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Clinical and hemodynamic effects of intra-aortic balloon pump therapy in chronic heart failure patients with cardiogenic shock

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hemodynamics

BACKGROUND: The role of the intra-aortic balloon pump (IABP) in acute decompensated heart failure (HF) with cardiogenic shock (CS) is largely undefined. In this study we sought to assess the hemodynamic and clinical response to IABP in chronic HF patients with CS and identify predictors of response to this device.
METHODS: We retrospectively reviewed all patients undergoing IABP implantation from 2011 to 2016 at our institution to identify chronic HF patients with acute decompensation and CS (cardiac index <2.2 liters/min/m^2 and systolic blood pressure <90 mm Hg or need for vasoactive medications to maintain this level). Clinical deterioration on IABP was defined as failure to bridge to either discharge on medical therapy or durable heart replacement therapy (HRT; durable left ventricular assist device or heart transplant) with IABP alone.
RESULTS: We identified 132 chronic HF patients with IABP placed after decompensation with hemodynamic evidence of CS. Overall 30-day survival was 84.1%, and 78.0% of patients were successfully bridged to HRT or discharge without need for escalation of device support. The complication rate during IABP support was 2.3%. Multivariable analysis identified ischemic cardiomyopathy (odds ratio [OR] 3.24, 95% confidence interval [CI] 1.16 to 9.06; $p = 0.03$) and pulmonary artery pulsatility index (PAPi) <2.0 (OR 5.04, 95% CI 1.86 to 13.63; $p = 0.001$) as predictors of clinical deterioration on IABP.
CONCLUSIONS: Overall outcomes with IABP in acute decompensated chronic HF patients are encouraging, and IABP is a reasonable first-line device for chronic HF patients with CS. Baseline right ventricular function, as measured by PAPi, is a major predictor of outcomes with IABP in this population.
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Chronic heart failure (HF) affects more than 5.5 million people in the United States, with an estimated 600,000 to 800,000 patients living with advanced HF (New York Heart Association [NYHA] Class IIIb to IV).[1] Although

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significant improvements in both medical- and device-based therapies have improved the prognosis of chronic HF,[2,3] episodes of acute decompensated heart failure (ADHF) may result in rapid deterioration and substantially worsen prognosis. Cardiogenic shock (CS) represents ADHF in its most severe form and is broadly defined as severe cardiac dysfunction resulting in impaired end-organ perfusion. Although inotropes and vasopressors remain as first-line therapies for CS, they have significant adverse side effects (e.g., arrhythmia) and may be insufficient to counteract this process.[4]

Temporary mechanical circulatory support devices (tMCSDs) are often utilized in CS refractory to medical therapy in an effort to stabilize patients sufficiently to allow for either removal of the tMCSD and discharge from the hospital or successful bridge to heart replacement therapy (HRT; e.g., durable left ventricular assist device [LVAD] or orthotopic heart transplantation [OHT]). Percutaneous tMCSD options include intra-aortic balloon pump (IABP), microaxial percutaneous LVAD, extracorporeal centrifugal-flow LVAD, and extracorporeal membrane oxygenation (ECMO).[5] Of these, the IABP is the most widely used by a substantial margin, largely due to its widespread availability, ease of insertion, and low complication rate.[6]

Despite decades of IABP experience, its appropriate clinical role in CS remains poorly defined, largely due to limited evidence to guide its use. The largest randomized, controlled trial in patients with CS demonstrated neither benefit nor harm with IABP use in CS after acute myocardial infarction (AMI).[7] Findings from that study have led to a paradigm shift away from routine IABP use in these patients. However, chronic HF patients with acute decompensation and CS represent a unique physiologic phenotype compared with AMI patients, which may lead to a differential response to device therapy. The objectives of our study were to assess the clinical and hemodynamic response to IABP in chronic HF patients with CS and identify predictors of clinical deterioration on IABP therapy in this population.

Methods

Study population

We retrospectively reviewed the medical records of all patients in the cardiac care unit who underwent IABP implantation at our institution from January 2011 to April 2016. All patients ≥18 years of age with chronic systolic HF (left ventricular ejection fraction [LVEF] <40% for >6 months) who underwent IABP placement for acute-on-chronic decompensated HF with hemodynamic evidence of CS were included in our cohort. Hemodynamic evidence of CS was defined as pre-IABP cardiac index (CI) <2.2 liters/min/m^2 *and* either systolic blood pressure <90 mm Hg *or* need for vasoactive medications to achieve this level. Exclusion criteria were: (1) diagnosis of AMI during the index hospitalization; (2) IABP placement after cardiac surgery; (3) concurrent support with another tMCSD at the time of IABP implantation (e.g., ECMO); (4) previous OHT; and (5) lack of pre-implant hemodynamic data. The study was approved by the institutional review board of Columbia University.

