Influence of compression rate on initial success of resuscitation and 24 hour survival after prolonged manual cardiopulmonary resuscitation in dogs

MICHAEL P. FENELEY, M.D., GEORGE W. MAIER, M.D., KARL B. KERN, M.D., J. WILLIAM GAYNOR, M.D., STANLEY A. GALL, JR., M.D., ARTHUR B. SANDERS, M.D., KEN RAESSLER, M.D., LAWRENCE H. MUHLBAIER, PH.D., J. SCOTT RANKIN, M.D., AND GORDON A. EWY, M.D.

ABSTRACT  The influence of chest compression rate on initial resuscitation success and 24 hr survival after prolonged manual cardiopulmonary resuscitation (CPR) was investigated in 26 morphine-anesthetized dogs (17 to 30 kg). After placement of aortic and right atrial micromanometers and induction of ventricular fibrillation, manual CPR was commenced immediately and continued for 30 min. One group of 13 dogs underwent manual CPR at a compression rate of 60/min, and the other group at a rate of 120/min. The compression durations in the two groups were not significantly different (51.7 ± 1.8% at 60/min vs 51.6 ± 1.9% at 120/min). No drugs other than sodium bicarbonate were administered during CPR. A maximum of three attempts was permitted to defibrillate the heart. Successfully defibrillated animals were followed for 24 hr, during which time no treatment, other than naloxone, was given to reverse the effects of morphine. Arterial blood pH, \( P_{CO_2} \), and \( P_{O_2} \) were not significantly different in the two groups throughout the CPR period. When compared with the compression rate of 60/min, the compression rate of 120/min produced more successfully defibrillated animals (12/13 at 120/min vs 2/13 at 60/min, \( p < .002 \)) and more 24 hr survivors (8/13 at 120/min vs 2/13 at 60/min, \( p < .03 \)). All 24 hr survivors were conscious and able to sit, stand, and drink normally. One 24 hr survivor in each group had difficulty walking. Improved survival with the high-rate compression technique was consistent with the significantly higher mean aortic (systolic and diastolic) and coronary perfusion pressures attained with high-rate compressions (all \( p < .002 \)). Although the clinical applicability of these findings has yet to be demonstrated, they provide empirical support for the recent decision to increase the chest compression rate for manual CPR recommended by the American Heart Association, and indicate that the hemodynamic and survival benefits of faster compression rates in this experimental preparation were not dependent on covariant alterations in compression duration.


THE RATE OF manual chest compression recommended for cardiopulmonary resuscitation (CPR) by the American Heart Association was recently increased from 40 to 60/min to 80 to 100/min.\(^1\) The experimental evidence supporting this alteration came from the work of Maier and Wolfe and their associates\(^2,3\) from Duke University, who demonstrated in a canine preparation of CPR that cardiac output, aortic pressure, and coronary blood flow increased with increasing manual compression rates up to an optimal compression rate of 120/min. In the only study that has addressed the impact of manual compression rate on survival after cardiac arrest, however, Kern et al.\(^5\) from the University of Arizona and Purdue University found no differences in initial resuscitation success or 24 hr survival in dogs after 17 min of manual CPR at 120/min when compared with a rate of 60/min. An important reservation concerning this finding was that, unlike Maier and Wolfe,\(^2,3\) Kern et al.\(^5\) did not find any improvement in hemodynamic variables with a compression rate of 120/min when compared with a rate of 60/min. Thus, the absence of a survival benefit with high-rate
compressions in the latter study was not surprising.

The question remained, therefore, as to whether differences between either the study design or the high-rate compression technique used by Maier and associates ("high-impulse CPR")² and those used by Kern et al.⁵ might explain the absence of hemodynamic and survival benefits with high-rate compressions when performed by the latter group. To answer this question, and to resolve the issue of whether faster manual CPR compression rates have the potential to improve survival, these two groups of investigators collaborated in a comparative study of initial resuscitation success and 24 hr survival in dogs after 30 min of manual CPR at rates of 60/min and 120/min.

