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Elective Intra-aortic Balloon Counterpulsation During High-Risk Percutaneous Coronary Intervention

A Randomized Controlled Trial

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PERCUTANEOUS CORONARY INTERVENTION (PCI) in patients with impaired left ventricular function can be associated with significant mortality and morbidity, particularly when a substantial proportion of viable myocardium is subtended by diseased coronary arteries.^{1,2} Such patients have diminished reserve to withstand the consequences of ischemia or arrhythmias that may occur during PCI and are at risk of entering a spiral of hemodynamic compromise, potentially culminating in cardiogenic shock or death. In these circumstances, vital hemodynamic support can be provided by an intra-aortic balloon pump (IABP), which simultaneously augments coronary blood flow and decreases myocardial oxygen demand.^{3,4}

Increased understanding of the physiological benefits of counterpulsation and evidence of its efficacy in cardiogenic shock⁵ have led to an expansion in the indications for IABP use. The Benchmark Registry showed that the most

Context Observational studies have previously reported that elective intra-aortic balloon pump (IABP) insertion may improve outcomes following high-risk percutaneous coronary intervention (PCI). To date, this assertion has not been tested in a randomized trial.

Objective To determine whether routine intra-aortic balloon counterpulsation before PCI reduces major adverse cardiac and cardiovascular events (MACCE) in patients with severe left ventricular dysfunction and extensive coronary disease.

Design, Setting, and Patients The Balloon Pump–Assisted Coronary Intervention Study, a prospective, open, multicenter, randomized controlled trial conducted in 17 tertiary referral cardiac centers in the United Kingdom between December 2005 and January 2009. Patients (n=301) had severe left ventricular dysfunction (ejection fraction $\leq 30\%$) and extensive coronary disease (Jeopardy Score $\geq 8/12$); those with contraindications to or class I indications for IABP therapy were excluded.

Intervention Elective insertion of IABP before PCI.

Main Outcome Measures Primary end point was MACCE, defined as death, acute myocardial infarction, cerebrovascular event, or further revascularization at hospital discharge (capped at 28 days). Secondary end points included all-cause mortality at 6 months, major procedural complications, bleeding, and access-site complications.

Results MACCE at hospital discharge occurred in 15.2% (23/151) of the elective IABP and 16.0% (24/150) of the no planned IABP groups ($P=.85$; odds ratio [OR], 0.94 [95% confidence interval [CI], 0.51-1.76]). All-cause mortality at 6 months was 4.6% and 7.4% in the respective groups ($P=.32$; OR, 0.61 [95% CI, 0.24-1.62]). Fewer major procedural complications occurred with elective IABP insertion compared with no planned IABP use (1.3% vs 10.7%, $P<.001$; OR, 0.11 [95% CI, 0.01-0.49]). Major or minor bleeding occurred in 19.2% and 11.3% ($P=.06$; OR, 1.86 [95% CI, 0.93-3.79]) and access-site complications in 3.3% and 0% ($P=.06$) of the elective and no planned IABP groups, respectively.

Conclusions Elective IABP insertion did not reduce the incidence of MACCE following PCI. These results do not support a strategy of routine IABP placement before PCI in all patients with severe left ventricular dysfunction and extensive coronary disease.

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common reason for IABP insertion is to electively support patients who are hemodynamically stable at the outset but perceived to be at high risk of major complications during angiography or PCI.⁶

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Several observational studies have reported fewer intra-procedural complications and reduced major adverse cardiovascular events with prophylactic IABP insertion compared with a provisional counterpulsation strategy during high-risk PCI.⁷⁻⁹ However, these series have been retrospective, subject to selection bias, and relatively underpowered to adequately address this assertion. As such, the current international guidelines for PCI do not offer formal recommendations for elective IABP use but suggest that “IABP support should be reserved only for patients at the extreme end of the spectrum of hemodynamic compromise.”¹⁰ The Balloon Pump–Assisted Coronary Intervention Study (BCIS-1) is, to our knowledge, the first randomized controlled trial to assess the efficacy and safety of elective IABP use in patients undergoing high-risk PCI.

