

## IMMEDIATE CORONARY ANGIOGRAPHY IN SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST

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**ABSTRACT**

**Background** The incidence of acute coronary-artery occlusion among patients with sudden cardiac arrest outside of the hospital is unknown, and the role of reperfusion therapy has not been determined. We therefore performed immediate coronary angiography and angioplasty when indicated in survivors of out-of-hospital cardiac arrest.

**Methods** Between September 1994 and August 1996, coronary angiography was performed in 84 consecutive patients between the ages of 30 and 75 years who had no obvious noncardiac cause of cardiac arrest.

**Results** Sixty of the 84 patients had clinically significant coronary disease on angiography, 40 of whom had coronary-artery occlusion (48 percent). Angioplasty was attempted in 37 patients and was technically successful in 28. Clinical and electrocardiographic findings, such as the occurrence of chest pain and the presence of ST-segment elevation, were poor predictors of acute coronary-artery occlusion. The in-hospital survival rate was 38 percent. Multivariate logistic-regression analysis revealed that successful angioplasty was an independent predictor of survival (odds ratio, 5.2; 95 percent confidence interval, 1.1 to 24.5;  $P=0.04$ ).

**Conclusions** Acute coronary-artery occlusion is frequent in survivors of out-of-hospital cardiac arrest and is predicted poorly by clinical and electrocardiographic findings. Accurate diagnosis by immediate coronary angiography can be followed in suitable candidates by coronary angioplasty, which seems to improve survival. (N Engl J Med 1997;336:1629-33.)

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**S**UDDEN out-of-hospital cardiac arrest remains a clinical problem. Despite community-based interventions, overall survival is still low.<sup>1,2</sup> The frequency of acute coronary occlusion in survivors of out-of-hospital cardiac arrest ranges from 36 percent in clinical studies that analyzed late coronary angiograms<sup>3</sup> to 95 percent in series based on autopsies.<sup>4</sup> The length of time from cardiac arrest to initial cardiopulmonary resuscitation remains a powerful predictor of survival.<sup>1,2</sup> Treatment of acute coronary-artery occlusion in myocardial infarction with either primary angioplasty or thrombolytic agents is routine and reduces morbidity and mortality in the hospital.<sup>5,6</sup> Prolonged cardiopulmonary resuscitation has been considered a

relative contraindication to thrombolytic therapy. Furthermore, it may be difficult to establish a clinical and electrocardiographic diagnosis of coronary-artery occlusion in patients with out-of-hospital cardiac arrest. Coronary angiography followed in suitable candidates by angioplasty could therefore be a therapeutic option in such cases.

To address this issue, we prospectively performed coronary angiography with angioplasty when indicated immediately after hospital admission in 84 consecutive survivors of out-of-hospital cardiac arrest. We assessed the prevalence of coronary artery disease and acute coronary-artery occlusion, the value of clinical and electrocardiographic data recorded before angiography in predicting coronary-artery occlusion, and the potential influence of primary angioplasty on survival during hospitalization.

**METHODS**

In Paris the management of out-of-hospital cardiac arrest involves emergency units based in five hospitals in the city and one dispatching center with two physicians. Each emergency unit is equipped with one or more ambulances with resuscitation equipment that are always staffed by one or two physicians trained in emergency medicine. Four emergency units participated in the study, covering a population of approximately 5 million during the day and 2.5 million at night. In suspected cases of sudden cardiac arrest, the closest emergency unit is dispatched to the scene. On arrival, cardiopulmonary resuscitation is initiated according to standard procedures. Successfully resuscitated patients were included in the study if they were between 30 and 75 years of age, if the sudden cardiac arrest occurred within six hours of the onset of symptoms in patients who were previously leading a normal life, and if there was no obvious noncardiac cause of cardiac arrest. Clinical and electrocardiographic preadmission data indicative of a cardiac cause of arrest were not required.

The patients who met the criteria were brought directly to the cardiac catheterization laboratory of one hospital (Cochin Hospital). Immediate coronary and left ventricular angiography was performed according to standard techniques. If a recent coronary-artery occlusion was found, coronary angioplasty was attempted, unless the infarct-related artery was too small or the operator considered the procedure to be technically impossible. Coronary stents were implanted in the case of occlusive dissection. Standard resuscitative and stabilization procedures were continued during the procedure. The patients were then transported to the medical intensive care unit and treated with the aid of noninvasive and invasive monitoring.