Methods

Experimental preparation. Twenty-six healthy adult mongrel dogs (weight 17 to 30 kg) that had not undergone any previous surgical manipulation were used in this study. All dogs tested negative for heartworm infestation (Knots's test). The 26 dogs were assigned in a blinded manner to undergo either high-rate CPR at 120 compressions/min or low-rate CPR at 60 compressions/min, thus forming two equal groups of 13 dogs. The animals were premedicated with morphine sulfate (0.8 mg/kg sc). After intravenous administration of morphine sulfate (2 mg/kg iv) and succinyl choline (1 to 2 mg/kg iv), each dog was endotracheally intubated and ventilated with a volume respirator (Bennett MA1, FIO₂ 0.70, rate 12/min). The tidal volume was adjusted to attain an arterial Pco₂ of approximately 40 mm Hg. Each animal was secured in a dorsal recumbent position in a V shaped cradle. The anterior and lateral regions of the thorax were shaved, and electrocardiographic leads were attached. Micro-manometer-tipped catheters (Millar MPC-500) zeroed and calibrated at 38°C were passed into the right atrium and the ascending aorta via the right external jugular vein and carotid artery, respectively. Catheter placement was guided by surface anatomic measurement of the approximate catheter length necessary to achieve the target position and by continuous monitoring of the pressure waveforms during insertion. A silicone rubber catheter was inserted in a femoral artery to permit sampling for arterial blood gas analyses. Normal saline was infused intravenously to achieve a mean right atrial pressure of 6 to 8 mm Hg; arterial pH and bicarbonate levels were corrected, if necessary, by intravenous infusion of sodium bicarbonate to achieve an arterial pH within 0.05 units of 7.40. The amounts of sodium bicarbonate administered for this purpose to the high-rate (29 ± 32 [SD] meq) and low-rate (40 ± 21 meq) CPR groups were not significantly different. Additional morphine sulfate (1 mg/kg iv) and succinyl choline (1 mg/kg iv) was then administered. In six animals, three each from the high-rate and low-rate groups, halothane anesthesia (0.5 to 1%) was used in place of paralysis with succinyl choline during the instrumentation period but was discontinued, allowing sufficient time for the aortic blood pressure to return to approximately 120/80 mm Hg, before control data were recorded.

Experimental protocol and data acquisition. After pressure and arterial blood gas data were recorded in the control state, ventricular fibrillation was induced by a 60 Hz alternating current applied for 30 sec to two paddles placed across the anterior thorax. Manual CPR was commenced immediately, and the compression rate was synchronized with a crystal-controlled digital beeper apparatus. Thirteen dogs underwent forceful, deep-chest compression at a rate of 60/min, and the other 13 dogs underwent chest compression at a rate of 120/min. The latter (high-rate) technique has been described previously as "high-impulse CPR."² In the first phase of the study, which was performed at Duke University, an investigator from the University of Arizona team performed the low-rate compressions in 10 dogs, and a member of the Duke University team performed the high-rate compressions in another 10 dogs. In the second phase of the study, which was performed at the University of Arizona, a member of the University of Arizona research team performed both the high-rate and the low-rate compressions in the remaining six dogs.

Manual CPR was continued for precisely 30 min in each study. The right atrial and aortic pressures were monitored continuously on a storage oscilloscope, permitting the resuscitators to adjust their compression site, duration, and force as necessary to obtain the greatest achievable aortic diastolic and coronary perfusion pressures at each compression rate. Pressure data were acquired within 30 sec after institution of CPR and at 5 min intervals until the last data collection point 29 min after the onset of CPR. Arterial blood gas samples were obtained at these same time intervals in the first phase of the study and at intervals of 5, 15, and 25 min in the second phase. Arterial Pco₂ was corrected by appropriate alterations in the tidal volume delivered by the respirator, and arterial pH was adjusted by intravenous infusion of sodium bicarbonate. The total amounts of sodium bicarbonate administered to the low-rate and high-rate groups during CPR were not significantly different (52.7 ± 4.4 (SD) and 56.6 ± 7.5 meq, respectively). No other pharmacologic agents were administered during CPR.

At the completion of the 30 min CPR period, electrical defibrillation (300 J) was attempted. No more than three attempts to defibrillate the heart were permitted, and no antiarrhythmic or inotropic drugs were administered. Successful defibrillation was defined as resumption of a spontaneous cardiac rhythm associated with a peak aortic pressure of at least 60 mm Hg. If spontaneous circulation did not resume after three attempts at defibrillation, the study was terminated. Because metabolic acidosis was expected after resumption of spontaneous circulation and restoration of effective perfusion to peripheral regions, a slow infusion of sodium bicarbonate (50 meq) was commenced at defibrillation. In the first phase of the study, hemodynamic and arterial blood gas data were obtained 5, 15, and 30 min after resumption of a spontaneous circulation to assess the time course of recovery of these variables.

Survivors were followed for a maximal observation period of 24 hr. No further attempts at resuscitation were permitted after the initial 30 min CPR period. Medical therapy was confined entirely to weaning the animals from artificial ventilation, which necessitated administration of naloxone (0.8 mg) to reverse the effects of morphine in some cases. No other pharmacologic agents were administered. At the completion of the 24 hr observation period, surviving animals were evaluated neurologically according to standard criteria,⁶ and then were killed by injection of potassium chloride after deep barbiturate general anesthesia. An autopsy was performed on all animals to assess thoracic and abdominal trauma. The brain was not autopsied.

