Effect of Protracted Dobutamine Infusion on Survival of Patients in Cardiogenic Shock Treated with Intraaortic Balloon Pumping*

Spyridon D. Moulopoulos, M.D.; Stamatis F. Stamatoelopoulos, M.D.; John N. Nanas, M.D.; Dimitrios A. Kontoyannis, M.D.; and Serafin N. Nanas, M.D.

The survival of subjects with postmyocardial infarction cardiogenic shock treated with intra-aortic balloon pumping (IABP) differs significantly among various reports. Differences in the criteria for IABP application and in the timing of its initiation have been considered as the main reasons for variations in survival. This study examines whether the way patients in cardiogenic shock are treated prior to IABP may affect their survival. Fifty-five patients in severe postmyocardial infarction cardiogenic shock were classified into three groups according to the rate of dobutamine infusion prior to IABP; the "nondobutamine" (group A, n = 31), the "high-dose dobutamine" (8 to 20 μg·kg⁻¹·min⁻¹, group B, n = 17), and the "low-dose dobutamine" (up to 7 μg·kg⁻¹·min⁻¹, group C, n = 7). All subjects seen from 1978 to 1983 were recruited for group A, from 1986 to 1990 for group B, and in years 1984, 1985, and 1991 for group C, without using any other classification criteria. It was shown a posteriori that the three groups did not differ in the features of the subjects, in the severity of shock, and in the time length between onset of shock and pumping initiation. None of the 17 subjects of group B could survive under pumping, while 10 of the 31 subjects in group A and 4 of the 7 subjects in group C were weaned off pumping. Conclusions: A protracted, high-dose pre-IABP administration of dobutamine may adversely affect the survival of patients with postmyocardial infarction cardiogenic shock.

(Chest 1993; 103:249-52)

IABP = intra-aortic balloon pumping

Table 1—Criteria for Diagnosis of Cardiogenic Shock Used in all Three Groups*

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-arterial systolic blood pressure ≤80 mm Hg</td>
</tr>
<tr>
<td>Urine output less than 20 ml·h⁻¹</td>
</tr>
<tr>
<td>Mental confusion, peripheral signs of low output</td>
</tr>
</tbody>
</table>

*From the Department of Clinical Therapeutics, Medical Division, School of Health Sciences, Athens University, Athens, Greece. Manuscript received March 3; revision accepted June 10
Reprint requests: Dr. Moulopoulos, Ws. Sofias 80, 11528 Athens, Greece

Dobutamine Effect on Survival in Cardiogenic Shock (Moulopoulos et al)

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Table 2—Classification Into Three Groups*

<table>
<thead>
<tr>
<th></th>
<th>Group A (Nondobutamine)</th>
<th>Group B (High-Dose Dobutamine)</th>
<th>Group C (Low-Dose Dobutamine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>60.4 ± 1.8</td>
<td>62.3 ± 1.9</td>
<td>57.6 ± 4.9</td>
</tr>
<tr>
<td>Sex</td>
<td>26 M, 5 F</td>
<td>15 M, 2 F</td>
<td>7 M</td>
</tr>
<tr>
<td>HR</td>
<td>105.3 ± 2.5</td>
<td>104.1 ± 3.8</td>
<td>112.7 ± 7.9</td>
</tr>
<tr>
<td>ia SBP</td>
<td>71 ± 1.3</td>
<td>74.4 ± 4</td>
<td>77.5 ± 5.9</td>
</tr>
<tr>
<td>CVP</td>
<td>17.1 ± 0.6</td>
<td>15.6 ± 0.7</td>
<td>16.9 ± 1.2</td>
</tr>
<tr>
<td>PWP</td>
<td>22.4 ± 0.8</td>
<td>23.4 ± 1.4</td>
<td>27.8 ± 2.8</td>
</tr>
<tr>
<td>Cardiac index</td>
<td></td>
<td>1.93 ± 0.28</td>
<td>1.96 ± 0.07</td>
</tr>
<tr>
<td>Systemic resistance</td>
<td></td>
<td>2,008 ± 220</td>
<td>1,906 ± 75.9</td>
</tr>
<tr>
<td>Urine output</td>
<td>8.0 ± 1.3</td>
<td>2.0 ± 0.9</td>
<td>6.3 ± 2.9</td>
</tr>
<tr>
<td>Shock duration</td>
<td>11.2 ± 1.5</td>
<td>19.9 ± 8</td>
<td>18.1 ± 10.3</td>
</tr>
<tr>
<td>Location AMI</td>
<td>21 ANT, 8 INF, 2 S</td>
<td>12 ANT, 4 INF, 1 S</td>
<td>4 ANT, 3 INF</td>
</tr>
<tr>
<td>Previous/acute MI</td>
<td>14 of 31</td>
<td>10 of 17</td>
<td>4 of 7</td>
</tr>
<tr>
<td>Dobutamine duration</td>
<td></td>
<td>17.5 ± 7.9</td>
<td>16.3 ± 10.4</td>
</tr>
</tbody>
</table>