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**Data Collection**

The clinical data gathered during resuscitation and hospitalization were prospectively entered in a computer data base. All the electrocardiograms recorded during resuscitation and the initial hospital phase were interpreted by two experienced cardiologists who were unaware of the patients' clinical and angiographic status. Decisions during angioplasty were guided by on-line quantitative analysis (Computerized Medical Technologies, Haifa, Israel). The 35-mm angiograms underwent final qualitative and quantitative review by two independent cardiologists who were

**TABLE 1. CLINICAL AND PREADMISSION CHARACTERISTICS OF 85 PATIENTS.\***

CHARACTERISTIC	VALUE
Male sex — no. (%)	70 (82)
Mean ( $\pm$ SD) age — yr	55.5 $\pm$ 11.5
History of coronary artery disease or surgery — no. (%)†	17 (20)
Risk factors for coronary artery disease — no.‡	
0	34
1	38
2	10
3	2
4	1
Location of out-of-hospital cardiac arrest — no. (%)	
At home	28 (33)
At work	16 (19)
Other	41 (48)
Chest pain before arrest — no. (%)	28 (33)
Bystander-initiated CPR — no. (%)	68 (80)
Median interval between cardiac arrest and CPR — min (10th–90th percentile)	3 (1–10)
Median interval between cardiac arrest and CPR by EMSP — min (10th–90th percentile)	10 (5–60)
Median interval between cardiac arrest and return of spontaneous circulation — min (10th–90th percentile)	25 (10–98)
Median interval between cardiac arrest and arrival at hospital — min (10th–90th percentile)	110 (65–160)
First rhythm recorded on preadmission electrocardiogram — no. (%)	
Ventricular fibrillation	61 (72)
Ventricular tachycardia	18 (21)
Asystole	2 (2)
Sinus rhythm	3 (4)
Atrioventricular block	1 (1)
Electrocardiographic changes after return to sinus rhythm — no. (%)§	
ST-segment elevation	36 (42)
ST-segment depression	8 (9)
Left bundle-branch block	18 (21)
Right bundle-branch block	2 (2)
No specific ST or T patterns	10 (12)
Normal ST segment and T wave	11 (13)

\*CPR denotes cardiopulmonary resuscitation, and EMSP emergency-medical-system personnel.

†Coronary artery disease or surgery was defined as angina, prior myocardial infarction, percutaneous transluminal coronary angioplasty, or coronary-artery bypass grafting.

‡The following were considered risk factors: hypertension (diastolic pressure, >90 mm Hg), diabetes mellitus, hypercholesterolemia (cholesterol, >263 mg per deciliter [6.8 mmol per liter]), smoking, and family history of coronary disease.

§ST-segment elevation and depression were defined as increases of more than 1 mm or decreases of less than 1 mm in two contiguous leads, respectively.

unaware of the patients' clinical status. Disagreement between observers was arbitrated by an independent third party. The left ventricular ejection fraction was estimated by the biplane area-length method described by Dodge et al.<sup>7</sup>

Each coronary lesion resulting in more than a 50 percent reduction in luminal diameter was considered clinically significant. We used the classification of Lo et al.,<sup>8</sup> derived from a previous classification by Ambrose et al.,<sup>9</sup> to separate coronary lesions into two groups: type I, smooth (eccentric or concentric, wide-based) lesions, and type II, irregular (unstable) lesions. Type II lesions were further divided into type IIA (single lesions with narrow bases, acute angles, serrated edges, or craters) and type IIB (lesions with long-segment stenosis with diffuse irregularities and at least two closely spaced high-grade stenoses). Flow in obstructed arteries was assessed with the Thrombolysis in Myocardial Infarction (TIMI) classification<sup>10</sup>; an artery was considered occluded if flow of TIMI grade 0 or 1 was present. A coronary-artery occlusion was considered recent if angiography revealed thrombus at the site of the occlusion; this classification was considered confirmed by the ability to pass a guidewire easily through the occlusion if angioplasty was attempted. Angioplasty was deemed successful if it resulted in residual stenosis of less than 50 percent with TIMI grade 3 flow.

The study protocol was reviewed and approved by the ethics committee of Cochin Hospital. Informed consent was impossible to obtain from the patients. The relatives of 26 patients were available to provide consent before the procedure. In the case of the remaining patients, the next of kin was informed as soon as possible during or immediately after the procedure.