Data analysis. At each data sampling point specified in the protocol above, analog pressure data were acquired for 10 sec, digitized, and stored for analysis on a microprocessor (DEC, model PDP 11/23). Each compression/release cycle was divided into a compression period (systole), defined as the period between the onset of the rise of aortic pressure and its return to the precompression level, and a relaxation period (diastole), defined as the remainder of the cycle. The compression duration was expressed as a percentage of the total compression-relaxation cycle time (duty cycle). The mean coronary perfusion
FIGURE 1. Comparison of 24 hr survival curves after manual CPR for 30 min at a compression rate of 60/min or 120/min in two groups of 13 dogs each. The p value refers to the statistical significance of the difference in survival between the two compression rates over the entire 24 hr observation period (see text).

Pressure was calculated as the difference between the mean diastolic aortic and right atrial pressures.

Statistical comparisons of prearrest, baseline characteristics of the low-rate and high-rate groups were made by unpaired t test. Statistical comparisons of blood gas and pressure data in the two groups were made by analyses of variance for repeated measures. All data are expressed as the mean ± SD. Because the frequency of blood gas samples in the last six studies was less than in the first 20 studies, analysis of variance of the blood gas data was based on the first 20 studies. The statistical significance of differences in survival between the two groups was determined over the entire 24 hr observation period with the Gehan-Wilcoxon test, and differences in survival at specific times in this period were isolated with the Fisher exact test.

Results

Survival data. The 24 hr survival curves for the low-rate and high-rate compression groups are shown in figure 1. Only two of the 13 animals in the low-rate compression group could be successfully defibrillated. Both of these animals were studied at Duke University, and both survived for 24 hr. In contrast, 12 of the 13 animals in the high-rate compression group were successfully defibrillated (p < .002 vs low-rate group), including all three of the dogs studied at the University of Arizona. Two of the successfully defibrillated dogs in the high-rate group died within 10 min of resuscitation, one due to recurrent ventricular fibrillation and the other secondary to hemorrhage from a liver laceration. Two other dogs in the high-rate group died 12 and 16 hr, respectively, after resuscitation, one due to pulmonary failure and the other suddenly, presumably

| TABLE 1 |
| Prearrest baseline characteristics of the two manual CPR groups |

<table>
<thead>
<tr>
<th>Compression rate</th>
<th>60/min</th>
<th>120/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>19 ± 1.5</td>
<td>19 ± 3.6</td>
</tr>
<tr>
<td>Mean pressures (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic systolic</td>
<td>145 ± 16</td>
<td>132 ± 23</td>
</tr>
<tr>
<td>Aortic diastolic</td>
<td>116 ± 16</td>
<td>105 ± 23</td>
</tr>
<tr>
<td>Right atrial</td>
<td>8 ± 4</td>
<td>6 ± 3</td>
</tr>
<tr>
<td>Coronary perfusion</td>
<td>108 ± 15</td>
<td>98 ± 22</td>
</tr>
<tr>
<td>pH</td>
<td>7.39 ± 0.04</td>
<td>7.38 ± 0.04</td>
</tr>
<tr>
<td>Po2 (mm Hg)</td>
<td>412 ± 16</td>
<td>411 ± 29</td>
</tr>
<tr>
<td>Pco2 (mm Hg)</td>
<td>40.6 ± 4.0</td>
<td>40.0 ± 7.5</td>
</tr>
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</table>

^4On volume respirator with Fio2 of 0.70.

FIGURE 2. Comparison of mean ± SD duty cycles (percentage compression durations) measured throughout the period of manual CPR at a compression rate of 60/min or 120/min in two groups of 13 dogs each. The duty cycles in the two groups were not significantly different.

FIGURE 3. Representative examples of hemodynamic recordings from two dogs within 1 min of the onset of manual CPR (EARLY) and 1 min before attempted defibrillation (LATE) at compression rates of 60/min and 120/min. Perfusion pressure is the difference between aortic and right atrial pressures.
secondary to an arrhythmia. As noted in Methods, the study protocol did not permit any attempts at resuscitation after the initial CPR study period, nor did it permit advanced life-support techniques. Thus, at the end of the 24 hr observation period, two dogs survived in the low-rate CPR group, and eight survived in the high-rate CPR group (p < .03). When determined over the entire 24 hr period of observation after 30 min of CPR, survival was significantly greater at a manual compression rate of 120/min than at a compression rate of 60/min (p < .005). All 24 hr survivors were conscious and able to sit, stand, and drink normally. One 24 hr survivor in each group had difficulty walking.

**Hemodynamic and arterial blood gas data.** No significant differences existed in the prearrest, baseline data from the two groups (table 1). Despite the different chest compression rates used in the two groups during the CPR period, the duty cycles for the two groups were virtually identical (figure 2). The duty cycle averaged 51.7 ± 1.8% at 60/min and 51.6 ± 1.9% at 120/min. That is, the total duration of compression-phase time in the two groups was the same.

