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SHOCK

Use of Intraaortic Balloon Counterpulsation in Patients Presenting With Cardiogenic Shock: Observations From the GUSTO-I Study

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Objectives. **We sought to examine the use, complications and outcomes with early intraaortic balloon counterpulsation (IABP) in patients presenting with cardiogenic shock complicating acute myocardial infarction and treated with thrombolytic therapy.**

Background. **The use of IABP in patients with cardiogenic shock is widely accepted; however, there is a paucity of information on the use of this technique in patients with cardiogenic shock who are treated with thrombolytic therapy.**

Methods. **Patients who presented within 6 h of chest pain onset were randomized to one of four thrombolytic regimens. Cardiogenic shock was not an exclusion criterion, and data for these patients were prospectively collected. Patients presenting with shock were classified into early IABP (insertion within one calendar day of enrollment) or no IABP (insertion on or after day 2 or never).**

Results. **There were 68 (22%) IABP placements in 310 patients presenting with shock. Early IABP use occurred in 62 patients (20%) and none in 248 (80%). Most IABP use occurred in the United States (59 of 68 IABP placements) involving 32% of U.S. patients presenting with shock. Despite more adverse events in the early IABP group and more episodes of moderate bleeding, this cohort showed a trend toward lower 30-day and 1-year mortality rates.**

Conclusions. **IABP appears to be underutilized in patients presenting with cardiogenic shock, both within and outside the United States. Early IABP institution is associated with an increased risk of bleeding and adverse events but a trend toward lower 30-day and 1-year all-cause mortality.**

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Despite advances in the treatment of acute myocardial infarction (MI), the group of patients who present with or develop cardiogenic shock continues to do poorly. A recent analysis of cardiogenic shock from the Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries (GUSTO-I) trial (1) revealed a mortality rate of 55% for all patients in cardiogenic shock and its contribution to 58% of all deaths at 30 days. This finding represents a small but disappointing improvement in patient outcome since early thrombolytic trials (2–4). In fact, a recent longitudinal study of shock from 1975 to 1988 (5) has shown that in-hospital mortality rates did not improve and may even have worsened (73.7% in 1975, 81.7% in 1988). Analyses have shown (6,7) the main cause of early mortality in thrombolytic-treated patients to be left ventricular failure.

In an attempt to improve the outcome in cardiogenic shock, the use of intraaortic balloon counterpulsation (IABP) became more common in the 1970s (8). However, despite its use two randomized trials (9,10) in the prethrombolytic era of <50 patients failed to show a survival benefit or a reduction in infarct size. Recent animal data suggest a role for IABP in patients with cardiogenic shock treated with thrombolytic therapy. Studies in a canine model of acute MI (11) showed that the rate and degree of thrombolysis, after intracoronary tissue-type plasminogen activator administration, were markedly depressed in the presence of hypotension. The use of IABP in this model increased the rate and extent of thrombolysis (12). Additional work in a canine model (13) revealed that augmentation of diastolic blood pressure with IABP decreased the average time to reperfusion with intravenous thrombolytic therapy by 26 min. Observations in humans treated with IABP (14) suggested that the increase in proximal coronary blood flow velocity was 50% greater in patients who were hypotensive than in those who were not. Observational studies (15,16)

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Abbreviations and Acronyms

ACC/AHA	=	American College of Cardiology/American Heart Association
CK	=	creatine kinase
ECG	=	electrocardiogram, electrocardiographic
GUSTO	=	Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries (trial)
IABP	=	intraaortic balloon counterpulsation
MI	=	myocardial infarction
TAMI	=	Thrombolysis and Angioplasty in Myocardial Infarction (trial)
TIMI	=	Thrombolysis in Myocardial Infarction

suggest an improved outcome with IABP use in patients experiencing cardiogenic shock treated with thrombolytic therapy. However, there are no randomized trials of this treatment regimen at present.

The investigators of the international GUSTO-I trial collected data on 41,021 patients treated with thrombolytic therapy. Patients in cardiogenic shock were included, and the trial prospectively collected information on their diagnosis, adjunctive treatment and outcomes. The present report summarizes the experience with IABP in the GUSTO-I trial, defining its use, complications and effect on outcome in patients presenting with cardiogenic shock.

