ORIGINAL ARTICLE

Angiography after Out-of-Hospital Cardiac Arrest without ST-Segment Elevation

S. Desch, A. Freund, I. Akin, M. Behnes, M.R. Preusch, T.A. Zelniker, C. Skurk, U. Landmesser, T. Graf, I. Eitel, G. Fuernau, H. Haake, P. Nordbeck, F. Hammer, S.B. Felix, C. Hassager, T. Engstrøm, S. Fichtlscherer, J. Ledwoch, K. Lenk, M. Joner, S. Steiner, C. Liebetrau, I. Voigt, U. Zeymer, M. Brand, R. Schmitz, J. Horstkotte, C. Jacobshagen, J. Pöss, M. Abdel-Wahab, P. Lurz, A. Jobs, S. de Waha-Thiele, D. Olbrich, F. Sandig, I.R. König, S. Brett, M. Vens, K. Klinge, and H. Thiele, for the TOMAHAWK Investigators*

ABSTRACT

BACKGROUND

Myocardial infarction is a frequent cause of out-of-hospital cardiac arrest. However, the benefits of early coronary angiography and revascularization in resuscitated patients without electrocardiographic evidence of ST-segment elevation are unclear.

METHODS

In this multicenter trial, we randomly assigned 554 patients with successfully resuscitated out-of-hospital cardiac arrest of possible coronary origin to undergo either immediate coronary angiography (immediate-angiography group) or initial intensive care assessment with delayed or selective angiography (delayed-angiography group). All the patients had no evidence of ST-segment elevation on postresuscitation electrocardiography. The primary end point was death from any cause at 30 days. Secondary end points included a composite of death from any cause or severe neurologic deficit at 30 days.

RESULTS

A total of 530 of 554 patients (95.7%) were included in the primary analysis. At 30 days, 143 of 265 patients (54.0%) in the immediate-angiography group and 122 of 265 patients (46.0%) in the delayed-angiography group had died (hazard ratio, 1.28; 95% confidence interval [CI], 1.00 to 1.63; P=0.06). The composite of death or severe neurologic deficit occurred more frequently in the immediate-angiography group (in 164 of 255 patients [64.3%]) than in the delayed-angiography group (in 138 of 248 patients [55.6%]), for a relative risk of 1.16 (95% CI, 1.00 to 1.34). Values for peak troponin release and for the incidence of moderate or severe bleeding, stroke, and renal-replacement therapy were similar in the two groups.

CONCLUSIONS

Among patients with resuscitated out-of-hospital cardiac arrest without ST-segment elevation, a strategy of performing immediate angiography provided no benefit over a delayed or selective strategy with respect to the 30-day risk of death from any cause. (Funded by the German Center for Cardiovascular Research; TOMAHAWK ClinicalTrials.gov number, NCT02750462.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Desch at the Department of Internal Medicine–Cardiology, Heart Center Leipzig at the University of Leipzig, Strümpellstr. 39, Leipzig 04289, Germany, or at steffen.desch@medizin.uni-leipzig.de.

*A list of the investigators in the TOMAHAWK trial is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Desch and Freund contributed equally to this article.

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The prognosis in patients who have out-of-hospital cardiac arrest is poor, with a mortality of up to 65% even among those who undergo successful resuscitation and admission to the hospital.[1] Acute coronary syndrome accounts for up to 60% of out-of-hospital cardiac arrests in which a cardiac cause has been identified.[2] The finding of ST-segment elevation on postresuscitation electrocardiography (ECG) has good positive predictive value for acute coronary lesions triggering the cardiac arrest.[3,4] In the far larger subgroup of patients without ST-segment elevation, the spectrum of underlying causes is considerably broader and includes both cardiac and noncardiac causes.[3,4]

In patients with myocardial infarction, early revascularization can preserve ventricular function and prevent negative consequences of myocardial injury, such as heart failure or arrhythmias. However, routine, unselected early coronary angiography may also result in negative effects, including procedural risks and delays in the identification and treatment of causes of cardiac arrest other than acute coronary syndrome.

A recent randomized trial involving patients with cardiac arrest without ST-segment elevation that compared immediate angiography with delayed angiography showed no significant between-group difference in the primary end point of survival at 90 days or in any of the secondary efficacy or safety end points.[5] However, the trial included only patients with a shockable rhythm, a population that makes up approximately 60% of the patients with out-of-hospital cardiac arrest without ST-segment elevation.[6] Therefore, evidence regarding the general indication and timing of coronary angiography in patients with out-of-hospital cardiac arrest, including those with nonshockable rhythm, is still limited.