Representative pressure recordings, obtained within 1 min of the onset of CPR and 1 min before attempted defibrillation in the two groups, are shown in figure 3. The mean systolic aortic pressure at a compression rate of 120/min significantly exceeded that at a rate of 60/min throughout the CPR period (p < .001; figure 4, A). Similarly, the mean diastolic aortic pressure in the high-rate group significantly exceeded that in the low-rate group (p < .001; figure 4, B). After 5, 15, and 29 min of CPR, the mean diastolic aortic pressures in the high-rate group were 35.8 ± 8.7, 33.4 ± 8.4, and 33.1 ± 6.5 mm Hg, respectively, while the corresponding pressures in the low-rate group were 29.6 ± 6.3, 20.0 ± 7.5, and 18.8 ± 8.1 mm Hg, respectively. In contrast, the mean diastolic right atrial pressures in the two groups were not significantly different (figure 4, C). Consequently, the mean coronary perfusion pressure was maintained at a significantly higher level in the high-rate group than in the low-rate group throughout the CPR period (p < .001; figure 4, D). After 5, 15, and 29 min of CPR, the mean coronary perfusion pressures in the high-rate group were 20.1 ± 7.2, 20.9 ± 5.8, and 21.2 ± 5.2 mm Hg, respectively, while the corresponding pressures in the low-rate group were 11.4 ± 6.3, 8.4 ± 7.1, and 8.4 ± 8.3 mm Hg, respectively.

The arterial pH was maintained at approximately constant and normal levels in both groups throughout the CPR period (figure 5, A). The arterial Po2 declined progressively in both groups throughout the CPR
different in the two groups (figure 5, C), but declined during the first 5 to 10 min due to the high-frequency ventilatory effect of repetitive chest compression, then returned toward normal levels as the rescuers made compensatory adjustments to the tidal volume delivered by the respirator.

The hemodynamic and arterial blood gas data obtained after CPR from those dogs that survived more than 5 min after defibrillation in the first phase of the study are given in table 2. Intergroup statistical comparisons were precluded by the small number of survivors in the low-rate group, but the hemodynamic variables had returned to essentially normal levels by 15 min after defibrillation in the high-rate group, and by 30 min in the two low-rate survivors, in the absence of any inotropic support. A particularly notable feature of the recovery period was the marked hypercapnia and acidosis 5 min after successful resuscitation, which resolved completely within 30 min. This observation is consistent with "washout" of peripheral regions that were poorly perfused during CPR after resumption of spontaneous circulation, indicating that arterial blood gas samples obtained during CPR are not representative of the acid-base balance of the whole organism. Finally, arterial Po2 increased rapidly after successful defibrillation, suggesting that the reduced Po2 during CPR resulted primarily from ventilation-perfusion mismatch.

**Postmortem findings.** The autopsy findings for both study groups are summarized in table 3. Rib fractures were uncommon, and never involved more than two ribs. The most common findings in both survivors and nonsurvivors were small amounts of serosanguineous peritoneal fluid in the absence of a bleeding site and minor degrees of intrapulmonary hemorrhage. The latter consisted of discrete hemorrhagic spots confined to

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**TABLE 2**

<table>
<thead>
<tr>
<th>Postresuscitation hemodynamic and arterial blood gas data</th>
<th>5 min after defib</th>
<th>15 min after defib</th>
<th>30 min after defib</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>60 compressions/ min (n = 2)</td>
<td>120 compressions/ min (n = 9)</td>
<td>60 compressions/ min (n = 2)</td>
</tr>
<tr>
<td>Mean systolic aortic pressure (mm Hg)</td>
<td>56.90 ± 1.26</td>
<td>87.50 ± 8.20</td>
<td>77.50 ± 3.59</td>
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<tr>
<td>Mean diastolic aortic pressure (mm Hg)</td>
<td>42.80 ± 1.07</td>
<td>67.10 ± 8.10</td>
<td>63.90 ± 4.38</td>
</tr>
<tr>
<td>Mean right atrial pressure (mm Hg)</td>
<td>6.39 ± 2.49</td>
<td>12.20 ± 0.90</td>
<td>11.58 ± 0.52</td>
</tr>
<tr>
<td>Coronary perfusion pressure (mm Hg)</td>
<td>36.40 ± 3.33</td>
<td>55.00 ± 8.50</td>
<td>53.09 ± 3.58</td>
</tr>
<tr>
<td>pH</td>
<td>7.21 ± 0.01</td>
<td>7.29 ± 0.04</td>
<td>7.32 ± 0.01</td>
</tr>
<tr>
<td>PCO2 (mm Hg)</td>
<td>74.60 ± 1.31</td>
<td>72.70 ± 5.10</td>
<td>53.40 ± 1.29</td>
</tr>
<tr>
<td>PO2 (mm Hg)</td>
<td>198.20 ± 42.00</td>
<td>310.90 ± 46.60</td>
<td>301.50 ± 13.08</td>
</tr>
<tr>
<td>HCO3 (meq)</td>
<td>29.50 ± 0.140</td>
<td>35.3 ± 3.70</td>
<td>27.30 ± 0.24</td>
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TABLE 3
Summary of autopsy findings after manual CPR