METHODS

The methods used in this trial have been described previously.¹¹ In brief, BCIS-1 was a prospective, open, multicenter, randomized controlled trial conducted to evaluate the efficacy of elective IABP therapy for reducing major adverse cardiac and cardiovascular events (MACCE) during high-risk PCI. The trial was approved by the UK National Health Service research ethics committee, and each patient provided written consent for inclusion in the trial. Data management and analysis was carried out by an independent data coordinating center, with oversight from a steering committee. An independent data and safety monitoring committee oversaw the safety and efficacy of the trial. The members of the steering committee had full access to the data after unblinding and vouch for the accuracy and completeness of the data and the analyses.

Study Population

Patients scheduled to undergo high-risk single-vessel or multivessel percutaneous intervention to native coronary arteries or bypass grafts were considered for inclusion in the trial. High-risk was defined as the presence

of impaired left ventricular function (ejection fraction $\leq 30\%$ on echocardiography or left ventricular angiography) and a large amount of myocardium subtended by stenosed vessels, characterized by a BCIS-1 Jeopardy Score of 8 or greater or a left main coronary artery stenosis or by a target vessel that provides collateral supply to an occluded second vessel that in turn supplies more than 40% of myocardium. The BCIS-1 Jeopardy Score (range, 0-12) has been described previously¹¹ but in brief is a modification of the Duke Jeopardy Score,¹² which allows broader classification of coronary anatomy, including left main coronary artery stenoses and bypass grafts. Diseased proximal native coronary segments are assigned a score of 2 points, with 2 additional points assigned for each major myocardial territory subtended by these segments, accounting for dominance. The protective effect of functioning bypass grafts is represented by negative scores.

The principal exclusion criteria were current class I or II indications for IABP use, including cardiogenic shock, acute myocardial infarction within the previous 48 hours, complications of acute myocardial infarction (including ventricular septal defect, severe mitral regurgitation, and intractable ventricular arrhythmias); and contraindications to IABP use, including significant iliac or femoral arterial disease and more than mild aortic regurgitation on echocardiography. Additional exclusion criteria were planned staged procedure within 28 days; bleeding diathesis or warfarin therapy with an international normalized ratio greater than 2.5; active internal bleeding (except menstruation); allergy to aspirin, clopidogrel, heparin, or glycoprotein IIb/IIIa inhibitors; thrombocytopenia (platelet count $< 100 \times 10^3/\mu\text{L}$); pregnancy; and previous enrollment in BCIS-1 or current enrollment in any other study.

Race/ethnicity was self-reported as part of standard hospital admission procedure and categorized as white, South Asian, or other.

Treatment

Eligible patients were randomized to receive elective IABP insertion prior to PCI or to have no planned IABP insertion. Randomization was carried out via a 24-hour automated interactive telephone response system, and treatment assignment was based on random permuted blocks, stratified by center, with 1:1 allocation to each group. It was recommended that PCI be performed within 24 hours of randomization, and clinical events were attributed to the assigned treatment on an intention-to-treat basis.

In the elective IABP group, the balloon catheter was inserted at the start of the procedure, before coronary intervention. Sheathless insertion was recommended in the trial. The IABP remained in situ for at least 4 but no more than 24 hours following PCI, unless otherwise indicated by the patient's clinical status. Rescue IABP insertion was permitted in the no planned IABP group in the event of procedural complications such as prolonged hypotension, pulmonary edema, or refractory ventricular tachycardia/fibrillation, at the discretion of the operator.

Patients were pretreated with aspirin and clopidogrel and received intravenous unfractionated heparin during the procedure to maintain the activated coagulation time between 200 and 250 seconds. The use of abciximab was recommended, administered as a 0.25-mg/kg bolus followed by intravenous infusion at 0.125 $\mu\text{g}/\text{kg}$ per minute for 12 hours. The choice of drug-eluting or bare-metal stents and use of adjunctive devices was at the operators' discretion.

Patients who had IABP insertion in either group received an intravenous heparin infusion following PCI to maintain an activated partial thromboplastin time ratio between 1.5 and 2.5; the infusion was commenced immediately after PCI or on completion of the abciximab infusion, if the latter was used. When it was felt appropriate to remove the IABP, the heparin infusion was discontinued and the balloon catheter removed when the activated coagulation time decreased to less than 160 seconds.

