Cardiac Arrest in the Critically Ill

I. A Study of Predisposing Causes in 132 Patients

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Paul K. Hanashiro, M.D., and Herbert Shubin, M.D.

SUMMARY

The events preceding cardiac arrest were investigated in 132 critically ill patients on the basis of the hemodynamic, respiratory, and metabolic status prior to cardiac arrest. Approximately one-half of the patients had respiratory acidosis prior to cardiac arrest and only one of these patients ultimately survived. An additional one-fourth had metabolic acidosis due to progressive perfusion failure (shock), and none survived. In the remaining one-fourth, an immediate catastrophic and potentially preventable event accounted for cardiac arrest, and all but one of the long-term survivors were included in this group. In thirteen patients, obstruction or dislodgment of endotracheal tracheostomy tubes, or interruption of ventilation, was recognized as the immediate cause. In an additional 20 patients, cardiac arrest was associated with an adverse effect of a drug. Twelve instances of cardiac arrest were associated with central venous injection of aminophylline.

The initial cardiac resuscitation attempt was effective in 38% of patients. However, the majority of patients who survived the first episode succumbed after a second or third episode. The cumulative survival was disappointingly small. Only six patients, or 5% of the total group of 132 patients, were long-term survivors. These data may provide the basis for more restricted use of routine and repetitive resuscitative measures particularly for elderly patients in whom acidemia is due to progressive ventilatory or circulatory failure.

Additional Indexing Words:
Acidemia  Acidosis  Aminophylline  Cardiac resuscitation  Inotropic agents

WHEN CARDIAC arrest occurs as a catastrophic event, current techniques of cardiac resuscitation are remarkably effective. Prompt action by well-trained personnel may restore more than one-half of otherwise fatal cases of airway obstruction, apnea, drowning, electric shock, or patients who have sustained an acute coronary episode. On the other hand, when cardiac arrest occurs in patients who are already critically ill, resuscitative measures are much less effective. Fewer than 5% of such patients are successfully resuscitated.1 In the present study, we searched for more objective understanding of mechanisms of cardiac arrest and the effectiveness of resuscitation in a large group of critically ill patients. Our efforts were in part promoted by practical and ethical considerations.

A unique opportunity for investigation was provided by the special monitoring facilities of

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our Shock Research Unit. Comprehensive facilities were used for monitoring alarms and recording of hemodynamic, pulmonary, and metabolic changes for periods as long as 10 days. The episode of cardiac arrest was immediately recognized since the electrocardiogram, intraarterial pressure pulses, and central venous pressure were prominently displayed on an oscilloscopic screen above the patient's bed and as a numerical output on an adjacent video screen. Detailed data were stored in part by use of a digital-computer system.

**Method of Study**

**Patients**

The patient group included 78 men and 54 women, ranging from 4 to 84 years of age, who were referred from medical and/or surgical services of the Los Angeles County/University of Southern California Medical Center to the shock ward for management of shock or other life-threatening cardiopulmonary crises. Primary diseases were due to infection (37%), cardiac cause (22%), blood or fluid loss (13%), and miscellaneous or multiple causes in the remaining patients (28%).

A total of 193 episodes of cardiac arrest were documented in the 132 patients. Each patient was under supervision of a nurse or physician constantly at the bedside. The electrocardiogram, intraarterial pressure pulse, and the central venous pressure were prominently displayed on a 24-inch oscilloscopic screen suspended from the ceiling above the patient's head and as a numerical output on an adjacent video screen. These three measurements were also preserved for retrospective analysis by use of a four-channel recorder and in part by acquisition of data utilizing a digital-computer system. Cardiac arrest was defined as the sudden cessation of effective cardiac action with the intraarterial pulse pressure in each instance reduced to levels of less than 60 mm Hg, absent heart sounds, and loss of consciousness. Patients in whom cardiac arrest occurred as a consequence of progressive blood loss, uncontrolled congestive heart failure, or protracted cardiac arrhythmia were excluded. Standard resuscitation maneuvers were employed including closed-chest cardiac massage, mechanical ventilation, endotracheal intubation, and direct-current defibrillation. Drugs were injected through a central venous catheter which had previously been inserted on a routine basis at the time of admission. Adrenergic amines, especially epinephrine and isoproterenol, and 10% solutions of calcium chloride or calcium gluconate were the primary inotropic agents. Hypertonic sodium lactate or bicarbonate was administered routinely in amounts ranging from 44 to 220 mEq.