Methods

Patients. The GUSTO-I trial was a randomized, international trial comparing four thrombolytic regimens for treatment of acute MI (17). In brief, patients experiencing chest pain for ≥20 min but <6 h accompanied by >0.1-m V ST segment elevation in two or more limb leads or >0.2-m V ST segment elevation in two or more contiguous precordial leads were eligible for enrollment. Patients were excluded from the trial for previous stroke, active bleeding, previous treatment with streptokinase or anistreplase, recent trauma or major operation, previous trial participation or noncompressible punctures. Patients with cardiogenic shock were not excluded.

Thrombolytic regimens. Participants were randomized to one of four thrombolytic regimens: 1) streptokinase (1.5 million U over 1 h) with 12,500 U of subcutaneous heparin twice daily beginning 4 h after streptokinase; 2) streptokinase (1.5 million U over 1 h) with intravenous heparin adjusted to maintain the activated prothrombin time between 60 and 85 s; 3) accelerated alteplase (15-mg bolus, 0.75 mg/kg body weight over 30 min [≤50 mg] and 0.5 mg/kg over 1 h [≤35 mg]) with the same intravenous heparin regimen; or 4) alteplase (1.0 mg/kg over 1 h, not to exceed 90 mg, with 10% given as a bolus) combined with streptokinase (1.0 million U over 1 h) and intravenous heparin.

Adjunctive therapy. Chewable aspirin (≥160 mg) was given as soon as feasible and continued daily at 160 to 325 mg. Intravenous atenolol was given in two 5-mg doses and followed by 50 to 100 mg of oral therapy daily if no contraindications to beta-adrenergic blocking agents were present. All other medications, including nitrates, antiarrhythmic drugs, calcium-channel blocking agents, angiotensin-converting-enzyme inhibitors and digitalis, were prescribed at the discretion of the attending physician. The use of coronary angiography, coronary angioplasty and coronary artery bypass graft surgery were also at the discretion of the attending physician.

End points. The primary end point of the trial was all-cause mortality at 30 days. Other prospectively defined composite end points were death and nonfatal stroke; death and nonfatal hemorrhagic stroke; or death and nonfatal, disabling stroke. Bleeding was categorized as severe or life threatening, moderate or minor.

Data collection. All primary data were collected on a three-page case report form. Additional data on cardiogenic shock were recorded on a two-page supplemental form.

Definitions. *Cardiogenic shock.* was defined as systolic blood pressure <90 mm Hg for ≥1 h, unresponsive to fluid administration alone, thought to be secondary to cardiac dysfunction and associated with signs of hypoperfusion or a cardiac index ≤2.2 liters/min per m^2. Patients in whom systolic blood pressure increased to >90 mm Hg within 1 h after positive inotropic drugs were given were still classified as having cardiogenic shock (1). *Reinfarction* as assessed by the treating physician was defined on the basis of the presence of two or more of the following: 1) recurrent ischemic symptoms lasting >15 min; occurrence of new ST-T wave changes or new Q waves; 2) a second elevation in cardiac enzymes to more than the normal upper limit or by an additional 20% if index levels had not resolved; or 3) angiographic reocclusion of a documented patent infarct-related artery. *Recurrent ischemia* was defined as symptoms (chest discomfort, arm pain, jaw pain, nausea), ECG changes or new hypotension, pulmonary edema or murmur thought by the physician to represent myocardial ischemia. *Stroke* was defined as an acute new neurologic deficit resulting in death or lasting >24 h and classified by a physician as a stroke.

Bleeding was classified as "none/mild" if it did not require transfusion or cause hemodynamic instability; "moderate" if it required the transfusion of blood but did not lead to hemodynamic instability; and "severe" if it involved intracranial hemorrhage or caused hemodynamic compromise leading to intervention.