Outcome Measures

The primary end point was the composite of MACCE, defined as death, acute myocardial infarction, cerebrovascular event, or further revascularization by PCI or coronary artery bypass graft (CABG) surgery at hospital discharge (capped at 28 days). The secondary end points were 6-month all-cause mortality, major procedural complications (including prolonged hypotension, ventricular tachycardia/fibrillation requiring defibrillation, or cardiorespiratory arrest requiring assisted ventilation), bleeding complications, access-site complications, transient ischemic attack, and duration of hospital stay. All end points and adverse events were predefined¹¹ and adjudicated by a clinical events committee blinded to treatment assignment.

Prespecified definitions of myocardial infarction were used in the trial, based on the timing of the event in relation to the index PCI procedure and cardiac biomarker levels at baseline. Within 72 hours of PCI, myocardial infarction was defined as an increase in creatine kinase MB levels by more than 3-fold the upper limit of the reference range (if normal at baseline) or by more than 1.5-fold the baseline value (if elevated at baseline). Beyond 72 hours after PCI, universal definitions of myocardial infarction applied, based on elevation of cardiac troponin levels in association with typical symptoms or electrocardiographic changes.¹³

Prolonged hypotension was defined as a mean arterial pressure less than 75 mm Hg for at least 10 minutes despite fluid resuscitation or requirement of inotropic support to maintain the mean arterial blood pressure above 75 mm Hg in the elective IABP group. In the no planned IABP group, prolonged hypotension was defined as above, with the additional criterion of the need for IABP insertion to maintain the mean arterial blood pressure above 75 mm Hg.

Major bleeding was defined as a decrease in hemoglobin concentration by

at least 4 g/dL in relation to the baseline value, with 1 unit of whole blood or packed cells considered equivalent to an additional 1-g/dL decrease in hemoglobin concentration if transfusion was required. Minor bleeding was defined as a decrease in hemoglobin concentration by 2 g/dL to 4 g/dL compared with baseline. Access-site complications were defined as a vascular complication at any access site resulting in hematoma or leg ischemia requiring surgical or percutaneous intervention, false aneurysm (on ultrasound imaging), or femoral artery occlusion.

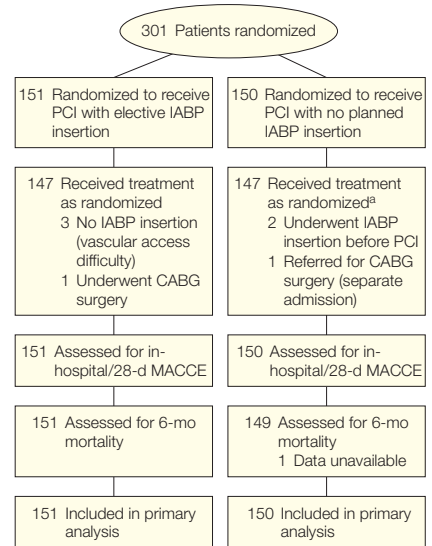
Statistical Analysis

The power calculation was based on a predicted MACCE rate of 15% in the no planned IABP group.⁸ A sample size of 300 would provide 80% power to detect a 10% absolute difference in MACCE rates between the elective and no planned IABP groups at a significance level of 5%, allowing 10% contingency for missing data. An independent statistician performed all statistical analyses. Primary and secondary end points were analyzed on an intention-to-treat basis. All tests of significance are 2-sided.

The proportions of in-hospital MACCE were compared and odds ratios (ORs) and 95% confidence intervals (CIs) calculated from logistic regression. The proportions of all-cause mortality at 6 months were compared using the χ^2 test, and cumulative event rates were estimated by the Kaplan-Meier method. Other categorical outcome measures were compared using a χ^2 test or Fisher exact test as required. Continuous variables were compared using a 2-sided unpaired *t* test. Continuous data that were not normally distributed were compared using the Wilcoxon rank-sum test.

Prespecified subgroup analyses (stratified by median glomerular filtration rate, diabetic status, glycoprotein IIb/IIIa or bivalirudin use, and BCIS-1 Jeopardy Score) were performed, with ORs and 95% CIs calculated by logistic regression, together with formal tests for interaction.

Figure 1. Study Flow



CABG indicates coronary artery bypass graft; IABP, intra-aortic balloon pump; MACCE, major adverse cardiac and cardiovascular events; PCI, percutaneous coronary intervention.