In the TOMAHAWK trial, we tested the hypothesis that routine immediate coronary angiography (possibly followed by revascularization) is superior to a deferred or selective approach regarding 30-day all-cause mortality in resuscitated patients with out-of-hospital cardiac arrest without ST-segment elevation.

Methods

Trial Design and Oversight

This investigator-initiated, randomized, international, multicenter, open-label trial had the primary objective of determining whether patients who have undergone successful resuscitation after out-of-hospital cardiac arrest of possible cardiac origin without ST-segment elevation benefit from immediate coronary angiography for the purpose of treating or ruling out acute coronary events, as compared with initial intensive care evaluation that includes delayed or selective coronary angiography. The design of the trial has been described previously.[7]

A Quick Take is available at NEJM.org

The trial was fully funded by the German Center for Cardiovascular Research. A data and safety monitoring board reviewed all the safety aspects of the trial. The protocol (available with the full text of this article at NEJM.org) was approved by the ethics committee at each participating site. The first author was responsible for the trial design, which was modified and approved by the steering committee. Data were gathered by investigators at the participating sites. The first author wrote the first draft of the manuscript, and all the authors made the decision to submit the manuscript for publication. All the investigators at the trial sites (including the authors) signed confidentiality agreements with the sponsor regarding the data. The steering committee vouches for the accuracy and completeness of the data and for the fidelity of the trial to the protocol. The trial statistician vouches for the accuracy of the data analysis.

Patients

Patients who were at least 30 years of age with resuscitated out-of-hospital cardiac arrest of possible cardiac origin without ST-segment elevation were eligible for inclusion. Patients with both shockable and nonshockable arrest rhythms were enrolled. A detailed list of inclusion and exclusion criteria and information regarding the stepwise consenting process are provided in the Supplementary Appendix, available at NEJM.org.

RANDOMIZATION AND TREATMENT

The patients were immediately screened for trial participation on admission to the emergency department. If the eligibility criteria were met, patients were randomly assigned in a 1:1 ratio to undergo either immediate coronary angiography (immediate-angiography group) or initial intensive care assessment and delayed or selective angiography (delayed-angiography group). Randomization was performed by means of randomly changing blocks and stratification according to trial site by means of a Web-based system.

The patients in the immediate-angiography group were transferred to the catheterization laboratory as soon as possible after hospital admission. Those in the delayed-angiography group were first transferred to the intensive care unit (ICU) for further evaluation of the cause of the cardiac arrest and for treatment. Further triage was dependent on the results of clinical examination and objective testing and was left to the clinical judgment of the treating physician. If the likelihood of an acute coronary trigger for the cardiac arrest was deemed to be high, the treating physician could proceed to coronary angiography after a minimum delay of 24 hours after cardiac arrest. Coronary angiography was allowed within the first 24 hours in case of substantial myocardial damage, which was defined as an increase in the cardiac troponin I or T level of at least 70 times the upper limit of the normal range (ULN) or an increase in the level of the creatine kinase myocardial band of at least 10 times the ULN on testing performed at least 6 hours after cardiac arrest, electrical instability possibly caused by acute myocardial ischemia, development of cardiogenic shock, or new ST-segment elevation. If the clinical examination and further testing indicated that a cardiac cause was unlikely, angiography could be either delayed (e.g., after the results of noninvasive stress testing were available) or abandoned.

Revascularization was to be attempted in both groups if at least one major coronary artery had disease that was deemed to be clinically relevant by the operator (e.g., substantial stenosis, occlusion, ulceration, or thrombus consistent with plaque rupture). Given the high-risk features of the trial population, the use of percutaneous coronary intervention (PCI), as opposed to coronary-artery bypass grafting (CABG), was favored whenever possible. However, the ultimate choice between PCI and CABG was left to the discretion of the individual operator, as was the interventional technique (e.g., stent choice). Further postresuscitation treatment in the ICU was provided according to the local standard of care.

PRIMARY AND SECONDARY END POINTS

The primary end point was death from any cause at 30 days. Key secondary efficacy end points were myocardial infarction at 30 days; severe neurologic deficit, which was defined as a Cerebral Performance Category value of 3 to 5 (with 3 indicating severe cerebral disability, 4 indicating coma or vegetative state, and 5 indicating brain death) at 30 days[8]; a composite of death from any cause or severe neurologic deficit at 30 days; length of stay in the ICU; serial values for the Simplified Acute Physiology Score (SAPS) II[9]; rehospitalization for congestive heart failure within 30 days; and peak release of myocardial enzymes. Secondary safety end points were moderate or severe bleeding (types 2 to 5 on the Bleeding Academic Research Consortium scale, which are detailed in the Supplementary Appendix),[10] stroke, and acute kidney failure leading to renal-replacement therapy.