Data collection

Demographic data were collected, including co-morbidities, etiology of cardiomyopathy (ischemic vs non-ischemic), and echocardiographic parameters. Hemodynamic data included measurements made by pulmonary artery (PA) catheter, including cardiac output (CO) and CI (Fick method) as well as the pulmonary artery pulsatility index (PAPi = [systolic pulmonary artery pressure – diastolic pulmonary artery pressure] / right atrial pressure). Laboratory data included serum creatinine, lactate, hemoglobin, and baseline estimated glomerular filtration rate (eGFR; using the Modified End-stage Renal Disease [MDRD] formula). We defined hemodynamic "super-responders" as those patients with increase in CO in the top quartile of the cohort.

Outcomes

The primary outcome was clinical deterioration despite IABP therapy. Patients were considered to have been stabilized on IABP if they were: (1) weaned from IABP and discharged from the hospital on medical therapy; or (2) bridged to durable HRT on IABP alone and survived to discharge. Patients not meeting these criteria (e.g., those who died or required escalation to another tMCSD device during IABP support) were considered to have clinical deterioration despite IABP. Secondary outcomes included 30-day mortality and immediate hemodynamic response (change in CO and CI, mean arterial pressure [MAP], and mean PA pressure). Adverse events were defined as: (1) bleeding—the need for packed red blood cell (PRBC) transfusions during IABP support related to access-site bleeding or the need for >2 PRBC transfusions during IABP support not related to access-site bleeding; (2) IABP malfunction—any pump malfunction requiring unplanned catheter exchange or removal; (3) vascular complication—limb ischemia that did not resolve with IABP removal or required endovascular or surgical intervention; and (4) embolic events—presence of new symptoms of an embolic event (e.g. neurologic deficit or visceral infarction) temporally related to IABP use.

Statistical methods

Continuous variables were compared using Student's *t*-test or Wilcoxon's rank sum test, as appropriate, and categorical variables were compared using chi-square tests. Categorical variables are reported as frequency, and continuous variables are reported as mean ± standard deviation or median with interquartile range, as appropriate. Logistic regression was used to identify pre-implant variables associated with clinical and hemodynamic response to IABP insertion. Variables with $p < 0.1$ on univariable analysis and those considered to be clinically important with respect to the primary outcome (e.g., age and gender) were included in a multivariable model. Collinear variables were excluded. All analyses were performed using STATA version 15.0 (StataCorp LP, College Station, TX).

Results

Figure 1 details IABP use at our institution during the study period for all indications, not solely for ADHF. In total, 776 patients in the cardiac critical care unit received an IABP during the study period. The primary indications for IABP implantation were active myocardial ischemia (430 patients, 55.4%), acute HF (e.g., fulminant myocarditis; 33 patients,

4.3%), and acute-on-chronic decompensated HF (202 patients, 26.0%). Of the 202 patients receiving IABP for ADHF, 70 were excluded for the following reasons: previous OHT ($n = 13$); transferred from outside hospitals with IABP already in place ($n = 11$); incomplete pre-implant hemodynamic data ($n = 21$); and pre-implant CI >2.2 liters/min/m^2 ($n = 25$). Our final cohort included 132 chronic systolic HF patients receiving IABP for ADHF with hemodynamic evidence of CS (Figure 1). All patients had insertion of the IABP in the femoral position, exception for 1 patient who had the device placed in the axillary position.