^aOf the 147 patients who received no planned IABP insertion prior to PCI, 18 required rescue IABP insertion.

Statistical analyses were performed using Stata version 10.1 (StataCorp, College Station, Texas).

RESULTS

Baseline and Procedural Characteristics

Three hundred one patients with multivessel coronary disease and impaired left ventricular function were enrolled at 17 interventional cardiology centers in the United Kingdom between December 2005 and January 2009; 69% of patients were enrolled at 5 centers at a mean rate of 15 patients per year. One hundred fifty-one patients were randomized to receive elective IABP support and 150 to have no planned IABP insertion during PCI. One patient in the elective IABP group did not have PCI but had CABG surgery instead (on the same admission), and 1 patient in the no planned IABP group did not have PCI but was referred for CABG surgery on a separate admission (FIGURE 1). All patients underwent follow-up until hospital discharge (capped at 28 days), and

6-month mortality data were available for the entire cohort. Cardiac markers were available for 97% of patients.

The groups were well balanced in terms of baseline characteristics (TABLE 1). Left ventricular ejection frac-

tion was 23.6% (SD, 5.2%) in the elective IABP group and 23.6% (SD, 5.5%) in the no planned IABP group. Mean BCIS-1 Jeopardy Scores in the respective groups were 10.4 (SD, 1.7) and 10.3 (SD, 1.7), with the maximum score of

12 found in 47% and 45% of patients in the respective groups. Twenty-seven percent of the elective IABP group and 29% of the no planned IABP group had a significant left main coronary artery lesion. Sixty-six percent and 72%, respectively, had New York Heart Association class III or IV dyspnea, while 48% and 45% had Canadian Cardiovascular Society class III or IV angina. Thirty-seven percent in the elective IABP group and 33% in the no planned IABP group had a diagnosis of diabetes at enrollment. Medical therapy at enrollment was also similar in both groups: 97% (147/151) and 96% (144/150) were taking aspirin, 93% in each group (140/151 and 139/150, respectively) were taking clopidogrel, and 89% (134/150) and 81% (121/150) were taking an angiotensin-converting enzyme inhibitor or angiotensin-II receptor blocker. Medication at discharge included aspirin in 99% (147/149) and 98% (146/149) of patients and clopidogrel in 99% (148/149) and 98% (146/149) in the elective IABP and no planned IABP groups, respectively.

An IABP was inserted at the start of the procedure in 97% of cases in the elective IABP group; the balloon catheter could not be inserted in 3 cases owing to vascular access difficulties. A stent was deployed in 94.2% and 92.5% of lesions treated in the elective IABP and no planned IABP groups, respectively. Patients in the 2 groups underwent comparable amounts of revascularization, with a mean of 2.15 (SD, 1.04) lesions attempted per patient in the elective IABP group and 2.05 (SD, 1.02) lesions in the no planned IABP group and with procedural success rates of 93.9% and 93%, respectively. In each group, 2.56 (SD, 1.33) and 2.31 (SD, 1.54) stents were deployed per patient, 67% of which were drug-eluting stents in both groups. Glycoprotein IIb/IIIa inhibitors were used in 39.3% and 43.3% of all cases in the elective IABP and no planned IABP groups, respectively.

Primary and Secondary End Points

The primary end point of MACCE at hospital discharge occurred in 15.2% (n = 23) of the elective IABP group and