The clinical end points of myocardial infarction, severe neurologic deficit, new congestive heart failure, bleeding, stroke, and acute kidney failure leading to renal-replacement therapy were adjudicated by a clinical events committee whose members were aware of trial-group assignments and were not otherwise involved in the trial conduct.

STATISTICAL ANALYSIS

At the time that the trial was designed, data were available from only one observational trial that exclusively evaluated clinical outcomes among survivors of out-of-hospital cardiac arrest without ST-segment elevation according to the timing of angiography.[11] In that trial, 30-day mortality was 34% among patients who had undergone emergency angiography and 46% among those who had undergone delayed or selective angiography. For the current trial, we selected a sequential statistical design in which one interim analysis was performed after the occurrence of 109 primary events. The global two-sided significance level was set at 0.05, with levels of 0.0242 for the interim analysis and 0.0342 for the final analysis. Thus, we determined that the enrollment of 558 patients would provide a power of 80% to reject the null hypothesis of no

difference between groups. Details regarding the sample-size calculation are provided in the Supplementary Appendix.

The primary efficacy analysis was performed in the intention-to-treat population, which included all the patients who had undergone randomization with the exception of four patients who were found to have not met the inclusion criteria. The per-protocol population was evaluated in a sensitivity analysis of efficacy end points, and the safety population was evaluated for the analysis of safety events according to the as-treated principle. (A full description of the trial populations is provided in the Supplementary Appendix.)

Predefined subgroup analyses were performed according to sex, diabetes status, age (<65 years or ≥65 years), targeted temperature management (received or not received), shockable or nonshockable rhythm, time from cardiac arrest to a return of spontaneous circulation (<15 minutes or ≥15 minutes), and the presence or absence of confirmed myocardial infarction as the event trigger.

For the primary analysis, we used a Cox model stratified according to trial site to calculate the hazard ratio and a two-sided log-rank test to calculate the P value. On the assumption of noninformative censoring, we treated the data for patients who were lost to follow-up in the same manner as the data for patients with administrative censoring. Sensitivity analyses were performed with the use of worst-case and worst-comparison imputation. For all end points, 95% confidence intervals have not been adjusted for multiple comparisons. A competing-risk model was added for several secondary end points.

RESULTS

PATIENTS

From November 2016 through September 2019, a total of 558 patients were found to be eligible for randomization at 31 trial sites in Germany and Denmark (Fig. S1 in the Supplementary Appendix), and 4 of these patients did not fully complete the randomization process because of technical reasons. Thus, 554 patients were randomly assigned to the immediate-angiography group (281 patients) or the delayed-angiography group (273 patients).

The characteristics of the patients at baseline were well balanced in the two treatment groups (Table 1 and Table S1). The median age in the overall population was 70 years (interquartile range [IQR], 60 to 78), and 30.4% of the patients were women. A total of 37.6% of the patients had known coronary artery disease. The median time from cardiac arrest to a return of spontaneous circulation was 15 minutes (IQR, 9 to 20). In the overall population, 55.5% of the patients had a shockable arrest rhythm. The majority of patients were comatose on admission, with a median score of 3 (IQR, 3 to 3) on the Glasgow Coma Scale, which ranges from 3 to 15, with 3 indicating that the patient is unresponsive and 15 indicating that the patient is fully alert.

TREATMENT AND PROCEDURES

Details regarding treatment and procedures in the early course after hospital admission are provided in Table 2. Coronary angiography was performed in 95.5% of patients in the immediate-angiography group and in 62.2% of those in the delayed-angiography group.

A total of 13 patients (4.6%) in the immediate-angiography group did not undergo immediate cardiac catheterization. Of those patients, 6 died before immediate coronary angiography. The remaining 7 patients did not receive the allocated intervention. In the delayed-angiography group, 22 patients (8.1%) underwent coronary angiography within the first 24 hours after hospital admission without fulfilling protocol-specified clinical criteria for early catheterization. (Details regarding these patients are provided in the Supplementary Appendix.) The median time from cardiac arrest to coronary angiography (defined as introduction of the access sheath) was 2.9 hours (IQR, 2.2 to 3.9) in the immediate-angiography group and 46.9 hours (IQR, 26.1 to 116.6) in the delayed-angiography group.

The prevalence of coronary artery disease among patients who underwent cardiac catheterization was 60.7% in the immediate-angiography group and 72.1% in the delayed-angiography group. One or more coronary lesions that were considered to be responsible for triggering cardiac arrest were identified in 38.1% of the patients in the immediate-angiography group and in 43.0% of those in the delayed-angiography group. The overall frequency of coronary revascularization was 39.6% (37.2% of the patients in the immediate-angiography group and 43.2% of those in the delayed-angiography group).