Baseline characteristics

The study cohort's baseline characteristics are represented in Table 1. Baseline CI was 1.56 ± 0.37 liters/min/m^2 and mean pulmonary capillary wedge pressure was 29.5 ± 8.3 mm Hg. Mean serum lactate was 2.5 ± 2.5 mmol/liter and mean eGFR was 47.6 ± 21.9 ml/min/1.73 m^2. The mean duration of cardiomyopathy in the whole cohort was 81.5 ± 65.5 months. In the clinical stabilization cohort, it was 84.3 ± 64.3 months, whereas in the clinical deterioration cohort it was 73.3 ± 69.0 months ($p = 0.42$). When compared with patients stabilized on IABP, those with clinical deterioration were more likely to have an ischemic cardiomyopathy (ICM; 58.8% vs 28.6%, $p = 0.002$) and to be receiving vasopressor medications at the time of implantation (44.1% vs 22.4%, $p = 0.02$). Comparison of baseline hemodynamics revealed that patients with clinical deterioration had lower diastolic blood pressure (60.8 mm Hg vs 65.3 mm Hg, $p = 0.04$), lower MAP (72.3 mm Hg vs 76.7 mm Hg, $p = 0.04$), higher central venous pressure (CVP; 18.9 mm Hg vs 13.1 mm Hg, $p = 0.0001$), lower PAPi (1.86 vs 3.39, $p = 0.03$), and smaller left ventricular end-diastolic diameter (6.56 cm vs 7.08 cm, $p = 0.02$). When comparing patients with ICM and non-ischemic cardiomyopathy (NICM), filling pressures were similar between the 2 groups (CVP: 15.2 ± 7.7 mm Hg vs 14.3 ± 6.9 mm Hg, respectively, $p = 0.50$; mean PA pressure: 38.9 ± 10.2 mm Hg vs 37.4 ± 8.8 mm Hg, respectively, $p = 0.39$), although patients with NICM had a lower cardiac index at baseline (1.65 ± 0.36 liters/min/m^2 vs 1.51 ± 0.34 liters/min/m^2, $p = 0.03$).

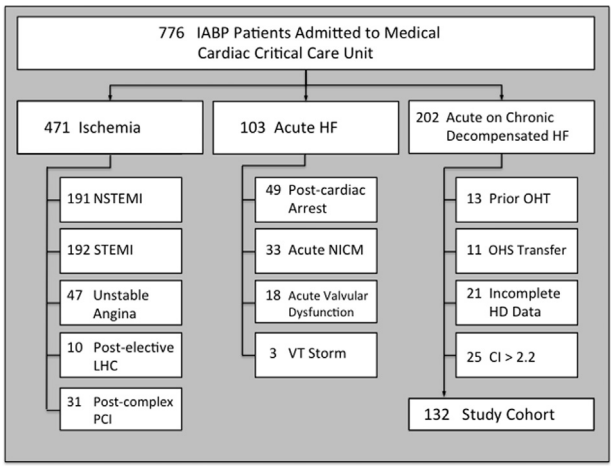

Figure 1 Patient selection flowchart. CI, cardiac index; HD, hemodynamic; HF, heart failure; IABP, intra-aortic balloon pump; LHC, left-heart catheterization; NICM, non-ischemic cardiomyopathy; NSTEMI, non–ST-elevation myocardial infarction; OHT, orthotopic heart transplant; OSH, outside hospital; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; VT, ventricular tachycardia.

Concomitant medical therapy

The mean blood pressure in the entire cohort was 98/64 mm Hg, and 37 (28.0%) of these patients were already on at least 1 vasopressor agent. The number of patients receiving vasopressors and the mean doses used were as follows: 1 (0.8%) patient was receiving phenylephrine at 150 μg/min; 4 (3.0%) were receiving norepinephrine at a mean dose of 13.9 ± 12.5 μg/min; 26 (19.7%) were receiving vasopressin at a mean dose of 2.4 ± 1.4 U/h; and 1 (0.8%) was receiving epinephrine at a dose of 1 μg/min. Inotropes were used frequently, with 115 (87.1%) patients receiving at least one inotrope at the time of IABP insertion. The number of patients receiving inotropes and the mean doses used were as follows: 72 (54.5%) patients were receiving milrinone at a mean dose of 0.31 ± 0.12 μg/kg/min; 45 (34.1%) were receiving dobutamine at a mean dose of 4.6 ± 2.0 μg/kg/min; and 23 (17.4%) were receiving dopamine at a mean dose of 2.9 ± 2.0 μg/kg/min.