Table 1. Baseline Characteristics

Characteristic	No. (%)	
	Elective IABP (n = 151)	No Planned IABP (n = 150)
Demographics		
Age, mean (SD), y	71 (9)	71 (10)
Men	122 (81)	117 (78)
Body mass index, mean (SD) ^a	28.4 (6.0)	27.4 (5.6)
Race/ethnicity		
White	144 (95)	141 (94)
South Asian	4 (3)	7 (5)
Other	3 (2)	2 (1)
Medical history		
Diabetes		
Type 1	3 (2)	6 (4)
Type 2	53 (35)	44 (29)
Smoking		
Current	32 (21)	29 (20)
Former	78 (52)	82 (55)
Hypertension	95 (63)	91 (61)
Prior MI	113 (75)	108 (73)
Prior PCI	17 (11)	14 (9)
Prior CABG surgery	25 (17)	20 (13)
Prior stroke	12 (8)	11 (7)
GFR, median (IQR) ^b	58.2 (45.0-78.6)	60.0 (41.9-80.0)
NYHA heart failure class		
I	8 (5)	11 (7)
II	43 (29)	31 (21)
III	63 (42)	64 (43)
IV	36 (24)	44 (29)
CCS angina class		
No angina	34 (23)	30 (20)
I	16 (11)	14 (9)
II	28 (19)	38 (25)
III	33 (22)	30 (20)
IV	39 (26)	38 (25)
Left ventricular ejection fraction, mean (SD), %		
Method of assessment		
Echocardiography	77 (51)	57 (38)
Left ventricular angiography	67 (44)	83 (55)
Other	7 (5)	10 (7)
Coronary anatomy		
BCIS-1 Jeopardy Score		
6	1 (1)	1 (1)
8	40 (26)	42 (28)
10	39 (26)	39 (26)
12	71 (47)	68 (45)
Left main coronary disease ^c	41 (27)	44 (29)

Abbreviations: BCIS-1, Balloon Pump–Assisted Coronary Intervention Study; CABG, coronary artery bypass graft; CCS, Canadian Cardiovascular Society; GFR, glomerular filtration rate; IABP, intra-aortic balloon pump; IQR, interquartile range; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

^a Calculated as weight in kilograms divided by height in meters squared.

^b Based on Cockcroft-Gault formula.¹⁴

^c >70% lesion in left main coronary artery.

16.0% (n=24) of the no planned IABP group ($P=.85$; OR, 0.94 [95% CI, 0.51-1.76]) (TABLE 2). There were 3 deaths in the elective IABP group and 1 death in the no planned IABP group ($P=.34$). Myocardial infarction occurred in 19 (12.6%) patients in the elective IABP group and 20 (13.3%) in the no planned IABP group ($P=.85$). Two cerebrovascular accidents occurred, both in patients who had received elective IABP insertion. One patient in the elective IABP group and 4 in the no planned IABP group underwent urgent further revascularization ($P=.21$). All-cause mortality at 6 months was 4.6% in the elective IABP group and 7.4% in the no planned IABP group ($P=.32$; OR, 0.61 [95% CI, 0.24-1.62]) (Table 2 and FIGURE 2). Elective IABP insertion had no significant effect on the rates of MACCE at hospital discharge in the subgroups stratified according to median glomerular filtration rate ($P=.29$ for interaction), diabetic status ($P=.86$), BCIS-1 Jeopardy Score (12 vs 8) ($P=.48$), or glycoprotein IIb/IIIa inhibitor use ($P=.97$) (FIGURE 3).

Predefined procedural complications occurred more often in the no planned IABP group (16 patients [10.7%]) than in the group undergoing elective IABP insertion (2 patients [1.3%]) ($P<.001$; OR, 0.11 [95% CI, 0.01-0.49]). The most common component of these complications was prolonged procedural hypotension, which occurred in 13 patients in the group with no planned IABP insertion and 2 patients in the group with elective IABP insertion. Overall, rescue IABP insertion was required in 18 patients (12%) assigned to have no planned IABP insertion, including 13 for procedural hypotension, 1 for pulmonary edema, and 1 for sudden vessel closure. Patients requiring rescue IABP in the no planned IABP group had an ejection fraction of 24.4% (SD, 5.5%) and a BCIS-1 Jeopardy Score of 11.2 (SD, 1.4) at baseline. A maximum BCIS-1 Jeopardy Score of 12 was present in 45% of the no planned IABP group overall and in 72% of those requiring rescue IABP insertion.