Only patients who presented with cardiogenic shock were included in the analysis and from those who were noted on the case report form to have met the definition of cardiogenic shock and who presented with a Killip IV classification. Patients who presented with cardiogenic shock and received IABP therapy within one calendar day of admission (day 0 or 1) were classified in the *early IABP group*. Patients who presented with cardiogenic shock and received IABP therapy after day 1 or not at all were classified in the *no-IABP group*. This classification was chosen with the assumption that any benefit of IABP therapy would occur if it was begun soon after admission. The time of IABP insertion was not available; therefore, we could not obtain a more precise estimate of time

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Table 1. Baseline Clinical Characteristics

	Early IABP (n = 62)	No IABP (n = 248)	p Value
Age (yr)	64 (55, 70)	68 (59, 75)	0.008
Men	68	62	0.39
Hypertension	37	40	0.64
Diabetes	23	23	0.98
Current smoker	49	34	0.03
Previous MI	30	27	0.68
Previous CABG	7	4	0.41
Infarct location			0.06
Anterior	64.5	50.8	
Inferior	35.4	44.7	
Other	0	4.5	
SBP (mm Hg)	90 (78, 104)	90 (75, 113)	0.59
DBP (mm Hg)	60 (51, 71)	60 (50, 72)	0.88
HR (beats/min)	87 (66, 108)	91 (60, 110)	0.89
Peak CK (IU)	4,000 (1,416, 7,575)	1,207 (204, 2,694)	0.0001
Peak CK-MB (IU)	341 (78, 701)	162 (24, 293)	0.07
Time to therapy (h)	2.6 (2.2, 3.4)	2.7 (1.9, 3.0)	0.85
Treatment received			0.97
Alteplase, IV heparin	25.8	25.4	
SK, SC heparin	21.0	23.8	
SK, IV heparin	25.8	24.6	
Combination therapy*	27.4	26.2	

*Streptokinase (SK) and alteplase with intravenous (IV) heparin. Data presented are percent of patients or median (25th, 75th percentiles). CABG = coronary artery bypass graft surgery; CK = creatine kinase; DBP = diastolic blood pressure; HR = heart rate; IABP = intraaortic balloon counterpulsation; MI = myocardial infarction; SBP = systolic blood pressure; SC = subcutaneous.

to device placement. The decision to use IABP was made by the treating physician.

Statistical analysis. Continuous data are summarized as median (25th, 75th percentiles) and were compared with the Wilcoxon rank-sum test. Categoric variables are shown as percentages and were compared with the chi-square test. All significance tests were two-tailed. The 30-day mortality rates were compared between the two IABP groups before and after adjustment for the known baseline clinical variable predictive of mortality in the GUSTO-I population (18). Unadjusted mortality during the 30-day and 1-year follow-up periods was also described by Kaplan-Meier curves. A Cox proportional hazards model was used to compare unadjusted mortality.

Results

Cardiogenic shock was found in 315 patients (0.8%) on presentation in the GUSTO-I trial. Of these 315 patients, IABP status was missing in 5 (1.6%). The remaining 310 patients make up the present analysis. IABP was used early in 62 patients (20%) and later or not at all in 248 (80%) (the no-IABP group). In the no-IABP group, 6 patients (2%) underwent IABP insertion at a median of 5 (2,8) days after enrollment.

Baseline characteristics. Patients in the early group were on average 4 years younger, and more of them were current smokers (Table 1). Patients who had early IABP also showed a trend toward more anterior MI. Patients in the early group had significantly higher creatine kinase (CK) levels and a trend toward higher CK-MB fractions. There were no differences in the time to administration of thrombolytic therapy or in the proportion of patients randomized to each thrombolytic regimen.

Table 2. Baseline Coronary Angiographic Characteristics

	Early IABP (n = 41)*	No IABP (n = 51)*	p Value
TIMI flow grade			0.06
0	42	34	
1	24	8	
2	10	17	
3	24	41	
CAD			0.29
0 VD	7	5	
1 VD	22	41	
2 VD	39	28	
3 VD	32	26	
LVEF (%)	40 (29, 50)	49 (33, 59)	0.13

*Number of patients who underwent coronary angiography and had Thrombolysis in Myocardial Infarction (TIMI) flow grade, coronary artery disease (CAD) and left ventricular ejection fraction (LVEF) data available. Data presented are percent of patients or median (25th, 75th percentiles). IABP = intraaortic balloon counterpulsation; VD = vessel disease.