**Procedures**

An inventory of hemodynamic and metabolic measurements was routinely obtained within 4 hours after admission of a patient to the Shock Research Unit. For this purpose, a polyethylene catheter was introduced into the right atrium through a surgically exposed basilic vein. Correct position was established by observation of intracardiac pressure pulses during advancement of the catheter into the right ventricle and its subsequent withdrawal to a position just proximal to the tricuspid valve. A red Odman catheter was inserted into the brachial, radial, or femoral artery over a guide wire by percutaneous technique or after surgical exposure and advanced for a distance of 10 cm. The catheters were connected to Statham 23 AA strain-gauge pressure transducers and flushed intermittently under pressure with normal saline solution containing 5 units/ml of heparin. Arterial and central venous pressures were recorded on a direct-writing multichannel recorder. The electrocardiogram (lead II) was monitored continuously, and heart rate was measured from it.

Blood was withdrawn from the arterial catheter at regular intervals of between 2 and 4 hours, and as frequently as every 11 minutes at time of clinical crises, for measurement of blood gases. Ventilation was assisted in a majority of patients with the use of a self-cycling positive-pressure ventilator (Bird Mark VIII) or a volume-controlled ventilator (Engstrom Respirometer model 200). The inspired gas contained between 40 and 100% oxygen. A Beckman 160 analyzer, with a flow-through pH electrode and subsequently a Radiometer system, was used for measurement of blood pH, pCO₂, and P O₂. Arterial oxygen saturation was measured by use of a Waters double-scale cuvette oximeter, the calibration of which was periodically confirmed by Van Slyke analyses.

**Results**

**Survival**

An initial episode of cardiac arrest was successfully reversed in 50 of the 132 patients (38%), but only five of these survived to leave the hospital. A second episode of cardiac arrest occurred in 45 of the surviving patients, and 17 (38%) were successfully resuscitated. Only one of these 45 patients ultimately
survived. A third attempt at cardiac resuscitation was made in 16 patients. Cardiac arrest was successfully reversed in seven (44%), but all of these patients ultimately died. Two patients had more than three episodes of cardiac arrest and both died during a subsequent episode. These data are summarized in table 1.

The percentages of successful resuscitations during each of the three successive resuscitative efforts were remarkably similar, i.e., 39, 38, and 44%. Assuming independence of episode outcome, the probability of successfully resuscitating a patient from three episodes of cardiac arrest, therefore, was $0.39 \times 0.38 \times 0.44 = 0.06$. However, survival to the time of hospital discharge was even less, for only six patients (5%) left the hospital alive.

**Predisposing Causes**

For purposes of analysis, three groups of patients were identified. In 98 patients, 74% of the total group, acidosis with arterial blood pH of less than 7.35 was detected prior to onset of cardiac arrest. Group I included 65 patients with predominant respiratory acidosis in whom arterial blood pH was less than 7.35, and concurrent pCO$_2$ was 41 mm Hg or more; pH averaged 7.16 and pCO$_2$, 67 mm Hg. Group II included 34 patients with predominantly metabolic acidosis with pH less than 7.35 and pCO$_2$ equal to or less than 39 mm Hg. Arterial blood pH averaged 7.21 and pCO$_2$, 28 mm Hg. A majority of these patients had clinical and hemodynamic changes characteristic of circulatory shock.

The remaining 33 patients constituted group III and accounted for 26% of the total group. Arterial blood pH prior to cardiac arrest was 7.37 or greater. In each of these cases, however, an unexpected and catastrophic event accounted for cardiac arrest. The mean value of pH and pCO$_2$ and the ranges of values for each of the three categories of patients are summarized in table 2.