Table 2. Trial Outcomes

Variable	No. (%)		OR (95% CI) ^a	P Value
	Elective IABP (n = 151)	No Planned IABP (n = 150)		
Primary end point				
MACCE ^b	23 (15.2)	24 (16.0)	0.94 (0.51-1.76)	.85
MI	19 (12.6)	20 (13.3)	0.93 (0.48-1.83)	.85
Death	3 (2.0)	1 (0.7)	3.02 (0.31-29.37)	.34
CVA	2 (1.3)	0		
Further revascularization	1 (0.7)	4 (2.7)	0.24 (0.03-2.20)	.21
Secondary end points				
6-mo mortality	7 (4.6)	11 (7.4) ^c	0.61 (0.24-1.62)	.32
Bleeding				
All	29 (19.2)	17 (11.3)	1.86 (0.93-3.79)	.06
Major	5 (3.3)	6 (4.0)	0.83 (0.20-3.36)	.77
Minor	24 (15.9)	11 (7.3)	2.39 (1.07-5.61)	.02
Procedural complications	2 (1.3)	16 (10.7)	0.11 (0.01-0.49)	<.001
Access-site complications	5 (3.3)	0		.06 ^d

Abbreviations: CI, confidence interval; CVA, cerebrovascular accident; IABP, intra-aortic balloon pump; MACCE, major adverse cardiac and cardiovascular events; MI, myocardial infarction; OR, odds ratio.

^aOdds ratios are unadjusted.

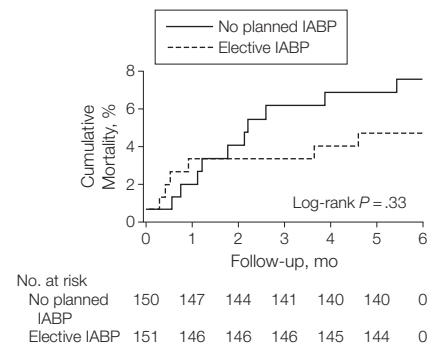
^bMACCE is hierarchical (death > MI > CVA > further revascularization); the sum of individual end points is greater than the total composite primary events, because 1 patient had an MI and died and 2 patients had MIs and further percutaneous coronary interventions.

^cData unavailable for 1 patient.

^dBy Fisher exact test.

MACCE occurred in 4 of rescue cases (22%), all of which were instances of periprocedural myocardial infarction. The IABP remained in situ for a median duration of 8.6 (interquartile range, 6-23) hours in the elective IABP group compared with 22.9 (interquartile range, 17-26) hours following rescue IABP insertion. A post hoc comparison of the no planned IABP group who required vs did not require rescue IABP use is summarized in TABLE 3.

Major or minor bleeding occurred in 19.2% of the elective IABP group and 11.3% of the no planned IABP group ($P=.06$; OR, 1.86 [95% CI, 0.93-3.79]). There was no difference between the groups in the incidence of major bleeding (5 and 6 patients, respectively), but there was more minor bleeding in the elective IABP group (15.9%) compared with the no planned IABP group (7.3%) ($P=.02$). Five patients in the elective IABP group and none in the no planned IABP group had an access-site complication ($P=.06$ by Fisher exact test). The median duration of in-hospital stay in both groups was 2 (interquartile range, 1-5) days ($P=.12$). No transient ischemic attacks were documented in either group.

Figure 2. Cumulative Mortality Estimates by Treatment Assignment

Mortality at 6 months was numerically lower in the elective intra-aortic balloon pump (IABP) group than in the no planned IABP group, although this was not statistically significant (4.6% vs 7.4%, $P=.32$ by the χ^2 test).

COMMENT

BCIS-1 addressed the hypothesis that elective IABP insertion in patients with poor left ventricular function and extensive coronary disease would reduce the incidence of MACCE at hospital discharge (capped at 28 days). The study has demonstrated that there is no difference in the incidence of the composite end point of death, myocardial infarction, cerebrovascular events, or further revascularization with elective

IABP insertion compared with a strategy of no planned IABP insertion. An absolute 2.8% difference in mortality at 6 months favoring the elective IABP group was observed, but this difference was not statistically significant. The present trial was not powered to

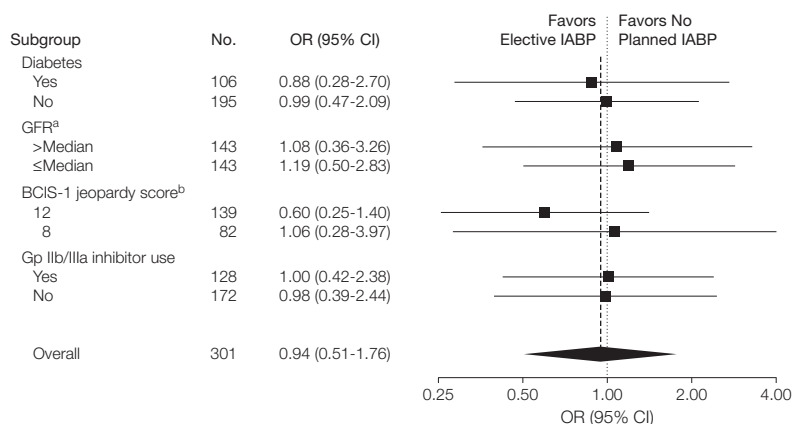
detect a difference in mortality at 6 months between the groups. Elective IABP use was associated with significantly fewer procedural complications but more minor bleeding and more access-site complications than when PCI was performed without