<table>
<thead>
<tr>
<th></th>
<th>Compression rate</th>
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<tr>
<td></td>
<td>60/min</td>
</tr>
<tr>
<td>Thorax</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>Normal</td>
</tr>
<tr>
<td>Lungs</td>
<td></td>
</tr>
<tr>
<td>Intrapulmonary hemorrhage</td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>11/13</td>
</tr>
<tr>
<td>Moderate</td>
<td>2/13</td>
</tr>
<tr>
<td>Extensive</td>
<td>—</td>
</tr>
<tr>
<td>Ribs</td>
<td></td>
</tr>
<tr>
<td>≤2 fractures</td>
<td>2/13</td>
</tr>
<tr>
<td>Abdomen</td>
<td></td>
</tr>
<tr>
<td>Serosanguineous peritoneal fluid</td>
<td>11/13</td>
</tr>
<tr>
<td>Liver laceration</td>
<td></td>
</tr>
<tr>
<td>Major</td>
<td>—</td>
</tr>
<tr>
<td>Minor (no significant hemorrhage)</td>
<td>—</td>
</tr>
</tbody>
</table>

one or two lung lobes. Moderate intrapulmonary hemorrhage, defined as discrete hemorrhagic areas involving more than two lobes or confluent hemorrhagic areas confined to one or two lobes, was less common. More extensive areas of intrapulmonary hemorrhage were found in two dogs from the high-rate group, although one of these dogs was ambulatory without respiratory difficulty 24 hr after resuscitation. Two deaths in the high-rate group were related to traumatic complications. One of these dogs died from respiratory failure 12 hr after resuscitation, and extensive areas of intrapulmonary hemorrhage were found at autopsy, although neither the lung nor any identifiable pulmonary vessels were lacerated. The other died due to intra-abdominal hemorrhage from a liver laceration. A small liver laceration, without significant intra-abdominal hemorrhage, was an incidental finding at autopsy examination of one 24 hr survivor in the high-rate group. No dogs in the low-rate group sustained serious trauma. There was no evidence of cardiac trauma in any of the dogs studied.

Discussion

The recent decision by the American Heart Association to increase the recommended chest compression rate for manual CPR from 40 to 60/min to 80 to 100/min was supported by those who believe that blood flow during CPR results primarily from cardiac compression. According to this view, provided sufficient compression time is permitted to maintain a constant extent of cardiac compression, the stroke volume will remain relatively constant when the compression rate is increased, with a consequent increase in the cardiac output. Based on their experimental evidence supporting this view, Maier et al. advocated the increase in the compression rate for human CPR.

During the last decade, however, it has been demonstrated that with some nonmanual CPR techniques, the primary driving force for blood flow is a generalized increase in intrathoracic pressure, the heart acting as a "passive conduit" for blood flow. This has been called the thoracic pump model of CPR. According to the thoracic pump model, blood flow is primarily determined by compression duration, rather than rate. Several investigators hold the view that the thoracic pump mechanism is also the primary mechanism of blood flow during manual CPR. Consequently, these authors have favored a greater emphasis on prolonging manual compression duration rather than increasing compression rate. It has been suggested by some of these investigators that the improved cardiac output noted by Maier et al. when compression rate was increased might have resulted from a covariant increase in the percentage compression duration.

Nevertheless, advocates of the thoracic pump mechanism supported the recent decision to increase the recommended chest compression rate on the basis that "the faster rate would make it easier to achieve the 50% chest compression-relaxation ratio" that they believe to be optimal, thus increasing the total time spent in the compression phase. A comprehensive review of the current controversy concerning the mechanism of manual CPR is given elsewhere.

Regardless of the primary mechanism of blood flow during manual CPR, it is clear that the ultimate justification for any alteration to the recommended manual CPR technique must be that this alteration improves survival. Under the conditions of the present study, a compression rate of 120/min significantly improved both immediate and 24 hr survival after 30 min of manual CPR when compared with a compression rate of 60/min. The improved survival with the high-rate technique correlated well with the greater aortic diastolic and coronary perfusion pressures produced with this technique; both of these pressures have been shown to directly influence measured coronary blood flow during CPR and resuscitation success. The improved hemodynamic variables with high-rate CPR are consistent with the previous observations of Maier and Wolfe and their associates that the increase in cardiac output with increased compression rates resulted in higher diastolic aortic pressures, and thus coronary perfusion pressures. Coronary blood flow was optimized at a compression rate of 120/min, since coronary perfusion was limited at higher rates by the abbreviation of diastolic perfusion time.
diastolic and coronary perfusion pressures tend to decline during prolonged CPR due to progressive loss of peripheral vascular tone in the presence of low systemic flow.2 Thus, the higher cardiac output associated with high-rate compressions2-4 is consistent with the observation that aortic diastolic and coronary perfusion pressures were well maintained over time in the high-rate group in the present study, but declined progressively in the low-rate group (figure 4). Importantly, the improved hemodynamics and improved survival with high-rate CPR in the present study were not dependent on differences in percentage compression duration: the percentage compression durations in the high-rate and low-rate groups were the same.