Among the 310 patients in the entire cohort, 112 underwent coronary angiography (Table 2). Of these 112 patients, 41 in the early IABP group and 51 in the no-IABP group had data available on Thrombolysis in Myocardial Infarction (TIMI) grade flow and number of diseased vessels. Although the number of patients with two- and three-vessel disease did not differ between groups, those in the early IABP group tended to have worse angiographic flow according to TIMI grade. There was no difference between groups in degree of left ventricular dysfunction.

Use of adjunctive therapies. Patients in the early-IABP group were treated significantly more often with inotropic agents (Table 3). They also had a greater use of hemodynamic monitoring, intubation and pacemaker support. The median time to catheterization in the entire cohort of 112 patients was

Table 3. Use of Medications and Procedures

	Early IABP (n = 62)	No IABP (n = 248)	p Value
Inotropic drugs	95	81	0.007
Lidocaine use	16	18	0.70
Pacemaker	48	19	0.0001
Swan-Ganz catheter	83	30	0.0001
Ventilator	81	50	0.0001
Cardioversion/defibrillation	50	33	0.01
Coronary angiography	84	28	0.0001
PTCA	42	9	0.0001
CABG	20	4	0.0001

Data presented are percent of patients. PTCA = percutaneous transluminal coronary angioplasty; other abbreviations as in Table 1.

Table 4. Bleeding Outcomes

	Early IABP (n = 62)	No IABP (n = 248)	p Value
Bleeding			
Moderate	47	12	0.0001
Severe or life-threatening	10	5	0.16
Packed red cell transfusion (U)			
≥1	66	13	0.0001
≥1 (excluding CABG-related transfusions)	60	10	<0.0001
Units transfused	3.9 ± 4.7	0.5 ± 1.5	0.0001

Data presented are percent of patients or mean value ± SD. Abbreviations as in Table 1.

9 h (4, 117). In the 51 patients undergoing angiography in the early IABP group, the median time to catheterization was 5.5 h (3.3, 28). Coronary angioplasty and bypass surgery were used more often in the early IABP group.

Bleeding outcomes. As expected, the early IABP cohort, containing the majority of counterpulsation devices inserted, had significantly more moderate bleeding (Table 4). The early group required a greater number of packed red blood cell transfusions, even if patients who underwent coronary bypass were excluded. Patients in the early group undergoing transfusion received a mean of 4 U of packed red cells each; the no-IABP group received ~1 U each.

Clinical outcomes. There was a trend toward lower 30-day mortality in the early IABP group; however, this became nonsignificant after adjustment for baseline clinical predictors of mortality (chi-square 2.54, p = 0.11) (Table 5). The unadjusted 1-year mortality rate was also significantly lower in those who received IABP early (Fig. 1). The median time to death was 67 h (2.8 days) in the early IABP group and 7.2 h in the no-IABP group (p = 0.0002). More than 50% of the overall 30-day mortality in the no-IABP group occurred in the first 8 h after enrollment (56.8%), whereas only 23.3% of the early group died during the same period (Fig. 2). Patients in the early-IABP group had significantly more recurrent ischemia and reinfarction. The incidence of stroke did not differ between groups.

Because of the greater proportion of patients undergoing angiography and revascularization in the early IABP group (Table 3), we analyzed 30-day mortality among these patients (Table 6). The 30-day mortality rate among patients who underwent either angioplasty or bypass did not differ between the early and no-IABP groups. After excluding patients who underwent revascularization in each group, a trend remained toward lower 30-day mortality in the early IABP group (47% vs. 64%, p = 0.07).