Clinical outcomes

The median time on IABP support for the entire cohort was 96.0 (interquartile range [IQR] 48.0 to 144.0) hours. For the clinical stabilization cohort, it was 96.0 (IQR 49.0 to 132.0) hours and for the clinical deterioration cohort it was 84.0 (IQR 44.0 to 235.0) hours ($p = 0.49$). Those who went on to LVAD or OHT had a median time on IABP support of 110.5 (IQR 48 to 168) hours. Thirty-day survival and survival to discharge were 84.1% and 78.0%, respectively. The primary outcome of clinical deterioration occurred in 34 (25.8%) patients, whereas 98 (74.2%) had stabilization on IABP. Among the latter group, 21 (21.4%) were discharged from the hospital on medical therapy alone, 69 (70.4%) were bridged to durable LVAD, and 8 (8.2%) were bridged to OHT. Of the 34 patients with clinical deterioration on IABP, 19 (55.9%) died or were discharged to hospice without needing another tMCSD, 10 (29.4%) were escalated to another tMCSD for further stabilization, and 5 (14.7%) died after having been bridged to durable LVAD on IABP alone. Of those receiving another tMCSD (ECMO or surgically implanted short-term ventricular assist device), 2 (20.0%) were ultimately bridged to durable LVAD, 3 (30.0%) to OHT, and 5 (50.0%) died (Figure 2). At our institution, we typically consider implantation of another more powerful device if there are signs of persistent shock or the need for substantial escalation of pharmacotherapy to maintain adequate CO, blood pressure, and end-organ function. The median time to escalation for those who required a more powerful device was 48.0 (IQR 38.0 to 91.0) hours. Among those in the stabilization cohort,

Table 1 Baseline Characteristics for Chronic HF Patients With IABP Placed for Cardiogenic Shock

	All ($n = 132$)	Clinical stabilization ($n = 98$)	Clinical deterioration ($n = 34$)	p-value
Demographic data				
Age	61.2 ± 13.0	60.2 ± 12.5	64.1 ± 14.2	0.13
Male gender (%)	111 (84.1)	82 (83.7)	29 (85.3)	0.84
Body surface area (m^2)	1.93 ± 0.25	1.95 ± 0.23	1.85 ± 0.28	0.06
Diabetes mellitus (%)	44 (33.3)	29 (29.6)	15 (44.1)	0.12
Ischemic cardiomyopathy (%)	48 (36.4)	28 (28.6)	20 (58.8)	0.002
Hemodynamic data				
Systolic blood pressure (mm Hg)	98.4 ± 14.6	99.5 ± 15.3	95.3 ± 11.8	0.16
Diastolic blood pressure (mm Hg)	64.2 ± 10.9	65.3 ± 11.3	60.8 ± 9.1	0.04
Mean arterial pressure (mm Hg)	75.6 ± 10.6	76.7 ± 11.1	72.3 ± 8.6	0.04
Heart rate (beats/min)	93.0 ± 19.3	91.5 ± 17.5	97.3 ± 23.5	0.14
Baseline cardiac index (liters/min/m^2)	1.56 ± 0.37	1.54 ± 0.35	1.64 ± 0.37	0.14
Central venous pressure (mm Hg)	14.6 ± 7.2	13.1 ± 6.6	18.9 ± 6.9	<0.0001
PA systolic pressure (mm Hg)	56.6 ± 14.0	56.3 ± 14.3	57.2 ± 13.2	0.75
PA diastolic pressure (mm Hg)	28.2 ± 8.1	27.9 ± 8.2	28.9 ± 7.9	0.55
Mean PA pressure (mm Hg)	37.9 ± 9.3	37.5 ± 9.3	39.1 ± 9.4	0.41
Pulmonary capillary wedge pressure (mm Hg)	29.5 ± 8.3	28.8 ± 8.5	31.7 ± 7.6	0.28
Cardiac power index	0.26 ± 0.07	0.26 ± 0.07	0.26 ± 0.06	0.98
PA pulsatility index	2.97 ± 3.39	3.39 ± 3.79	1.86 ± 1.49	0.03
LV stroke work index	12.13 ± 4.40	12.75 ± 4.44	10.39 ± 3.81	0.11
RV stroke work index	5.61 ± 3.00	5.84 ± 3.08	4.98 ± 2.73	0.16
Inotropes (baseline % on)	115 (87.1)	84 (85.7)	31 (91.2)	0.41
Pressors (baseline % on)	37 (28.0)	22 (22.4)	15 (44.1)	0.02
Additional data				
Baseline eGFR (ml/min/1.73 m^2)	47.6 ± 21.9	48.1 ± 20.1	46.3 ± 26.8	0.69
Baseline lactate. serum (mmol/liter)	2.5 ± 2.5	1.8 ± 1.0	3.4 ± 3.5	0.07
LVEF (%)	18.0 ± 8.9	17.6 ± 9.4	19.0 ± 7.0	0.38
LVEDD (cm)	6.95 ± 1.14	7.08 ± 1.13	6.56 ± 1.12	0.02
Mitral regurgitation (moderate–severe)	90 (68.2)	71 (72.4)	19 (55.9)	0.07

eGFR, estimated glomerular filtration rate; IABP, intra-aortic balloon pump; LV, left ventricle. LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; PA, pulmonary artery; RV, right ventricle.