The mechanism of cardiac arrest for one of the patients in group I is illustrated in figure 1. A 34-year-old woman was admitted after ingestion of an overdose of barbiturates. Because of aspiration of oral and gastric contents prior to admission, the clinical course was complicated by bronchopneumonia. A progressive fall in pH and rise in pCO$_2$ preceded cardiac arrest. The patient was successfully resuscitated, maintained on a mechanical ventilator with dedicated airway care for a protracted period, and ultimately survived. This case is specifically cited because among the 99 patients included in groups I and II this is the only patient who was a long-term survivor.

Illustrative of patients in group II is the case of a 63-year-old man who had massive

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**Table 1**

<table>
<thead>
<tr>
<th>Survival following Cardiac Resuscitation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Attempted resuscitations</strong></td>
</tr>
<tr>
<td>No. survivors</td>
</tr>
<tr>
<td>Success of each attempt (%)</td>
</tr>
<tr>
<td>Cumulative survival (%)</td>
</tr>
<tr>
<td>No. long-term survivors</td>
</tr>
</tbody>
</table>

*More than three resuscitation efforts were made in only two patients.
†Weighted average of individual resuscitation attempts.

**Table 2**

Arterial Blood pH and pCO$_2$ within Four Hours preceding Cardiac Arrest

<table>
<thead>
<tr>
<th>Patient group</th>
<th>No. of patients</th>
<th>pH</th>
<th>pCO$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>I: Respiratory acidosis</td>
<td>65</td>
<td>7.16</td>
<td>67</td>
</tr>
<tr>
<td>(pH &lt; 7.35; pCO$_2$ &gt; 40 mm Hg)</td>
<td></td>
<td>(6.61-7.35)</td>
<td>(41-120)</td>
</tr>
<tr>
<td>II: Metabolic acidosis</td>
<td>34</td>
<td>7.21</td>
<td>28</td>
</tr>
<tr>
<td>(pH &lt; 7.35; pCO$_2$ &lt; 40)</td>
<td></td>
<td>(6.96-7.35)</td>
<td>(11-39)</td>
</tr>
<tr>
<td>III: Catastrophic event</td>
<td>33</td>
<td>7.45</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(7.37-7.59)</td>
<td>(19-54)</td>
</tr>
</tbody>
</table>
Table 3

Presumptive Causes of “Catastrophic” Cardiac Arrest (Group III)

<table>
<thead>
<tr>
<th>Event</th>
<th>No. of Catastrophic patients</th>
<th>Events (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug therapy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aminophylline</td>
<td>12</td>
<td>36</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Digoxin (Lanoxin)</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Potassium penicillin G</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Chlorpromazine (Thorazine)</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Airway manipulation — anoxia:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endotracheal manipulation</td>
<td>9</td>
<td>27</td>
</tr>
<tr>
<td>Dislodgment of tracheostomy tube</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Accidental interruption of</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ventilation</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>40</td>
</tr>
</tbody>
</table>

Pulmonary infarction due to embolic occlusion of the left pulmonary artery. Cardiac arrest followed a progressive fall in pH from 7.29 to 7.11 and pCO₂ from 25 to 18 mm Hg. A concomitant decline in blood pressure from 150/78 to 88/49 mm Hg and an increase in lactate content of arterial blood from 14.8 to 23.0 mm were observed. Cardiac arrest was reversed shortly after admission to the shock ward, but progressive decline in cardiac output and arterial pressure ensued, terminating in irreversible cardiac arrest within 5 hours after admission.

The catastrophic events which accounted for the 33 patients in group III were related to an adverse reaction to drugs (60%) or acute anoxia (40%). Specific causes are summarized in Table 3. The cardiac catastrophies in 13 or

**Figure 1**

A progressive fall in pH and rise in PCO₂ preceding cardiac arrest.

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40% of the patients in this group were associated with interruption of mechanical ventilation, most commonly while the nurse or physician was manipulating the airway. Accidental dislodgment of a tracheostomy cannula and temporary interruption of mechanical ventilation accounted for four episodes of cardiac arrest. In each instance, these interruptions occurred while the patient's body position was changed during nursing procedures and especially for washing or changing bed sheets.

An example of ventricular standstill following temporary interruption of mechanical ventilation for readjustment of a ventilator is demonstrated in figure 2. The patient was a 68-year-old man in whom mesenteric artery occlusion was demonstrated on surgical exploration.