The majority of patients in both treatment groups received targeted temperature manage-

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Immediate Angiography (N=265)	Delayed or Selective Angiography (N=265)
Median age (IQR) — yr	69 (59–78)	71 (60–79)
Female sex — no. (%)	80 (30.2)	81 (30.6)
Median body-mass index (IQR)†	26.5 (24.5–29.4)	26.2 (24.2–29.4)
Medical condition or risk — no./total no. (%)		
Diabetes mellitus	71/244 (29.1)	74/251 (29.5)
Hypertension	161/240 (67.1)	162/234 (69.2)
Current smoker	49/164 (29.9)	59/171 (34.5)
Dyslipidemia	80/227 (35.2)	84/228 (36.8)
Coronary artery disease	79/229 (34.5)	93/229 (40.6)
Previous myocardial infarction	44/228 (19.3)	45/227 (19.8)
Previous PCI	40/217 (18.4)	58/220 (16.4)
Previous CABG	19/237 (8.0)	25/236 (10.6)
Peripheral artery disease	27/220 (12.3)	21/224 (9.4)
Previous stroke or transitory ischemic attack	24/228 (10.5)	20/225 (8.9)
Circumstance during cardiac arrest — no./total no. (%)		
Arrest witnessed	236/259 (91.1)	226/257 (87.9)
Shockable first monitored rhythm	126/241 (52.3)	142/242 (58.7)
Bystander cardiopulmonary resuscitation	142/247 (57.5)	152/252 (60.3)
Before hospital admission		
Median time from arrest to basic life support (IQR) — min	2 (0–8)	1 (0–5)
Median time from arrest to return of spontaneous circulation (IQR) — min	15 (10–20)	15 (8–20)
Prehospital extracorporeal life support — no./total no. (%)	2/262 (0.8)	1/264 (0.4)
After hospital admission		
Median score on Glasgow Coma Scale (IQR)‡	3 (3–3)	3 (3–3)
Median systolic blood pressure (IQR) — mm Hg	110 (95–130)	110 (95–130)
Median left ventricular ejection fraction (IQR) — %	45 (38–56)	44 (30–50)
Median laboratory value (IQR)		
Blood pH	7.22 (7.11–7.31)	7.24 (7.12–7.31)
Lactate — mmol/liter	5.0 (2.4–8.1)	4.9 (2.9–8.4)
Creatinine — μmol/liter	118 (94–115)	111 (93–141)
Troponin T — μg/liter	0.09 (0.04–0.19)	0.08 (0.04–0.16)
Troponin I — μg/liter	0.40 (0.10–0.90)	0.10 (0.06–0.58)
Blood glucose — mmol/liter	11.5 (8.9–15.7)	11.5 (8.9–15.9)

* To convert the values for creatinine to milligrams per deciliter, divide by 88.4. To convert the values for glucose to milligrams per deciliter, divide by 0.05551. CABG denotes coronary-artery bypass grafting, IQR interquartile range, and PCI percutaneous coronary intervention.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ The Glasgow Coma Scale is the summation of scores for eye, verbal, and motor responses and ranges from 3 (indicating deep coma) to 15 (indicating fully awake status).

ment (77.6% in the immediate-angiography group and 78.6% in the delayed-angiography group); the median time from hospital admission to the initiation of targeted temperature management was 153 minutes (IQR, 67 to 242) and 119 minutes (IQR, 30 to 205), respectively.

Table 2. Prevalence, Characteristics, and Treatment of Coronary Artery Disease.

Variable	Immediate Angiography (N=265)	Delayed or Selective Angiography (N=265)
Coronary angiography performed — no. (%)	253 (95.5)	165 (62.2)
Median time from arrest to coronary angiography (IQR) — hr	2.9 (2.2–3.9)	46.9 (26.1–116.6)
Catheterization access — no./total no. (%)		
Femoral	179/250 (71.6)	96/161 (59.6)
Radial	70/250 (28.0)	65/161 (40.4)
Brachial	1/250 (0.4)	0/161
Severity of coronary artery disease — no./total no. (%)		
No substantial disease	99/252 (39.3)	46/165 (27.9)
1-vessel disease	37/252 (14.7)	21/165 (12.7)
2-vessel disease	32/252 (12.7)	26/165 (15.8)
3-vessel disease	84/252 (33.3)	72/165 (43.6)
Culprit lesion identified — no./total no. (%)	94/247 (38.1)	67/156 (43.0)
PCI performed — no./total no. (%)	93/250 (37.2)	70/162 (43.2)
Median amount of contrast dye (IQR) — ml	107 (70–178)	125 (70–202)

PRIMARY END POINT

A total of 530 patients (95.7%) were available for primary analysis in the intention-to-treat population (Fig. S1). At 30 days, the primary end point of death from any cause had occurred in 143 of 265 patients (54.0%) in the immediate-angiography group and in 122 of 265 patients (46.0%) in the delayed-angiography group. In time-to-event analyses, there was no significant difference between the treatment groups (hazard ratio, 1.28; 95% confidence interval [CI], 1.00 to 1.63; P=0.06 by the log-rank test); after worst-case imputation, the hazard ratio was 1.24 (95% CI, 0.97 to 1.57; P=0.08 by the log-rank test) (Fig. 1 and Table 3). Additional results according to other imputation scenarios are provided in the Supplementary Appendix.