22 (22.4%) had a significant increase in vasopressor or inotrope requirement (defined as addition of 1 of these agents or a >25% increase in the doses administered), whereas 13 (38.2%) in the deterioration group had a significant increase in these medications ($p = 0.07$).

Immediate hemodynamic response

The median duration of time between pre- and post-implant hemodynamic measurement was 5.0 (IQR 4.0 to 9.0) hours. For those who clinically stabilized the median was 5.0 (IQR 4.0 to 9.0) hours, and for those with clinical deterioration it was 5.5 (IQR 3.0 to 10.0) hours ($p = 0.96$). The mean increase in CO and CI after IABP implantation was 0.51 (IQR 0.08 to 0.98) liter/min and 0.26 (IQR 0.01 to 0.48) liters/min/m^2, respectively. The change in mean PA pressure was –5 (IQR –9 to 1) mm Hg. The mean change in MAP was –2.0 (IQR –10.0 to 7.3) mm Hg. Patients stabilized on IABP had a change in CO of +0.54 (IQR 0.08 to 1.01) liter/min, whereas those with further clinical deterioration had a change in CO of +0.30 (IQR 0 to 0.83) liter/min ($p = 0.31$). No significant differences existed between the groups with regard to mean PA pressure change (clinical stabilization group: –5 [IQR –11 to 0] mm Hg vs clinical deterioration group: –5 [IQR –8 to –1] mm Hg; $p = 0.67$) or change in MAP (clinical stabilization group: –2.8 [IQR –11.5 to 7.2] mm Hg vs clinical deterioration group: –1.2 [IQR –7.3 to 7.3] mm Hg; $p = 0.38$) after IABP implantation.

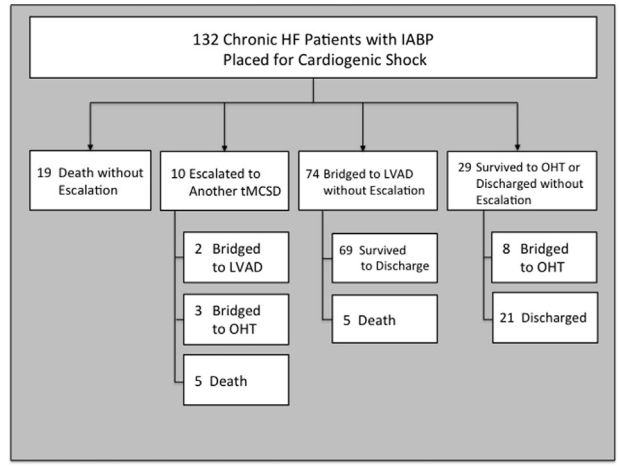

Figure 2 Study cohort clinical outcomes. HD, hemodynamic; HF, heart failure; HRT, heart replacement therapy; IABP, intra-aortic balloon pump; LVAD, left-ventricular assist device; MCS, mechanical circulatory support; OHT, orthotopic heart transplant.

Predictors of clinical response

Univariable analysis identified ICM (odds ratio [OR] 3.57, 95% confidence interval [CI] 1.59 to 8.04; $p = 0.002$), vasopressor use at the time of implantation (OR 2.73, 95% CI 1.19 to 6.23; $p = 0.02$), higher CVP (OR 1.13, 95% CI 1.06 to 1.21; $p < 0.001$), and lower PAPi (OR 5.14, 95% CI 2.04 to 12.94; $p = 0.001$) as predictors of clinical deterioration on IABP. In multivariable analysis, ICM (OR 3.24, 95% CI 1.16 to 9.06; $p = 0.03$) and PAPi <2.0 (OR 5.04, 95% CI 1.86 to 13.63; $p = 0.001$) were independent predictors of clinical deterioration on IABP (Table 2). This cut-point for PAPi was guided by the cohort's median value and previous reports of this index as a predictor of outcomes in multiple phenotypes of shock.[8–10] Patients with 0, 1, or 2 of these risk factors had rates of clinical deterioration of 6.8%, 25.4%, and 55.2%, respectively ($p < 0.001$; Figure 3).