International use of IABP. The use of IABP was far more common in the United States. Of the 185 patients who presented with cardiogenic shock in the United States, only 59 (32%) received an IABP, 47 (80%) of which were placed on the day of admission. Non-U.S. countries accounted for 125 patients who presented with shock, 9 (7.2%) of whom had an IABP inserted, all on the day of admission. The six late insertions of IABP in the no-IABP group were all in the United States. In the United States, the majority of IABP insertions occurred on the same day as catheterization or angioplasty (Table 7). All procedures performed in non-U.S. patients occurred on the day of IABP insertion, which was also the day of study enrollment.

Data on hospital size were available for 189 of the 310 patients in the study group. Using the number of inpatient beds as a surrogate measure of hospital size (<300, 300 to 600, >600 beds), 34%, 43% and 23% of patients in the early IABP group and 38%, 52% and 11% of patients in the no-IABP cohort were enrolled, respectively, in these groups. Although not statistically significant (p = 0.12), this suggests that IABP use may have been greater in larger or tertiary medical centers in the present study.

Discussion

The use of IABP has been recommended for patients with cardiogenic shock. Indeed, the 1990 American College of Cardiology/American Heart Association (ACC/AHA) task force report on the management of acute MI (19) suggests that cardiogenic shock is a class I indication for IABP. These recommendations are based on data suggesting that IABP use reduces myocardial oxygen demand (20) and increases coronary blood flow velocity (21). However, the clinical information available was observational and not supported by randomized data (22,23).

According to the ACC/AHA guidelines, therefore, IABP was underused in patients presenting with cardiogenic shock in the multicenter, randomized GUSTO-I trial of thrombolytic therapy for acute MI. A minority of patients received this therapy, with the majority of these at the time of admission. Overall, 86% of all patients who presented with shock and were treated with this modality were enrolled in the United States. There were 1,487 patients who at some point during their hospital stay had IABP (1,354 [91%] within and 133 [9%] outside the United States) (24), which represents only 5.9% of all U.S. and 1% of all non-U.S. patients enrolled in the trial.

Table 5. Clinical Outcomes

	Early IABP (n = 62)	No IABP (n = 248)	p Value
Mortality			
In-hospital	48	59	0.12
30 day	47	60	0.06*
1 yr	57	67	0.04
Stroke			
Hemorrhagic	0	0.4	0.62
Nonhemorrhagic	1.6	1.6	1.0
Recurrent ischemia	20	9	0.02
Reinfarction	5	0.8	0.03

*Adjusted p = 0.11. Data presented are percent of patients. IABP = intraaortic balloon counterpulsation.

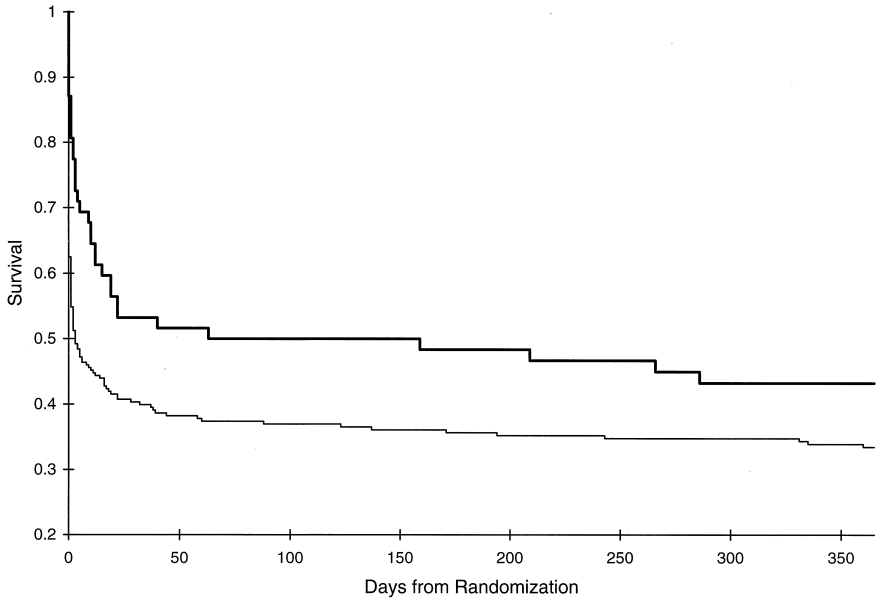

Figure 1. One-year Kaplan-Meier survival curves for the early IABP (**bold line**) and no-IABP groups (**light line**). The 1-year mortality rate was 57% in the early IABP group versus 67% in the no-IABP group ($p = 0.04$).