**Statistical Analysis**

Factors potentially relevant to survival and the prediction of coronary-artery occlusion were assessed by univariate analysis with the chi-square test for categorical variables and simple logistic regression for continuous variables. A two-tailed P value of less than 0.05 was considered to indicate statistical significance. Predictors found to be significant on the basis of univariate analysis were then included in a forward, stepwise multiple logistic-regression model to identify the independent factors associated with survival and with the presence of coronary-artery occlusion. Statistical analysis was performed with the Stata 4.0 statistical package for Macintosh (Stata, College Station, Tex.).

**RESULTS****Patient Population**

From September 1994 to August 1996, four emergency units in Paris responded to 1762 cases of suspected out-of-hospital sudden cardiac arrest. Cardiopulmonary resuscitation was not attempted in 852 patients because of late arrival of the medical team or a severe, preexisting pathologic state. Cardiopulmonary resuscitation was attempted in the remaining 910 patients, and a stable hemodynamic state obtained in 312. Fatal recurrent cardiac arrest occurred during transportation to the hospital in 126; 186 were therefore successfully transported. A total of 101 patients were excluded from the study, either because they had an obvious noncardiac cause of cardiac arrest (71 patients) or because they were outside the age range for the study (30 patients). Eighty-five eligible patients were therefore admitted to the cardiac-catheterization laboratory. In all 85 patients the onset of symptoms was within one hour before the loss of consciousness. Clinical and pre-admission data are presented in Table 1.

### Cardiac Catheterization and Angioplasty

Coronary angiography was impossible to perform in one patient because of extensive peripheral artery disease; the patient died four hours later. Autopsy revealed inferior myocardial infarction. Data collected in the catheterization laboratory on the remaining 84 patients are summarized in Tables 2 and 3. Coronary-artery occlusions were found in 40 patients (48 percent); percutaneous transluminal coronary angioplasty (PTCA) was attempted in 37 and was successful in 28. Failure was due to recurrent thrombosis in four of the remaining nine patients and to low coronary flow in five. Twenty patients had clinically significant coronary-artery lesions with no acute occlusion; 18 of the 20 had irregular lesions (type II). Two patients with normal coronary arteries had clinically significant aortic valvular stenosis. The cause of cardiac arrest remained undetermined at the end of the procedure in 15 of the patients with normal coronary arteries and 7 patients with clinically insignificant lesions and was sought through an extensive clinical workup during follow-up in the intensive care unit.

### Follow-up in the Intensive Care Unit

Coronary-artery spasm was diagnosed in four patients with clinically insignificant lesions of the left anterior descending artery; transient ST-segment elevation in the anterior leads occurred in all four and disappeared after the intravenous administration of nitrates. In six patients a final diagnosis of idiopathic dilated cardiomyopathy was based on a history of heart failure and on echocardiographic or coronary and ventricular angiographic findings obtained before the arrest. Two patients with normal coronary arteries underwent electrophysiologic studies that revealed sustained monomorphic ventricular tachycardia. Each subsequently received an internal defibrillator. A noncardiac cause of out-of-hospital cardiac arrest was found in three patients with normal coronary arteries (subarachnoid hemorrhage in two, and extensive pneumonia due to *Streptococcus pneumoniae* in one). No cause of cardiac arrest was found before death in seven patients: autopsies were performed in two and found no cause of arrest; autopsies were not performed in the remaining five at the request of the next of kin.

### Repeated Coronary and Left Ventricular Angiography

Fourteen patients who underwent successful PTCA survived with no major neurologic sequelae. Coronary and left ventricular angiography was repeated in all 14 an average ( $\pm$ SD) of  $21 \pm 14$  days after the arrest to assess the outcome of angioplasty with respect to coronary-artery patency and left ventricular function. No reocclusion was noted. The mean left ventricular ejection fraction increased from  $34 \pm 21$  percent to  $46 \pm 20$  percent (mean change,  $12 \pm 11$  percentage points).

**TABLE 2.** ANGIOGRAPHIC DATA IN THE 84 PATIENTS WHO UNDERWENT ANGIOGRAPHY.\*

VARIABLE	VALUE
Normal coronary arteries — no. (%)	17 (20)
Clinically insignificant coronary artery disease ( $\leq 50$ percent stenosis) — no. (%)	7 (8)
Clinically significant coronary artery disease — no. (%)	60 (71)
Single-vessel disease	22
Two-vessel disease	13
Three-vessel disease	24
Isolated left main coronary artery disease	1
Left ventricular ejection fraction — %	$33.9 \pm 10.5$
Left ventricular end-diastolic pressure — mm Hg	$25.3 \pm 9.5$

\*Plus-minus values are means  $\pm$ SD. Because of rounding, the percentages do not total 100.