planned IABP insertion. These results do not support a strategy of prophylactic placement of an intra-aortic balloon catheter during PCI in all patients with severe left ventricular dysfunction and a high myocardial Jeopardy Score.

It is important to note that rescue IABP insertion was required in 12% of the group assigned to a strategy of PCI without planned balloon pump insertion. Rescue IABP use was at the discretion of the operators and was largely driven by the occurrence of prolonged hypotension. This finding is consistent with the observations of Briguori et al,⁸ who found that 15% of patients undergoing high-risk PCI experienced sufficient hypotension to warrant emergency IABP placement during the procedure. In the current study, rescue IABP placement appeared to be associated with a worse in-hospital outcome than did elective IABP insertion. Patients receiving rescue IABP placement also required a longer duration of IABP support and had a more prolonged in-hospital stay than those in the elective IABP group, which accords with previous registry data.⁹ In the absence of clear markers that would allow prospective identification of patients who will require rescue IABP insertion, a standby IABP approach is advisable when undertaking PCI in the presence of severe left ventricular impairment and extensive coronary disease, to allow timely emergency placement of a balloon catheter if required.

The lack of benefit for routine elective balloon counterpulsation in reducing MACCE in this study contrasts with data from previous registries and merits further consideration. First, did the patients enrolled in this study comprise a sufficiently high-risk cohort? The presence of severe left ventricular dysfunction (mean ejection fraction, 24%), extensive coronary disease (mean Jeopardy Score, 10), a high prevalence of diabetes, and an urgent indication for revascularization in nearly half of the population would certainly place these patients at the upper end of the spectrum of risk following PCI.^{15,16} Further-

Figure 3. Elective Intra-aortic Balloon Pump Insertion and Rates of Major Adverse Cardiac and Cardiovascular Events



BCIS-1 indicates Balloon Pump–Assisted Coronary Intervention Study; CI, confidence interval; GFR, glomerular filtration rate; Gp, glycoprotein; IABP, intra-aortic balloon pump; OR, odds ratio. Vertical dashed line indicates overall estimate. Elective IABP insertion had no significant effect on the occurrence of major adverse cardiac and cardiovascular events in the overall study population or any of the predefined groups.

^aMedian estimated GFR, 59.1 mL/min.

^bFor clarity, only the comparison between BCIS-1 Jeopardy Scores 8 and 12 are shown; there was no significant interaction between Jeopardy Scores 8 vs 10 or 10 vs 12.

Table 3. No Planned IABP Group by Requirement for Rescue IABP

Variable	No. (%)		P Value
	Rescue IABP Required (n = 18)	No IABP Inserted (n = 132)	
Baseline and procedural characteristics			
Age, mean (SD), y	74 (8)	71 (10)	.26
Men	12 (67)	105 (80)	.22
Diabetes	6 (33)	44 (33)	>.99
GFR, median (IQR), mL/min ^a	50.1 (38.5-78.7)	60.8 (43.3-80.7)	.46
Ejection fraction, mean (SD), %	24.4 (5.5)	23.5 (5.6)	.56
BCIS-1 Jeopardy Score			
Mean (SD)	11.2 (1.4)	10.2 (1.7)	.02
Patients with maximum score ^b	13 (72)	55 (42)	.02
Vessels attempted, mean (SD)	1.94 (0.87)	1.60 (0.71)	.06
Vessels revascularized, mean (SD)	1.82 (0.88)	1.61 (0.71)	.25
Outcome			
MACCE at hospital discharge	4 (22)	20 (15)	.49 ^c
Major or minor bleeding	2 (11)	15 (11)	>.99 ^c
Access-site complications	0	0	NA
In-hospital stay, median (IQR), d	4 (3-7)	2 (1-4)	<.001

Abbreviations: BCIS-1, Balloon Pump–Assisted Coronary Intervention Study; GFR, glomerular filtration rate; IABP, intra-aortic balloon pump; IQR, interquartile range; MACCE, major adverse cardiac and cardiovascular events; NA, not applicable.