The hospital size data suggest a trend toward greater IABP use in larger medical centers. The distributions of patients in the two smaller size categories between the early and no-IABP groups were similar. The data from the largest hospital size suggest that patients in the early IABP group may have been more likely to be treated in larger medical centers. The potential relation between hospital size and IABP use may therefore be one factor affecting utilization of this therapy.

IABP use in GUSTO-I. To our knowledge, the present analysis represents the largest report to date of patients with acute MI complicated by shock who were treated with the combination of thrombolytic therapy and IABP. In the unadjusted comparison of the early and no-IABP groups, a trend toward lower 30-day mortality with the early use of this therapy was found. When adjusted for clinical variables known to predict mortality in the GUSTO-I population (18), the association (even though less significant) persisted and was still evident at 1 year.

Inspection of the Kaplan-Meier survival curves (Fig. 1 and 2) reveals an early high mortality rate in both groups. In fact, >50% of the overall 30-day mortality in patients presenting with shock occurred within the first 8 h. This group represents patients who were critically ill at presentation and in whom earlier initiation of counterpulsation did not affect survival. The survival curves then diverge, with the no-IABP group continuing to exhibit higher early mortality. This finding raises the possibility that earlier use of IABP could have improved survival.

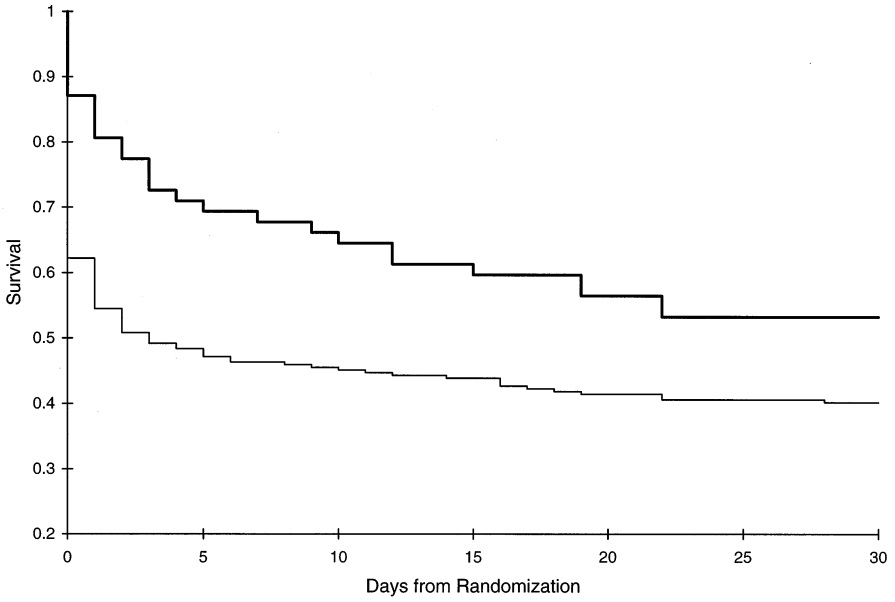

Figure 2. Thirty-day Kaplan-Meier survival curves for the early IABP (**bold line**) and no-IABP groups (**light line**).

Table 6. Thirty-Day Mortality After Revascularization

	Early IABP (n = 62)	No IABP (n = 248)
Revascularization category		
PTCA	n = 21	n = 16
	13 (62)	7 (44)
CABG	n = 12	n = 11
	3 (25)	2 (18)
None	n = 30	n = 218
	14 (47)	139 (64)
Time to angiography (d)		
U.S.	6 (3, 28)	—
Outside U.S.	4.5 (3, 11)	—
Time to angioplasty (d)		
U.S.	3.5 (3, 4.5)	—
Outside U.S.	4.5 (3,78)	—

Data presented are the number (%) of patients or median (25th, 75th percentiles). d = days; U.S. = United States; other abbreviations as in Tables 1 and 3.