*Mean values ± SE of age in years, sex, heart rate prior to IABP (HR), intra-arterial systolic blood pressure prior to IABP in mm Hg (ia SBP), central venous pressure prior to IABP in mm Hg (CVP), pulmonary wedge pressure prior to IABP in mm Hg (PWP), cardiac index in Lmin⁻¹m⁻², systemic resistance in dynes·sec⁻¹·cm⁻⁵, urine output prior to IABP in ml·h⁻¹ (urine output), time lag between onset of shock and IABP initiation in hours (shock duration), location of acute myocardial infarction (AMI, ANT = anterior, INF = inferior, S = septal), proportion of subjects presented with a coexisting previous infarction on top of the acute one (previous/acute MI), and duration of dobutamine infusion in hours (dobutamine infusion).

for at least 2 h despite the application of the specific (see below) treatment applied in each of the 3 groups into which were classified the 55 subjects; (3) subjects submitted to corrective surgery or coronary angioplasty while under pump assist were not included in the study; thus, "survivors" were subjects improved by IABP alone so that they could be weaned off pump and leave hospital surviving for over 1 month, independently of the type of treatment (conservative or corrective surgery or transluminal angioplasty) to which they were submitted afterwards.

The 55 subjects were classified into 3 groups (Table 2) according to the protocol of treatment applied following the establishment of cardiogenic shock and prior to the initiation of IABP. The only variable considered for this classification was whether they had received dobutamine during the above period of time, and if they had received it whether its infusion rate was higher or lower than 7.5 µg·kg⁻¹·min⁻¹. It must be made clear that the infusion rate of dobutamine was independent of the severity of shock since the classification of subjects into the three groups was performed as follows: all subjects with cardiogenic shock seen from 1978 to 1983 were recruited for group A (see below), from year 1986 to 1990 for group B, and within years 1984, 1985, and 1991 for group C. No other classification criteria were used. More specifically, the three protocols used for pre-IABP conventional treatment were as follows.

**Group A (Nondobutamine Group)**

This group consisted of 31 subjects treated with intravenous fluid infusion until central venous pressure and/or pulmonary wedge pressure were approaching 20 cm H₂O and 15 mm Hg, respectively. Intra-aortic balloon assistance was decided upon if the signs listed in Table 1 persisted for more than 2 h after this goal was reached. All these subjects were treated before the introduction of dobutamine in our institution, so none of them received the drug. Norepinephrine had to be infused, for a few minutes, in 6 of the 31 subjects with very severe blood pressure reduction, as a "bridge" to balloon insertion. The significant delay between shock establishment and IABP initiation (Fig 1) was due to two main factors: first, many of the patients had been transferred from other hospitals after the establishment of shock and second, balloons were inserted through a graft on the femoral artery at that time (year 1978 to 1983) and the surgical operation was often delayed for considerable time.

**Group B (High-Dose Dobutamine Group)**

This group consisted of 17 subjects. Dobutamine infusion was initiated if the signs listed in Table 1 persisted for 30 min despite left ventricular filling pressure increase to the level of 15 mm Hg or higher by means of intravenous fluid infusions. The initial rate of dobutamine infusion was 8 µg·kg⁻¹·min⁻¹. The infusion rate increased gradually to a maximum of 20 µg·kg⁻¹·min⁻¹ if the signs in Table 1 persisted or reappeared following an initial improvement. The IABP application was decided only if the signs of shock

![FIGURE 1. Maximal dobutamine dose, used during the prepumping period of treatment, plotted against shock duration, that is, the time passed from the onset of shock (criteria listed in Table 1) to the initiation of intra-aortic balloon pumping. Survival is indicated by plus sign and death by triangle. The dotted horizontal lines separate the three groups of subjects: the high-dose dobutamine group (upper), the low-dose dobutamine group (middle), and the nondobutamine group (lower).](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21663/ on 06/24/2017)
A and t = 0.89, NS for groups B vs C). The difference in the duration of dobutamine infusion (Table 2) between low-dose (16.33 ± 10.42 h) and high-dose (17.52 ± 7.99 h) dobutamine groups was also nonsignificant (t = 0.95, NS). The difference in dobutamine infusion rates between the above two groups (4.33 ± 0.42 µg·kg⁻¹·min⁻¹ and 11.52 ± 0.99 µg·kg⁻¹·min⁻¹, respectively) was, as expected, highly significant (t = 6.68, p < 0.001, n = 24).