Outstanding among the drugs implicated in sudden cardiac arrest was aminophylline, a theophylline ethylenediamine compound, which was slowly injected through the central venous catheter in doses ranging from 250 to 750 mg. Injection of epinephrine and digoxin through the central venous catheter also was associated with catastrophic cardiac arrest. In two instances, cardiac arrest followed intravenous administration of potassium penicillin G in an amount of 2 million and 5 million units over a period of 15–30 min. The adverse effect may have been due to the potassium ion, but an undetected sensitivity to penicillin is not excluded.

Illustrative is the case of a 68-year-old patient in whom surgical repair of an esophageal diverticulum was complicated by mediastinitis and shock. Ventricular fibrillation followed rapid infusion of 5 million units of potassium penicillin G containing 9 mEq of potassium ion into the right atrium over a period of 15–30 min (fig. 3).

The possibility that the route of administration or the speed of infusion of aminophylline in relation to the underlying cardiopulmonary defects accounted for cardiac arrest is not excluded. What does emerge is that the incidence of cardiac arrest after aminophylline under these conditions was selectively high. In the shock ward, aminophylline was used less than one-tenth as often as digoxin or penicillin, yet the incidence of cardiac arrest within 5 min after its administration was six times as great. This estimated 60-fold greater incidence of cardiac arrest with aminophylline than with the other drugs is presumptive evidence of a specific reaction to aminophylline.

Figure 2
Ventricular standstill following temporary interruption of mechanical ventilation for readjustment of a ventilator.
Electrical Mechanism of Cardiac Arrest

The relative incidence of ventricular asystole and ventricular fibrillation was analyzed for the 132 initial episodes of cardiac arrest. Pertinent data are summarized in table 4. In 76 patients (57%), ventricular asystole was the primary arrhythmia, and in 56 patients (43%) cardiac arrest was due to ventricular fibrillation. There were no significant differences in the relative incidence of cardiac standstill and ventricular fibrillation among the three categories of patients included in this study.

Discussion

The patients on whom this report is based were selectively the most critically ill patients in a large general hospital. The mortality of patients admitted to the shock ward was 61%. Even when patients are excluded in whom cardiac arrest occurred as a terminal event complicating exsanguination, protracted arrhythmias, or congestive heart failure which fails to improve promptly on medical management, this patient population still represents a selected group of very ill persons. This

| Table 4 |
|---|---|---|---|---|
| Patient group | No. of patients | Incidence | Successfully reverted | Incidence | Successfully reverted |
| | No. | % | No. | % | No. | % | No. | % |
| I: Respiratory acidosis | 65 | 34 | 52 | 7 | 20 | 31 | 48 | 15 | 50 |
| II: Metabolic acidosis | 34 | 22 | 65 | 16 | 72 | 12 | 35 | 2 | 7 |
| III: Catastrophic event | 33 | 20 | 60 | 0 | 0 | 13 | 40 | 5 | 30 |
| Total | 132 | 76 | 57 | 23 | 30 | 56 | 43 | 22 | 40 |

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precludes extrapolation of the information gathered during this study to the considerable information now available on previously healthy patients in whom sudden obstruction of the airway, immediate reactions to medication, electric shock, or sudden cardiac failure following myocardial infarction is the cause of cardiac arrest.

On the other hand, useful information emerges from the analysis which has both clinical and ethical implications. For practical purposes, there was no salvage of patients in whom progressive respiratory or circulatory failure accounted for acidosis prior to onset of cardiac arrest. This failure to ultimately reverse cardiac arrest in this large group of patients is of interest in the light of current traditions to attempt resuscitation on all except patients with terminal neoplasms or cerebrovascular accidents. Successful resuscitations were therefore primarily limited to those patients in whom cardiac arrest was catastrophic and potentially preventable.

The success of initial resuscitation is considerably greater in coronary care units. However, our resuscitative experience is more comparable to that reported by mobile resuscitation teams in teaching hospitals. The disappointingly small number of long-term survivors reflects the very high incidence of recurrence of cardiac arrest and the ultimate lethality of the primary disease which accounted for protracted acidosis prior to the onset of cardiac arrest.