These findings are consistent with the predictions of the cardiac compression model of blood flow during manual CPR.2, 4 More direct evidence for the cardiac compression model comes from the recent echocardiographic observation in dogs that the mitral valve was closed during the compression phase of manual CPR, preventing anterograde transmitral blood flow, with all but very prolonged, low-momentum compression techniques.30 Similar observations have been made during mechanical chest compressions in minipigs, where persistence of mitral valve closure during the compression phase was associated with survival.31 These observations are antithetical to the thoracic pump model of CPR, the central tenet of which is that blood flows anterograde through the open mitral valve during chest compression,14, 15 In the absence of anterograde transmitral blood flow during compression, net systemic arterial flow during compression can be attributed only to displacement of blood from the left ventricle (i.e., cardiac compression).30 On the other hand, there is little doubt that the thoracic pump mechanism is primarily responsible for blood flow during cough CPR and probably during vest CPR with simultaneous ventilation.8, 9, 13-15

As the pressure tracings shown in figure 3 exemplify, there was little difference between aortic and right atrial pressures during the compression phase of CPR. When averaged over the period of CPR, the mean systolic aortic pressure exceeded the mean systolic right atrial pressure by 4.4 ± 1.1 mm Hg in the low-rate group and 10.5 ± 0.8 mm Hg in the high-rate group. Similar observations have been made by many previous investigators.5, 15, 32-34 Competent venous valves at the thoracic inlet and the high systemic venous compliance prevent full transmission of the high right atrial systolic pressure to the extrathoracic veins, however, thereby ensuring an arteriovenous pressure gradient for systemic blood flow, particularly to the brain.13, 14, 35 Myocardial blood flow, on the other hand, occurs almost entirely during diastole, when the right atrial pressure falls.

By comparison with the hemodynamics of open-chest cardiac massage, some investigators have argued that the high right atrial systolic pressures generated by closed-chest, manual CPR are not compatible with a cardiac compression mechanism of blood flow.14, 15 This argument ignores the important distinction that compressive force is applied selectively to the ventricular surfaces of the heart during open-chest cardiac massage, but all cardiac chambers are exposed to compressive force during closed-chest CPR.34 Some non-uniformity of the pressures generated in the different cardiac chambers by closed-chest cardiac compression would be expected nonetheless due to differences in the anatomic relationships of the different chambers to the compression vector and differences in the impedance to venting of the pressure changes in the different chambers.30 Thus, the recent observation of mitral valve closure during manual chest compression30 was consistent with the finding from the same study that the peak and mean left ventricular systolic pressures exceeded the corresponding left atrial systolic pressures by 38.5 ± 4.0 and 13.5 ± 2.9 mm Hg, respectively. The tricuspid valve also has been observed to close during manual chest compression,30, 36 and some investigators have noted the presence of tricuspid regurgitation.13, 37 In the light of these observations, the high right atrial systolic pressures generated by manual CPR cannot be construed as evidence against the cardiac compression mechanism of blood flow.

In their previous comparative study of high-rate (120/min) and low-rate (60/min) manual CPR, Kern et al.,5 who collaborated in performing the present study, found that high-rate CPR did not improve either initial resuscitation success or 24 hr survival. In that study, however, manual CPR was not commenced until 3 min after cardiac arrest. CPR was performed for 17 min, and advanced cardiac life support techniques were employed for a period of 2 hr and 10 min after completion of the initial CPR period (including administration of pressor and antiarrhythmic drugs and further manual CPR and defibrillation attempts when required). Thus, the experimental design incorporated several variables that may have influenced the ultimate end point (i.e., survival) independent of the differences in initial manual compression technique.

In contrast, the present study was designed to ensure that any differences in survival outcome could be related only to differences between the manual compression techniques employed. Thus, the protocol did
not include either advanced cardiac life support techniques or secondary attempts at CPR, and electrical defibrillation was limited to three attempts at the completion of the initial CPR period. Optimal ventilatory support was provided for both groups of dogs. Sodium bicarbonate was given to both groups in an attempt to prevent metabolic acidosis and its potential arrhythmogenic effects, although little objective evidence exists that administration of sodium bicarbonate influences resuscitation success. In any case, equivalent amounts of sodium bicarbonate were administered to the two groups during CPR. As described previously, intravenous fluids were given to ensure normal and equal levels of central venous pressure in the two CPR groups before cardiac arrest, whereas infusions were not used in the previous study by Kern et al. If this difference in study design contributed significantly to the different outcome of the two studies, then this finding may have important implications for the clinical management of cardiac arrest. It seems unlikely, however, that preload limitation is a major factor in most human cardiac arrest situations. CPR was begun immediately after cardiac arrest in the present study and was continued for 30 min, a period exceeding that usually associated with successful resuscitation in the clinical setting. These features of the study design would be expected to increase the discriminative power of the comparison of CPR techniques.