**TABLE 3.** TYPES OF CORONARY-ARTERY LESIONS AND RESULTS OF PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY (PTCA) IN THE 60 PATIENTS WITH CLINICALLY SIGNIFICANT CORONARY ARTERY DISEASE.

VARIABLE	VALUE
Type II lesion — no. (%)	18 (30)
IIA	7
IIB	11
Type I lesion — no. (%)	2 (3)
Recent coronary-artery occlusion — no. (%)	40 (67)
PTCA attempted — no.	37
Median interval between admission and PTCA — min (10th–90th percentile)	32 (18–55)
Median duration of procedure — min (10th–90th percentile)	62 (40–120)
PTCA successful — no.	28
Stent implanted — no.	5
Intraaortic balloon inserted — no.	9

### Discharge and Follow-up

Thirty-two patients were discharged alive (38 percent), 30 of whom had no or minimal neurologic complications. All patients were followed for at least 6 months (median, 13; 10th to 90th percentiles, 7 to 28). Three patients died, two of complications related to severe neurologic sequelae and one of recurrent pulmonary embolism after aortic-valve surgery. Five patients initially treated with PTCA were readmitted for recurrent angina: four underwent successful PTCA, and one underwent successful coronary-artery bypass surgery. None of the survivors had recurrent cardiac arrest during follow-up.

### Predictive Value of Clinical and Electrocardiographic Features

Clinical and electrocardiographic data collected before coronary angiography were analyzed by multivariate logistic regression to determine whether they could be used to predict the presence of recent coronary-artery occlusion on angiography. ST-segment elevation (odds ratio, 4.3; 95 percent confidence interval, 1.6 to 2;  $P=0.004$ ) and chest pain before the arrest (odds ratio, 4.0; 95 percent confidence interval, 1.3 to 10.1;  $P=0.016$ ) were the only independent predictive factors. The presence of one of these two factors was associated with positive and negative predictive values of 0.63 and 0.74, respectively, and the presence of both with values of 0.87 and 0.61. Nine patients presented with no ST-segment elevation or chest pain and were found on angiography to have had a recent coronary-artery occlusion (Table 4).

### Factors Predictive of Survival

Multivariate analysis revealed that the following factors were predictive of survival: absence of the need for inotropic drugs during transportation to the hospital (odds ratio, 3.6; 95 percent confidence interval, 1.1 to 11.8;  $P=0.03$ ) and successful coronary angioplasty (odds ratio, 5.2; 95 percent confidence interval, 1.1 to 24.5;  $P=0.04$ ). A longer time between the onset of cardiac arrest and the return of spontaneous circulation was associated with a lower rate of survival, with an odds ratio for mortality of 1.1 per minute of delay (95 percent confidence interval, 1.02 to 1.12;  $P=0.003$ ). A cardiac cause of arrest, the presence of coronary-artery lesions, attempted angioplasty, and recent coronary-artery occlusion were not associated with survival. Furthermore, there were no significant differences in age, sex, the interval between cardiac arrest and cardio-

pulmonary resuscitation or return of spontaneous circulation, the presence of risk factors, the rate of bystander-initiated cardiopulmonary resuscitation, or the first rhythm recorded among the various subgroups of patients, including those who underwent successful angioplasty.

### DISCUSSION

In this series of patients who had sustained cardiac arrest outside of the hospital, we found a high prevalence of acute coronary occlusions (48 percent of the patients). We found irregular lesions in 18 (21 percent) of the patients.

Davies,<sup>11</sup> in post-mortem examinations of 168 victims of sudden coronary death, reported intracoronary mural thrombi in 43.5 percent, occlusive intraluminal thrombi in 29.8 percent, plaque fissure in only 7.7 percent, and no acute lesion in 19 percent. Lo et al.<sup>8</sup> analyzed angiograms performed in 49 long-term survivors; 16 had so-called type II lesions ("irregular lesions").