Ventricular fibrillation was not the predominant cause of cardiac arrest. A majority of the patients initially manifested ventricular standstill. We would therefore not favor defibrillation on an empirical basis prior to electrocardiographic confirmation.

In comparison to previous studies, the present investigation provides special advantages which stem from the routine monitoring of patients employed in the shock ward. Continuous recording of the intraarterial pressure in addition to the electrocardiogram provides an immediate indication of mechanical cardiac arrest. This is particularly important since alterations in electrocardiographic complexes in instances of cardiac arrest in patients with cardiogenic shock may follow rather than precede cessation of an effective arterial pulse.

Ventilatory failure appears to be the single most common cause of death in critical care facilities including shock units. This also emerges from the present data. Approximately one-half of the patients were in respiratory acidosis at the time of cardiac arrest. Mechanical ventilators were used in almost all of the patients who demonstrated respiratory acidosis. While anoxemia was initially reversed in most instances by increasing the oxygen content of the inspired gas, progressive increases in the airway pressures, a decline in arterial oxygen tension and saturation, and increases in pCO₂ terminated in cardiac arrest. A reduction in pulmonary compliance and progressive pulmonary arteriovenous shunting characterize the syndrome of pulmonary failure associated with shock. The incidence of this syndrome has rapidly increased but its mechanism is as yet poorly understood.

In approximately one-fourth of the patient group, cardiac arrest occurred in patients with metabolic acidosis. This was usually associated with a concomitant increase in blood lactate and occurred in patients with advanced clinical signs of shock. The carbon dioxide tension was reduced and oxygen tension in arterial blood was normal in the majority of these patients. These observations suggest that, normal arterial oxygen tensions notwithstanding, perfusion failure, anoxic metabolism, and consequent metabolic acidosis predispose to cardiac arrest. Our observations confirm previous experimental and clinical studies in which cardiac output was observed to increase with acidosis. It is therefore more likely that acidosis itself rather than a decline in cardiac output accounted for cardiac arrest.

In 33 patients or approximately 25% of the total 132 patients (group III), neither respiratory nor metabolic acidosis was implicated. In each instance, however, cardiac arrest occurred as an unexpected event. The hazards of airway obstruction in patients who have...
endotracheal tubes or tracheostomy, particularly in the ventilator-dependent patient, is now generally appreciated. This was the cause of cardiac arrest in 13 patients included in group III. The seriousness of this problem is underscored in the present study in which mechanical failure accounted for interruption of ventilation and consequent cardiac arrest in two instances. In each of these cases, effective ventilation had been established and arterial blood gases had previously reflected normal pulmonary gas exchange while the patients were maintained on the ventilator. These catastrophies represent human error and provide incentive for more intense training of bedside personnel in respiratory management.

In 20 patients, catastrophic causes were attributable to adverse effects of drugs. The relative incidence of such adverse reactions is undoubtedly related to the selective practices in various centers. In our own unit, it was only on retrospective analysis that we recognized an inordinately high incidence of cardiac arrest which followed the intravenous administration of aminophylline. The hazards of this agent have been previously suggested. The doses which were used and protracted injection over a period of between 3 and 5 min were in accordance with established practice. The only additional variable was the site of injection. The possibility that the catastrophic reaction to this drug would have been avoided by more peripheral injections at a slower rate and in greater dilution is not excluded. For the present, we have discarded the intravenous use of aminophylline in favor of alternate routes of administration or we have used other bronchodilator or diuretic agents for treatment of the critically ill.

Finally, we are brought face-to-face with the ethical issues that stem from long-term survival of only one 34-year-old woman from among the 99 cases of cardiac arrest which occurred in patients who had progressive acidosis due either to ventilatory or to circulatory failure. The extraordinary demands on staff and the need for equipment and supplies during resuscitation inevitably tax the resources of the hospital and, more important, detract from intensive care of other patients. These data may therefore provide an objective basis for more restricted use of routine and repetitive cardiac resuscitation, particularly of elderly patients in whom acidosis reflects progressive ventilatory and circulatory failure.

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