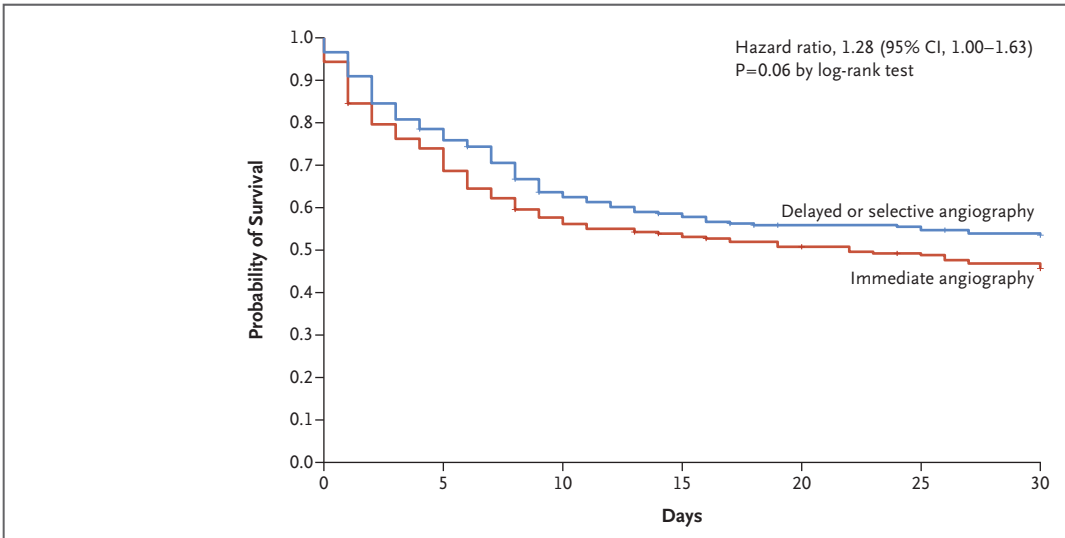
Only a minor variation in the risk estimates for the primary end point was observed when the analyses were performed in the per-protocol population (hazard ratio, 1.21; 95% CI, 0.94 to 1.56) (Fig. S4) and in the safety (as-treated) population (hazard ratio, 1.15; 95% CI, 0.90 to 1.46) (Fig. S5). The majority of patients died from severe anoxic brain injury or from circulatory collapse, with similar numbers in the two groups (Table S4).

SECONDARY END POINTS

Results for secondary end points are provided in Table 3. The severity of disease as measured by the SAPS II instrument and the length of ICU stay were similar in the two groups. The composite secondary end point of death from any cause or severe neurologic deficit occurred more frequently in the immediate-angiography group than in the delayed-angiography group (relative risk, 1.16; 95% CI, 1.00 to 1.34). The peak levels of both troponin and creatinine were similar in the two groups. Predefined subgroup analyses did not identify large differences in the results across subgroups (Fig. 2). Results of competing-risk analyses are provided in the Supplementary Appendix.

DISCUSSION

In this randomized, international trial, we found that among patients with successfully resuscitated out-of-hospital cardiac arrest and no ST-segment elevation, a strategy of immediate unselected coronary angiography provided no benefit over a delayed and selective approach with respect to the primary end point of death from any cause. Furthermore, a prespecified composite secondary end point of death or severe neurologic deficit occurred more frequently among patients assigned to undergo immediate angiography — a finding that should be interpreted with caution because of statistical concerns regarding multiple testing. However, if it was a true finding, then a possible cause would be that immediate



No. at Risk

Delayed or selective angiography	265	207	163	149	139	138	133
Immediate angiography	265	195	151	138	129	123	117

Figure 1. Kaplan–Meier Estimates of Death from Any Cause at 30 Days.

Shown is the risk of death at 30 days (the primary end point) among patients who underwent either immediate angiography or delayed or selective angiography after out-of-hospital cardiac arrest without ST-segment elevation.

coronary catheterization could lead to delays in diagnosing other triggers of out-of-hospital cardiac arrest.