Patients in the early IABP cohort had a higher rate of recurrent ischemia, reinfarction and complications, such as ventricular tachycardia and acute mitral regurgitation. They also exhibited a greater use of adjunctive therapies and procedures. A likely explanation for these differences is that the patients in the early IABP group were able to live longer, had more adverse events and underwent more procedures. Hence, once the early mortality of the no-IABP group had occurred, the survivors in this cohort represented a less critically ill population, with a lower rate of adverse events than patients who survived in the early IABP group. An alternative possibility is that clinicians selected patients in the early IABP group as more in need of an intervention. However, despite this possibility, the trend in mortality favored those who had IABP initiated early, and this trend was maintained at 1 year.

Studies of IABP have been confounded by a high rate of concomitant revascularization procedures (15,16). This limits our ability to identify the sole contribution of IABP in these patients. In the present study, we found a higher use of angiography, angioplasty and bypass surgery in the early IABP group, suggesting that revascularization may have been the reason for the improved mortality. However, when the 30-day mortality of patients with revascularization in each group was compared, there were no significant differences. More important, although patient numbers were small, a trend toward a lower 30-day mortality rate remained among patients in the early IABP group after exclusion of patients who underwent revascularization. In addition, the median times to angiography or angioplasty both in and outside the United States—3.5 to 6 days after the placement of most IABP devices—were sufficiently long to suggest that IABP use was not just supportive.

Table 7. Procedures Performed With Intraaortic Balloon Counterpulsation

	U.S. (n = 59)	Outside U.S. (n = 9)
Cardiac catheterization	51 (86)	6 (67)
IABP inserted*	35	6
PTCA	18 (30)	3 (33)
IABP inserted*	15	3
CABG	13 (22)	3 (33)
IABP inserted*	7	3

*Patients in the group with intraaortic balloon counterpulsation (IABP) on the same day as the procedure. Data presented are number (%) of patients unless otherwise indicated.

Previous studies. Our finding of a trend toward lower short- and long-term mortality in patients who presented with cardiogenic shock and were treated early with IABP is consistent with previous studies. The use of IABP in patients with cardiogenic shock became very popular in the 1970s. There was considerable experimental evidence suggesting physiologic benefits from its use (8,20,21). Despite this optimism, the two randomized trials of this technique (9,10), before the use of thrombolytic therapy, failed to show a benefit. Data for the use of IABP in the thrombolytic era are accumulating and appear more promising. On the basis of canine experiments (12,13), in which the use of IABP augmented the degree and rate of reperfusion with thrombolytic therapy, the poor results seen after thrombolytic therapy alone in patients with cardiogenic shock might be improved with the use of IABP.

Recent observational studies in humans have also shown promise. Waksman et al. (15) reported improved in-hospital survival in a group of 24 patients with cardiogenic shock treated with IABP compared with 21 similar patients not given IABP (46% vs. 19%, $p < 0.001$). Although there was a high rate of revascularization in the former group, they had survival rates similar to historical control subjects (n = 35) who did not undergo revascularization (46% vs. 45%). Stomel et al. (16) showed that thrombolytic-treated patients who also received IABP therapy had a significant in-hospital survival advantage over those treated with thrombolysis alone (68% vs. 23%, $p = 0.005$); however, the number of patients was small (n = 64). In the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock?) registry (25), survival of patients treated with IABP was 43% compared with 28% without IABP (n = 173, $p = 0.039$). However, when adjusted for age and rate of catheterization, there was no significant association. Bengtson et al. (26) reported on 200 consecutive patients admitted to the Duke cardiac care unit. Patients who received an IABP had an in-hospital mortality of 48% versus 57% in those who did not ($p = 0.23$) (26). Patients in this group who were treated with IABP and percutaneous revascularization had an in-hospital mortality rate of 38% compared with 63% in those treated with IABP alone ($p = 0.01$) (26). The interpretation of these results and others (27) is made difficult by their retrospective nature and the concomitant use of revascularization. This lack of consensus on the use of IABP and the absence of randomized trials may partly explain its infrequent use in the GUSTO-I trial.