Plotting dobutamine infusion rate against the corresponding shock duration for the 55 subjects in the three groups is shown in Figure 1. The survival rate (designated as the percentage of subjects improved to the extent to be weaned off IABP and to survive for more than 1 month, without being submitted to corrective surgery or other intervention while under pumping) was 10 of 31 subjects for the nondobutamine group and 4 of 7 for the low-dose dobutamine group, while none of 17 subjects in the high-dose dobutamine group survived (Fig 1). The survival rates did not differ between low-dose and nondobutamine groups (χ² = 2.77, NS). No significant (t = 1.32, NS) difference existed in shock duration among the 4 survivors of the low-dose (8.6 ± 1.76 h) and the 10 survivors of the nondobutamine (7.55 ± 1.49 h) groups.

As shown in Figure 1, and more clearly in Figure 2, the mean duration of shock before the initiation of IABP in the 14 survivors (7.75 ± 1.21 h) was significantly (t = 2.52, p < 0.01) shorter than in the 41 nonsurvivors (17.8 ± 3.79 h), when the total number of 55 subjects was examined. In the nondobutamine group, the same variable in the 10 survivors (7.55 ± 1.49 h) was significantly (t = 2.18, p < 0.02) shorter than in the 21 nonsurvivors (12.95 ± 1.97 h). In the high-dose dobutamine group, there was not a single survivor despite the fact that shock duration in 9 of the 17 subjects was shorter than 7 h (Fig 2).

As soon as the diagnosis of shock was established, that is, prior to the initiation of dobutamine infusion,
the urine output was $9.31 \pm 3.34$ ml·h⁻¹ for the high-dose and $13.6 \pm 2.78$ ml·h⁻¹ for the low-dose dobutamine group. The two values did not differ significantly ($t = 0.91$, NS). As soon as IABP was decided upon, that is following the failure of the (maximal for the specific group) conventional treatment (in which dobutamine was included) to improve the patient's hemodynamic condition, the same variable was, respectively, $2.0 \pm 0.9$ ml·h⁻¹ and $6.3 \pm 2.9$ ml·h⁻¹ (Table 2). Again, no significant difference existed between the two values ($t = 1.36$, NS). However, a statistically significant ($t = 2.10$, $p < 0.05$) difference existed between urine output before and after high-dose dobutamine infusion; the difference between the same values before and after low-dose dobutamine infusion was nonsignificant ($t = 1.79$, NS). Another statistically significant difference ($t = 3.75$, $p < 0.01$) existed in urine output before pumping between nondobutamine and high-dose dobutamine groups ($8.0 \pm 1.3$ and $2.0 \pm 0.9$ ml·h⁻¹, respectively, Table 2). No statistical difference existed either between the low-dose and the non-dobutamine groups or the low-dose and the high-dose dobutamine groups concerning the same variable (Table 2).

The location of acute myocardial infarction was as follows: 21 anterior, 8 inferior, and 2 septal infarctions for the nondobutamine, 12 anterior, 4 inferior, and 1 septal infarctions for the high-dobutamine, and 4 anterior and 3 inferior infarctions for the low-dobutamine groups. A previous infarction existed in 14 of the 31 subjects of the first, in 10 of the 17 subjects of the second, and in 4 of the 7 subjects of the third group of the above three groups. No difference could be established among the three groups concerning the location of acute myocardial infarction (Z test) or the percentage of coexisting previous infarctions ($\chi^2$ test). No statistically significant difference existed among the three groups concerning the values (shown in Table 2) of heart rate, intra-arterial systolic blood pressure, central venous pressure, and pulmonary wedge pressure before pumping. No statistically significant difference existed between groups B and C concerning the values (Table 2) of cardiac index and systemic resistance (flow was not measured in subjects of group A).