The current findings support the results from the randomized Coronary Angiography after Cardiac Arrest (COACT) trial, which showed no significant differences in clinical outcome among patients with out-of-hospital cardiac arrest between immediate and delayed coronary angiography at 90 days and at 1 year.[5,12] Although the COACT trial enrolled only patients with a shockable arrest rhythm, the TOMAHAWK trial recruited patients with both shockable and nonshockable rhythms, thereby extending the findings to a broader spectrum of risk. In addition to the COACT trial, two small, randomized pilot trials involving 79 and 99 patients, respectively, also showed no benefit of emergency angiography.[13,14]

Several findings may explain the lack of benefit of immediate coronary angiography in the patient cohort that we studied. First, the percentage of patients who had a coronary culprit lesion that was deemed to be causative as an event trigger was 40% in the overall population. A potential benefit of coronary angiography would be expected only in the subgroup of patients in whom coronary disease had been identified and in whom revascularization had been considered for reversing ongoing ischemia.[15] In all other patients, immediate unselected coronary angiography would increase the risk of procedural complications without any benefit and possibly delay the identification of the cause of the cardiac arrest and the provision of subsequent treatment.

Second, neurologic rather than cardiac injury may have the most substantial effect on overall prognosis in many patients with cardiac arrest, thereby attenuating a possible beneficial effect of coronary revascularization. Of note, brain injury was by far the most frequent cause of death among the patients in our trial. Both arguments point to the necessity of further refinements in selecting the appropriate patients for cardiac catheterization. Several markers such as shockable arrest rhythm, clinical history, ECG changes other than ST-segment elevation, echocardiographic abnormalities, and troponin values have been proposed to predict the presence of acute coronary lesions in such patients without ST-segment elevation. However, the sensitivity and specificity of such markers are only modest.[16-22] Observational data indicate a possible survival benefit for early coronary angiography only in patients at low risk for a poor neurologic outcome.[23] However, the assessment of neurologic

Table 3. Clinical Outcomes at 30 Days.*

End Point	Immediate Angiography (N=265)	Delayed or Selective Angiography (N=265)	Effect Size (95% CI)†
Primary end point			
Death from any cause — no. (%)	143 (54.0)	122 (46.0)	Hazard ratio, 1.28 (1.00 to 1.63)
Secondary efficacy end points‡			
Myocardial infarction — no./total no. (%)	0/248	2/250 (0.8)	Relative risk, 0 (0 to 1.93)
Severe neurologic deficit — no./total no. (%)§	21/112 (18.8)	16/126 (12.7)	Relative risk, 1.48 (0.82 to 2.67)
Death from any cause or severe neurologic deficit — no./total no. (%)	164/255 (64.3)	138/248 (55.6)	Relative risk, 1.16 (1.00 to 1.34)
Median length of ICU stay (IQR) — days	7 (3–11)	8 (4–13)	HLE, –1 (–2 to 0)
Median peak SAPS II (IQR)¶	70 (55–83)	69 (54–82)	HLE, 0 (–4 to 4)
Rehospitalization for congestive heart failure — no./total no. (%)	1/246 (0.4)	1/249 (0.4)	Relative risk, 1.00 (0.19 to 1.85)
Median peak release of myocardial enzymes (IQR)			
Troponin T — μg/liter	0.39 (0.14–1.26)	0.34 (0.12–1.07)	HLE, 0.04 (–0.03 to 0.11)
Troponin I — μg/liter	1.46 (0.42–5.69)	1.10 (0.40–5.75)	HLE, 0.06 (–0.37 to 0.49)
Median peak creatinine (IQR) — μmol/liter	133 (101–193)	133 (98–199)	HLE, 2.08 (–8.06 to 12.22)
Secondary safety end points — no./total no. (%)‡			
Moderate or severe bleeding‖	12/260 (4.6)	8/232 (3.4)	Relative risk, 1.34 (0.57 to 3.14)
Stroke	4/258 (1.6)	5/242 (2.1)	Relative risk, 1.13 (0.33 to 3.84)
Acute kidney failure leading to renal-replacement therapy	49/259 (18.9)	38/241 (15.8)	Relative risk, 1.14 (0.78 to 1.68)

* ICU denotes intensive care unit.
† The delayed-angiography group was used as the reference group for the calculation of hazard ratios, relative risk estimates, and Hodges–Lehmann estimator (HLE) for location shift. (Hodges–Lehmann estimates were used to calculate differences in medians and normal approximation for differences in proportions because of the robustness of differences regardless of the underlying distribution.) The 95% confidence intervals for the secondary end points have not been adjusted for multiplicity, so inferences drawn from these intervals may not be reproducible.
‡ Efficacy end points were analyzed in the intention-to-treat population; safety end points were analyzed in the safety (as-treated) population.
§ A severe neurologic deficit was defined as a score of 3 to 5 on the Cerebral Performance Category scale, which ranges from 1 to 5. A score of 3, 4, or 5 reflects a poor prognosis (severe neurologic disability, persistent vegetative state, or brain death).
¶ The Simplified Acute Physiology Score (SAPS) II measures the severity of disease in patients admitted to the ICU and ranges from 0 (best) to 163 (worst).
‖ Moderate or severe bleeding was defined as types 2 to 5 on the Bleeding Academic Research Consortium scale, which are detailed in the Supplementary Appendix.

prognosis during the very early clinical course of such patients is unreliable.