The high prevalence of coronary-artery occlusion and unstable lesions in our study substantiates the role of the rupture of atherosclerotic plaque as a trigger of acute coronary syndromes. Angiographic morphology suggestive of plaque rupture (such as type II irregular lesions) has been identified in the majority of stenoses associated with acute myocardial infarction and unstable angina.<sup>9,12,13</sup> Plaque rupture and platelet aggregation may lead to intraluminal thrombosis, occlusion, and thrombus fragmentation with microembolism, all of which may be important pathogenic factors in sudden cardiac arrest.<sup>12,14,15</sup>

The second important finding of our study is the poor predictive value of clinical and electrocardiographic data, such as chest pain or ST-segment elevation, for coronary-artery occlusion. Transient ST-segment variations in patients with subarachnoid hemorrhage<sup>16</sup> and reversible myocardial depression in survivors of cardiac arrest<sup>17</sup> have been described. Acute coronary-artery occlusion is therefore difficult to predict in survivors of out-of-hospital cardiac arrest on the basis of clinical and electrocardiographic data alone. Furthermore, early recognition of coronary or noncoronary causes of out-of-hospital cardiac arrest can result in profoundly different therapeutic strategies; immediate coronary angiography could therefore be warranted on this basis alone.

The third relevant finding of our study is the potential value of immediate coronary angioplasty in improving clinical outcome. Survival rates in various studies are difficult to compare because of differences in inclusion criteria. However, our results compare favorably with those of previous studies,<sup>1,18</sup> and only one recent study reported a similar survival rate.<sup>2</sup> Thrombolytic therapy<sup>19,20</sup> and emergency coronary angioplasty<sup>21</sup> have been proposed as reperfusion therapies in survivors of out-of-hospital cardiac

**TABLE 4.** RELATION BETWEEN ST-SEGMENT ELEVATION, CHEST PAIN BEFORE CARDIAC ARREST, AND RECENT CORONARY-ARTERY OCCLUSION IN THE 84 PATIENTS WHO UNDERWENT CORONARY ANGIOGRAPHY.\*

VARIABLE	NO. OF PATIENTS	NO. WITH RECENT CORONARY-ARTERY OCCLUSION (%)
ST-segment elevation and chest pain		
Present	15	13 (87)
Absent	69	27 (39)
ST-segment elevation or chest pain		
Present	49	31 (63)
Absent	35	9 (26)

\*ST-segment elevation was defined as an elevation of more than 1 mm in two contiguous leads.

arrest who have electrocardiographic evidence of transmural injury. The relative value of these two approaches is still unclear despite numerous studies.<sup>22,23</sup> Nevertheless, mechanical reperfusion may be the preferred option since thrombolytic therapy is often considered contraindicated after prolonged cardiopulmonary resuscitation because of the high risk of bleeding complications.<sup>24</sup> Finally, our study shows that a strategy of immediate coronary angiography in patients who survive cardiac arrest allows reperfusion therapy in the subgroup with no obvious electrocardiographic signs of ongoing ischemia.

Several limitations of our study must be stressed. First, the benefit of immediate angioplasty on survival was limited to patients in whom PTCA was successful. Attempted angioplasty was not a predictor of survival. Second, our results may only reflect a better prognosis in patients with cardiac arrest due to recent coronary-artery occlusion; the better outcome may not necessarily have been due to emergency angioplasty. However, there was no difference in base-line clinical data, such as the interval between cardiac arrest and the return to spontaneous circulation, between patients with and those without recent occlusion. Furthermore, multivariate analysis showed no association between survival and recent coronary-artery occlusion, suggesting that successful angioplasty alone improves survival. Third, angiography may not distinguish acute from chronic total occlusion; an attempt to perform PTCA in the case of a chronic occlusion in this setting could be deleterious. Finally, the number of patients included in our study is relatively small. The efficacy of emergency angiography with angioplasty when indicated in this setting should therefore be studied in a larger group of patients before definite conclusions can be drawn.

Marked improvement in the left ventricular ejection fraction was noted when angiography was repeated in 14 patients who underwent successful PTCA. Reversal of myocardial depression has been reported in survivors of cardiac arrest<sup>17</sup> or in patients after transthoracic shock.<sup>17,25</sup> However, an additional effect of successful PTCA on myocardial salvage seems highly probable.<sup>26</sup>

Coronary angiography was not performed in the patients who were excluded from the study. Therefore, we cannot estimate the prevalence of coronary artery disease among unselected patients after out-of-hospital cardiac arrest.

In conclusion, immediate coronary angiography with angioplasty as indicated in survivors of out-of-hospital cardiac arrest who have no obvious noncardiac cause of the arrest is safe and feasible when performed by an experienced team. Our results show a high incidence of acute coronary-artery occlusion, and successful PTCA was an independent predictor of survival. This approach may improve the long-term outcome in survivors of out-of-hospital cardiac arrest.

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