It must be noted that there is frequently some delay before the institution of CPR in human victims of cardiac arrest, and that this delay is a major determinant of survival outcome. It is to be expected, therefore, that any survival advantages associated with alterations in conventional CPR techniques will diminish with increasing delay before the institution of CPR, and may be marginal in many instances of prolonged out-of-hospital cardiac arrest. Similarly, the immediate onset of CPR after cardiac arrest in the present study, in contrast to the 3 min delay in the previous study by Kern et al., probably contributed to the differences between the two studies in survival outcome.

It is doubtful, however, whether this or other variations in study design can account fully for differences between the two studies in the aortic diastolic and coronary perfusion pressures at a compression rate of 120/min. The significant improvement in these variables in the present study probably was the major factor contributing to enhanced success of resuscitation. The fact that several animals survived CPR at both compression rates in the previous study by Kern et al. indicates that the 3 min delay was not sufficient to preclude restitution of adequate systemic blood flow. Under such conditions, the same mechanical factors that led to hemodynamic improvement with faster compression rates in the present study would be expected to be operative. albeit with a reduced survival benefit, unless systematic differences existed between the compression techniques used in the two studies. The low-rate compressions in both studies were performed by the same group of investigators from the University of Arizona. The high-rate CPR techniques used in the two studies differed, however, in at least one important respect: the absolute compression duration per cycle at 120/min in the previous study was only 100 msec, but was approximately 250 msec in the present study. The stroke volume displaced by cardiac compression will remain constant when the compression rate is increased only if sufficient compression time is permitted to ensure that the extent of cardiac compression remains constant. The absolute compression duration employed in previous studies in which stroke volume remained constant when compression rate was increased was approximately 200 msec. Since Kern et al. used deliberately deep, forceful compressions of 500 msec duration at 60/min, the extremely brief duration of their high-rate compressions probably was insufficient to ensure that the stroke volume remained constant. The concept of a minimum threshold duration for cardiac compression should not be confused with the prediction from the thoracic pump model that blood flow is determined by percentage compression duration: the percentage compression durations in the low-rate and high-rate groups in the present study were the same.

The important implication of these observations is that when compression rate is increased, the absolute compression duration should not be unduly abbreviated. An absolute compression duration of 200 to 250 msec is sufficient to ensure a constant extent of cardiac compression when compression rate is increased, and is equivalent to a percentage compression duration of 40% to 50% at a compression rate of 120/min. Fortunately, at compression rates exceeding 100/min, this is the compression duration that can be most easily maintained.

Halperin et al. have reported that when the percentage duration of compression was maintained constant during manual CPR in dogs, increasing the compression rate from 60/min to 150/min did not increase myocardial or cerebral perfusion pressures or blood flow. This finding was presented as evidence that the thoracic pump mechanism was primarily responsible for blood flow during manual CPR but is at variance with the findings of the present study and the previous...
studies by Maier and Wolfe and their associates\textsuperscript{2, 3} from Duke University. This discrepancy may reflect differences in the manual compression techniques used in these studies. Certainly, the aortic or left ventricular pressure waveforms generated during manual compression by these two research groups are distinctly different.\textsuperscript{2, 30, 38} The pressure waveforms generated by Halperin et al.\textsuperscript{38} are almost indistinguishable from those observed during vest CPR, a technique in which the thoracic pump mechanism of blood flow is thought to be dominant.\textsuperscript{15, 39} Since the Duke University group has directly demonstrated by echocardiography that there is no anterograde transmural blood flow during manual compression with their technique,\textsuperscript{30} a similar echocardiographic study of the manual compression technique used by Halperin et al.\textsuperscript{15, 38} might establish the mechanistic basis for the different hemodynamic findings reported by these investigators. If the thoracic pump mechanism is the primary mechanism of blood flow with their manual compression technique, as they believe, then anterograde transmural blood flow should be readily demonstrable during the compression phase.

The more important issue, however, is whether the manual compression technique used by these investigators confers the same survival benefit as the high-rate compression technique used by the Duke University group. Recently, Halperin et al.\textsuperscript{38} reported that after 26 min of manual CPR at a rate of 60/min with their standard compression technique (sternal force 300 N), only one of seven dogs survived for 24 hr, despite the use of epinephrine during CPR and advanced cardiac life support techniques (including antiarrhythmic and pressor agents) for up to 3 hr after defibrillation. Similarly, Niemann et al.\textsuperscript{40} reported that one of nine dogs survived after 30 min of conventional manual CPR. These results are quite comparable with those achieved with low-rate compressions (60/min) in the present study without the use of epinephrine or advanced cardiac life support techniques. Two of the dogs studied by Halperin et al., however, sustained severe trauma (liver laceration or flail chest), but none of the dogs in the low-rate group in the present study sustained comparable trauma. In another group of dogs, Halperin et al.\textsuperscript{38} used much more forceful chest compressions (up to 480 N) at a rate of 60/min. Three of these seven dogs survived for 24 hr, but one had difficulty walking and another was stuporous. Moreover, four of the dogs in the high-force group sustained liver lacerations, three had flail chests, and one had diffuse myocardial hemorrhage with hemopericardium. Thus, even with extremely forceful compressions at 60/min, these investigators achieved a poorer survival benefit at the expense of appreciably more trauma than was achieved with high-rate (120/min) compressions in the present study. Maier et al.\textsuperscript{2} have demonstrated previously that increasing compression force beyond moderate levels with the high-impulse CPR technique does not further augment stroke volume, but only increases the risk of serious trauma.