Our trial has several limitations. First, because of the trial design, physicians and ICU staff members were aware of treatment assignments, which could have influenced decisions regarding further treatment. Second, patients with hemodynamic or electrical instability, ST-segment elevation, or in-hospital cardiac arrest were excluded. Third, 4% of the patients who underwent randomization were not available for the analysis of the primary end point owing to withdrawal of informed consent or violation of inclusion or exclusion criteria, which led to a minimal reduction in statistical power from the desired 80% to the actual 79%. Fourth, data

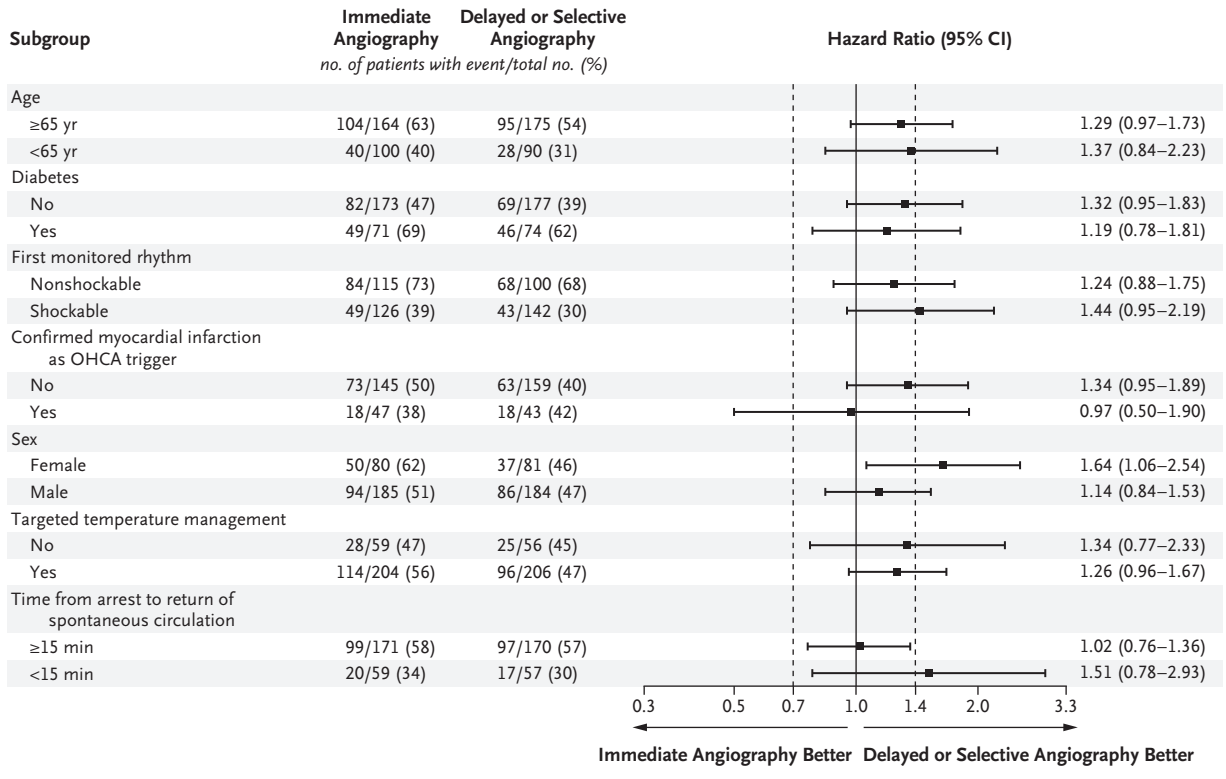


Figure 2. Subgroup Analyses of the Primary End Point.