The mean age of subjects was $60.4 \pm 1.8$ years for the nondobutamine group, $62.3 \pm 1.9$ years for the high-dose dobutamine group, and $57.6 \pm 4.9$ years for the low-dose dobutamine group. No statistical difference existed among the three groups ($t = 0.98$, NS for groups A vs B, $t = 1.13$, NS for groups A vs C, and $t = 1.07$, NS for groups B vs C). Five of the 31 subjects of group A and 2 of the 17 subjects in group B were women. No statistical difference existed between the two groups in the proportion of women. All seven subjects in group C were men.

**DISCUSSION**

All subjects with cardiogenic shock due to acute myocardial infarction included in this study were treated with IABP but without thrombolysis or angioplasty or surgical intervention while under pumping. Some of them were in protracted cardiogenic shock, when first seen, for reasons mentioned in the Methods section.

Since cardiac output was not measured in patients of group A, the criteria of cardiogenic shock used in this study were based on changes in intra-arterial blood pressure, central venous pressure, capillary wedge pressure, and urine output, as well as clinical evidence of reduced flow to the brain and the periphery, as in previous reports.¹ ²

Patients with predominantly right ventricular failure due to acute infarction of the right ventricle were not included in this study since (1) care had been taken to reject patients with initial evidence of right ventricular infarction in the ECG, and (2) following optimal loading of the circulation by intravenous fluid infusion, pulmonary wedge pressure was above 17 mm Hg in all subjects of the three groups and in no case was this variable lower than the corresponding value of central venous pressure.

The existence of a pulmonary wedge pressure higher than the corresponding central venous pressure in this series of patients excluded tamponade.

The only reason for not administering dobutamine, prior to IABP, to the patients in group A was the fact that the drug was not yet available in our institution at the time of their hospital admission (years 1978 to 1983). Without exception, all subjects with postmyocardial infarction cardiogenic shock seen within this specific time period of 6 years were submitted to the same protocol of treatment, in which dobutamine infusion was not included. High-dose dobutamine infusion was administered prior to IABP to all subjects with postmyocardial infarction shock seen within another, well-defined time period of 5 years (1986 to 1990). Low dobutamine doses were given under the same conditions to all patients seen within a third, also well-defined time period of 3 years (1984, 1985, and 1991). The similarity of the three groups was shown a posteriori. Thus, patients in group B were not sicker than patients in groups A and C, since the following occurred: (1) the three groups did not differ in severity and duration of shock as shown in Table 2; (2) the subjects in group B were consecutive cases of cardiogenic shock treated during the time period 1986 to 1990, as already mentioned. It seems very unlikely that all serious cases occurred within this specific period of 5 years, given that the same staff made the decision for assisting the patients of all three groups with the intraaortic balloon pump. (3) The groups did not differ in regard to age, sex, location of the acute...
infarction, in the proportion that a previous infarction coexisted, or even in the duration of dobutamine infusion.

Under these circumstances, none of the 17 subjects in the high-dose dobutamine group could be weaned off the pump, while 4 of the 7 subjects in the low-dose and 10 of the 31 subjects in the nondobutamine groups survived and were able to leave the hospital.

Considering the total number of 55 subjects, as well as the 31 subjects of the nondobutamine group, survival depended on the duration of shock prior to IABP, as expected.2 The mean value of the above variable was 7.75 h for the 14 survivors out of the total number of 55 subjects and when taken separately, 7.55 h for the 10 survivors of the nondobutamine and 8.25 h for the 4 survivors of the low-dose dobutamine group. It is obvious from Figure 2 that although a wide range existed in the values of shock duration for the 17 subjects of the high-dose dobutamine group, none of these 17 subjects survived, although this variable was less than 7 h in 9 and less than 3 h in 5 of them.

The fact that not a single patient survived while a high dose of dobutamine preceded IABP, although there were survivors in the nondobutamine or the low-dose dobutamine groups, is the main finding of this study. Since there is no difference among the groups in other parameters affecting IABP success, the findings may be related to further evidence provided by this work: a “high-dose” dobutamine infusion may significantly reduce the urine output. This finding was not observed following “low-dose” dobutamine infusion. The same variable was lower before IABP in the “high-dose” dobutamine group compared with the nondobutamine group. The findings may be related to the vasoconstrictive effect of high-dose dobutamine.

Experimental evidence that dobutamine administration may result in a depression of the regional myocardial function if a stenotic coronary artery lesion exists,8 might also have played a role in reducing a patient's survival under high-dose dobutamine infusion.

In conclusion, protracted pre-IABP use of dobutamine in doses equal or higher than 10 µg·kg⁻¹·min⁻¹ may adversely affect the survival of patients with postmyocardial infarction cardiogenic shock.

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