Bleeding outcomes. In previous studies, IABP use after thrombolytic therapy was shown to be an independent risk

factor for bleeding complications. In a review of hemorrhagic complications in the first Thrombolysis and Angioplasty in Myocardial Infarction (TAMI-1) study (28), IABP was shown by linear regression to be associated with an increased bleeding risk, even after patients who underwent operation were removed from the analysis. In a later review of several of the TAMI studies, IABP use also was shown (29) to impart a 4.5-fold increased risk of losing a femoral pulse or of needing vascular repair. In an analysis of the TIMI-II trial (30), 41% of the major and minor hemorrhagic events in the conservative treatment arm were associated with vascular instrumentation. The importance of certain clinical and procedural characteristics of GUSTO-I patients in predicting bleeding events has been shown (31). This study revealed that even after adjustment for baseline characteristics, the use of an IABP was significantly related to an increased risk of bleeding. The type and incidence of vascular trauma associated with IABP use were not collected in the GUSTO-I trial; however, that these events occurred should be expected on the basis of the above data.

There was no difference in the incidence of severe or life-threatening bleeding between patients treated with IABP at any time and those who were not. However, there was a significantly higher incidence of moderate bleeding among the early IABP group compared with the no-IABP group. This difference persisted even after those patients who ultimately underwent bypass surgery were removed from the analysis. The use of IABP to maintain infarct-related artery patency has been shown (32) to carry a very low rate of vascular or hemorrhagic complication when used in a group of patients without shock who had a lower rate of thrombolytic therapy use. However, the present analysis confirms that in patients with shock treated with thrombolysis, the use of IABP is associated with an increased risk of moderate bleeding and demands a cautious approach. This increased risk of hemorrhagic complications may also contribute to the infrequent use of this therapy.

Study limitations. There are several limitations to this study, including the small number of patients in the group who presented with cardiogenic shock. A larger population of patients would more easily allow detection of any true difference in mortality if it exists. This was also a retrospective analysis; however, the data were collected in a prospective fashion and known biases were adjusted for in the mortality analysis.

These data apply only to patients who are treated with thrombolytic therapy. Of the patients with MI who reach the hospital alive, typically only 40% are ultimately eligible to receive thrombolytic therapy (33). Therefore, these data may not apply to a large proportion of the patients in shock. The data from the prethrombolytic days of treating acute MI do not provide definitive answers as to the usefulness of IABP in cardiogenic shock. It remains for a large randomized trial of patients with MI complicated by shock to sort out these potential benefits.

A potentially significant source of bias in this analysis may arise from the fact that many patients in the no-IABP group died within the first hours of enrollment. This early mortality may have rendered these patients ineligible for IABP therapy. Additionally, the higher use of tertiary care (inotropic drugs, hemodynamic monitoring, pacemakers and ventilatory assistance) among patients in the early IABP group may have contributed to their reduced mortality. Adjusting for these potential biases is very difficult with the available statistical techniques, and removal of these patients from the above analysis would significantly decrease the number of patients in the study.

Conclusions. IABP is used infrequently in patients who present with cardiogenic shock complicating an acute MI. The majority (86%) of IABP use in patients with shock in the GUSTO-I trial occurred in the United States. The infrequent use of IABP therapy is most likely the result of several factors, including the lack of definitive data on its use and higher bleeding and vascular injury rates.

Patients who received IABP therapy within 1 day of study enrollment had a higher rate of adverse events and use of procedures than those receiving it later or not at all, but this observation is most likely due to the higher early mortality in the latter group. Despite the increased number of adverse events in the early IABP group patients, there was a trend toward lower 30-day and 1-year mortality rates in this group. As expected, there were more moderate bleeding events in the patients receiving early IABP, but there was no difference in the incidence of severe or life-threatening bleeds. These data support a continued role for the use of IABP in patients who present with cardiogenic shock. They further point to the need for a well executed, randomized trial of this mode of therapy.

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