In the same study by Halperin et al.,\textsuperscript{38} all seven dogs in which a modified vest CPR technique was used without simultaneous ventilation survived for 24 hr, with no instances of serious trauma. This result compares favorably with the report by Niemann et al.\textsuperscript{40} that seven of nine dogs survived after 30 min of vest CPR with simultaneous ventilation. Direct comparison with the high-rate manual CPR technique used in the present study is difficult because Halperin et al. administered epinephrine during the CPR period and used advanced cardiac life support techniques after defibrillation. Nevertheless, the hemodynamic measurements made during modified vest CPR before administration of epinephrine were quite comparable to those made during high-rate manual compression in this study, and initial resuscitation success with these two techniques was comparable. A direct comparison of these two techniques under identical experimental conditions would be of interest.

It should be noted, however, that while there is considerable evidence that blood flow during vest CPR with simultaneous ventilation is primarily mediated by the thoracic pump mechanism, there is as yet no evidence that the same mechanism remains dominant during vest compressions without simultaneous ventilation. In the absence of the opposing effect of simultaneous ventilation, a given change in intrathoracic vascular pressures by vest compression would require a greater reduction in intrathoracic volume, which may be associated with significant cardiac compression. Moreover, while vest CPR may prove useful in the management of prolonged in-hospital cardiac arrests, it has limited applicability in most situations of sudden cardiac arrest, in which the immediate application of effective manual CPR, often by nonmedical bystanders, has the greatest potential to significantly increase the number of survivors of cardiac arrest. The survival outcome obtained with high-rate manual CPR in this study is the highest yet reported with any manual CPR technique, despite the fact that no advanced life support techniques were employed.

As the foregoing discussion demonstrates, most of the data pertaining to the mechanisms and effectiveness of different CPR techniques have been obtained from experiments in animals, predominantly dogs. Differ-
ences in size, chest shape, and thoracic anatomy between human subjects and dogs may influence the clinical relevance of these data. Thus, while different investigators have derived evidence from canine experimental preparations to support either the cardiac compression mechanism\textsuperscript{2, 4, 30} or the thoracic pump mechanism\textsuperscript{14, 15} of blood flow during manual CPR, any or all of the above differences between human subjects and dogs may favor dominance of one or other mechanism of blood flow during human CPR. Similarly, the important experimental observation that closure of venous valves at the thoracic inlet protects the cerebral veins from the high right atrial systolic pressures generated by CPR, thus ensuring a cerebral flow gradient,\textsuperscript{13} awaits confirmation during human CPR, although the phenomenon has been demonstrated in human subjects during coughing.\textsuperscript{35} Moreover, several factors in addition to the CPR technique are important and often critical determinants of survival from cardiac arrest in human subjects, including the delay before the institution of CPR, the cause of cardiac arrest, and coexistent disease processes. In many instances, these additional factors may outweigh the benefits of any CPR technique. Finally, the dog provides a rather limited preparation for the assessment of neurologic function. Thus, the grossly normal neurologic function observed in most 24 hr survivors in the present study may have limited implications for the preservation of distinctively human intellectual function after prolonged CPR.

In conclusion, this study demonstrates that when CPR is initiated early after the onset of cardiac arrest and the percentage compression duration is constant, a compression rate of 120/min significantly improves both immediate and 24 hr survival in dogs after prolonged manual CPR when compared with a compression rate of 60/min. The significantly greater aortic diastolic and coronary perfusion pressures attained with the high-rate compression technique probably account for this survival benefit. These findings are consistent with the predictions of the cardiac compression model of blood flow during manual CPR.\textsuperscript{2, 4} Of more importance than the mechanistic implications is the direct empirical support that these findings provide for the recent decision by the American Heart Association\textsuperscript{1} to increase the recommended chest compression rate for manual CPR. Whether the findings of experiments in animal preparations are applicable to human subjects, however, must always be questioned, and survival from cardiac arrest in human subjects is determined by several factors in addition to the CPR technique. For these reasons, the present findings require confirmation in human victims of cardiac arrest. Scientifically designed clinical trials of the influence of chest compression rate on survival from cardiac arrest may now be warranted.

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