^aBased on Cockcroft-Gault formula.¹⁴

^bJeopardy Score ranges from 0-12.

^cBy Fisher exact test.

more, the congruence of predicted and observed MACCE rates in the no planned IABP group suggests that the risk profile of the enrolled population matches that anticipated when determining the sample size for this study.

Second, the decreased efficacy of elective balloon pump support may reflect advances in PCI techniques in the past decade, which in turn have resulted in better procedural outcomes and reduced complications. These advances are exemplified by rates of stent use during PCI (approximately 94% in BCIS-1 but <50% in previous registries).⁹

Third, there is an established relationship between institutional volume and outcome following PCI.^{17,18} This trial was conducted across 17 high-volume centers in the United Kingdom (a mean of 1695 [SD, 573] PCI procedures were performed at each center per year of recruitment to BCIS-1¹⁹), and the majority of operators were cardiologists experienced at performing complex PCIs and using percutaneous hemodynamic support devices. It is unclear whether inclusion of a more heterogeneous group of centers and operators may have affected the incidence of major complications overall and, therefore, the relative efficacy of elective counterpulsation. Nevertheless, BCIS-1 provides clarification of the conflicting signals that had emerged from observational and retrospective registries regarding the role of elective IABP support during high-risk PCI. Our findings mirror the conclusions of a recent meta-analysis of IABP therapy in the context of primary PCI for STEMI in patients who are hemodynamically stable at the outset.⁵

Albeit primarily designed to evaluate the efficacy of elective balloon counterpulsation, BCIS-1 also represents one of the largest contemporary cohorts of patients undergoing PCI for ischemic cardiomyopathy. Treatment of coronary disease in patients with significant left ventricular dysfunction has traditionally been associated with a poor outcome, regardless of the mode of revascularization.^{20,21} Although randomized efficacy trials of revascularization

are awaited, observational data suggest that advances in procedural techniques and adjunctive medical therapy may have resulted in a gradual improvement in survival following percutaneous^{22,23} or surgical²⁴ revascularization in this group of patients. The excellent short- and medium-term survival demonstrated in this study provides further evidence of this trend.

Study Limitations

The BCIS-1 Jeopardy Score provided a semiquantitative estimate of the amount of myocardium at risk in the event of hemodynamic compromise, on the basis of the distribution and extent of coronary disease.¹¹ However, the Jeopardy Score has several limitations as a marker of risk during PCI. First, it does not take into account the characteristics of coronary lesions, which directly translate to the complexity of PCI and hence outcome. The Syntax Score²⁵ had not been described and validated when the current study was designed; as a consequence, this information was not collected prospectively. Second, the Jeopardy Score does not incorporate viability of the myocardium subtended by the diseased coronary vessels, which affects the importance of each vessel as a potential source of ischemia and consequent compromise during PCI and also predicts the long-term outcome following revascularization.²⁶ Viability testing was not mandated in BCIS-1, because the trial only enrolled patients already scheduled to undergo PCI; the decision to proceed to percutaneous revascularization had been made by the clinical team managing the patient, based on a combination of symptoms, noninvasive testing, or both before inclusion in the trial. Third, the study was powered to detect a 10% difference in MACCE and we cannot exclude a smaller treatment effect, although it should be noted that this is the largest randomized study to date involving this high-risk group of patients.

CONCLUSIONS

In summary, BCIS-1 randomized 301 patients with severe left ventricular dysfunction and extensive coronary

disease to undergo elective IABP insertion before PCI or to undergo PCI without planned IABP support. The study did not demonstrate a difference in MACCE at hospital discharge and therefore does not support routine elective IABP insertion before high-risk PCI. However, 12% of patients who underwent PCI without elective IABP insertion required rescue IABP support, which highlights the importance of adopting a standby IABP strategy when undertaking high-risk PCI.

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Author Contributions: Dr Redwood had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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