Shown is a forest plot of the risk of death from any cause at 30 days among the patients with out-of-hospital cardiac arrest (OHCA) who were included in the primary analysis.

regarding patients who had been screened but not enrolled were collected only at the very beginning of the trial. Finally, early revascularization may have benefits outside the outcome measures that were studied in the current analysis — for example, the immediate strategy may have a positive effect on cardiac functional indexes (e.g., left ventricular ejection fraction) or on clinical end points, such as subsequent rehospitalization for heart failure. Several ongoing randomized trials that are addressing a similar research question will provide further evidence regarding early coronary angiography in patients with out-of-hospital cardiac arrest.[24,25]

Thus, among patients with resuscitated out-of-hospital cardiac arrest with a possible cardiac cause without ST-segment elevation, an immediate coronary angiography strategy was not found to be beneficial over a delayed or selective strategy with respect to the 30-day risk of death from any cause.

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

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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APPENDIX

The authors' full names and academic degrees are as follows: Steffen Desch, M.D., Anne Freund, M.D., Ibrahim Akin, M.D., Michael Behnes, M.D., Michael R. Preusch, M.D., Thomas A. Zelniker, M.D., Carsten Skurk, M.D., Ulf Landmesser, M.D., Tobias Graf, M.D., Ingo Eitel, M.D., Georg Fuernau, M.D., Hendrik Haake, M.D., Peter Nordbeck, M.D., Fabian Hammer, M.D., Ph.D., Stephan B. Felix, M.D., Christian Hassager, M.D., Thomas Engstrøm, M.D., Stephan Fichtlscherer, M.D., Jakob Ledwoch, M.D., Karsten Lenk, M.D., Michael Joner, M.D., Stephan Steiner, M.D., Christoph Liebetrau, M.D., Ingo Voigt, M.D., Uwe Zeymer, M.D., Michael Brand, M.D., Roland Schmitz, M.D., Jan Horstkotte, M.D., Claudius Jacobshagen, M.D., Janine Pöss, M.D., Mohamed Abdel-Wahab, M.D., Philipp Lurz, M.D., Ph.D., Alexander Jobs, M.D., Suzanne de Waha-Thiele, M.D., Denise Olbrich, Ph.D., Frank Sandig, Inke R. König, Ph.D., Sabine Brett, Maren Vens, Ph.D., Kathrin Klinge, Ph.D., and Holger Thiele, M.D.

The authors' affiliations are as follows: Heart Center Leipzig at the University of Leipzig, Departments of Internal Medicine–Cardiology (S.D., A.F., J.P., M.A.-W., P.L., A.J., H.T.) and Cardiac Surgery (S.W.-T.), Leipzig Heart Institute (S.D., A.F., A.J., H.T.), and University Clinic Leipzig (K.L.), Leipzig, University Heart Center Lübeck (S.D., T.G., I.E., G.F., A.J.) and the Center for Clinical Trials (D.O., S.B., K.K.) and the Institute for Medical Biometry and Statistics (F.S., I.R.K., M.V.), University of Lübeck, Lübeck, the German Center for Cardiovascular Research (S.D., A.F., I.A., M. Behnes, M.R.P., T.A.Z., C.S., U.L., T.G., I.E., G.F., F.H., S.B.F., S.F., J.L., M.J., C.L., C.J., A.J., D.O., F.S., I.R.K., S.B., M.V., K.K.) and University Clinic Charité, Campus Benjamin Franklin (C.S., U.L.), Berlin, University Clinic Mannheim, Mannheim (I.A., M. Behnes), the Department of Cardiology, Angiology, and Pneumology, University Hospital of Heidelberg, Heidelberg (M.R.P., T.A.Z.), Kliniken Maria Hilf, Mönchengladbach (H.H.), University Clinic Würzburg, Würzburg (P.N.), University Clinic Greifswald, Greifswald (F.H., S.B.F.), University Clinic Frankfurt, Frankfurt (S.F.), Rechts der Isar Hospital, Technical University (J.L.), and the Department of Cardiology, German Heart Center (M.J.), Munich, the Department of Cardiology, Pneumology and Intensive Care, St. Vincenz Hospital, Limburg (S.S.), Kerckhoff Clinic, Bad Nauheim (C.L.), the Departments of Acute and Emergency Medicine and of Cardiology and Angiology, Elisabeth Hospital Essen, Essen (I.V.), Klinikum Ludwigshafen, Ludwigshafen (U.Z.), University Clinic Marien Hospital Herne, Klinikum der Ruhr–Universität Bochum, Herne (M. Brand), the University Heart Center, Bad Krozingen (R.S.), Diakonissenkrankenhaus Flensburg, Flensburg (J.H.), University Medicine Göttingen, Göttingen (C.J.), and Vincentius–Diakonissen Hospital, Karlsruhe (C.J.) — all in Germany; the Division of Cardiology, Medical University of Vienna, Vienna (T.A.Z.); and the Department of Cardiology, Rigshospitalet, and the Department of Clinical Medicine, University of Copenhagen — both in Copenhagen (C.H., T.E.).

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