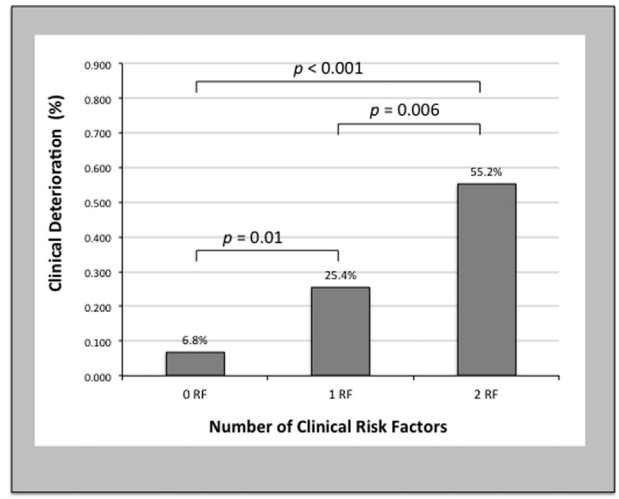

Figure 3 Predictors of clinical response. Association between identified risk factors and inadequate clinical response leading to death or device escalation. RF, risk factor.

Hemodynamic "super-response"

The top quartile of hemodynamic improvement included patients whose CO increased by ≥0.98 liter/min (Figure 4). When compared with the remainder of the study cohort, this subgroup of IABP "super-responders" also had a greater reduction in mean PA pressures (–8 [IQR –17 to –2] mm Hg vs –4 (IQR –9 to 0) mm Hg; $p = 0.004$) as well as CVP (–4 [IQR –6 to –1] mm Hg vs –2 [IQR –4 to 1] mm Hg; $p = 0.01$]. At baseline, super-responders had a right ventricular power index of 0.13 ± 0.05 W/m^2 and a left ventricular power index of 0.24 ± 0.26 W/m^2, whereas the remainder of the cohort had a right ventricular power index of 0.13 ± 0.03 W/m^2 ($p = 0.91$) and a left ventricular power index of 0.27 ± 0.06 W/m^2 ($p = 0.01$). In the multivariable analysis including those univariable predictors meeting our criteria and both type of cardiomyopathy and heart rate as prespecified variables, higher mean PA pressure was an independent predictor of robust hemodynamic response (OR 1.07, 95% CI 1.01 to 1.13; $p = 0.008$; Table 3). Finally, super-responders had an increased likelihood of stabilization on IABP (87.9% vs 70.8%; $p = 0.049$). If super-response was instead defined as the top quartile of reduction in mean PA pressures, corresponding to a reduction of at least 9 mm Hg, super-responders were more likely to have clinical stabilization, although this difference was not statistically significant and not as pronounced as seen when using the previous definition of hemodynamic super-response (clinical stabilization in 82.1% of super-responders vs 71.0% of the remainder of the cohort; $p = 0.19$).

IABP-associated complications

A total of 4 complications occurred in 3 patients during IABP support, corresponding to a complication rate of

Table 2 Analysis of Potential Predictors of Inadequate Response to IABP Therapy

	Univariable analysis		Multivariable analysis	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age	1.02 (0.99 to 1.06)	0.14	0.97 (0.96 to 1.04)	0.85
Male	1.13 (0.38 to 3.37)	0.82	0.73 (0.21 to 2.58)	0.63
Ischemic cardiomyopathy	3.57 (1.59 to 8.04)	0.002	3.24 (1.16 to 9.06)	0.03
Mean arterial pressure (mm Hg)	0.96 (0.92 to 1.0)	0.04	0.99 (0.94 to 1.04)	0.58
Heart rate (beats/min)	1.02 (0.99 to 1.03)	0.14		
Baseline cardiac index (liters/min/m^2)	2.32 (0.75 to 7.15)	0.14		
Central venous pressure (mm Hg)	1.13 (1.06 to 1.21)	<0.001		
Mean PA pressure (mm Hg)	1.02 (0.98 to 1.06)	0.4		
Cardiac power index	1.10 (0.01 to 490.2)	0.98		
PA pulsatility index <2.0	5.14 (2.04 to 12.94)	0.001	5.04 (1.86 to 13.63)	0.001
LV stroke work index	0.86 (0.71 to 1.04)	0.12		
RV stroke work index	0.90 (0.78 to 1.04)	0.16		
Multiple inotropes (>2)	1.05 (0.48 to 2.29)	0.91		
Pressors (≥1)	2.73 (1.19 to 6.23)	0.02	2.24 (0.81 to 6.18)	0.12
Mitral regurgitation (moderate–severe)	0.48 (0.21 to 1.08)	0.08	0.49 (0.19 to 1.27)	0.14

CI, confidence interval; IABP, intra-aortic balloon pump; LV, left ventricle; OR, odds ratio; PA, pulmonary artery; RV, right ventricle.

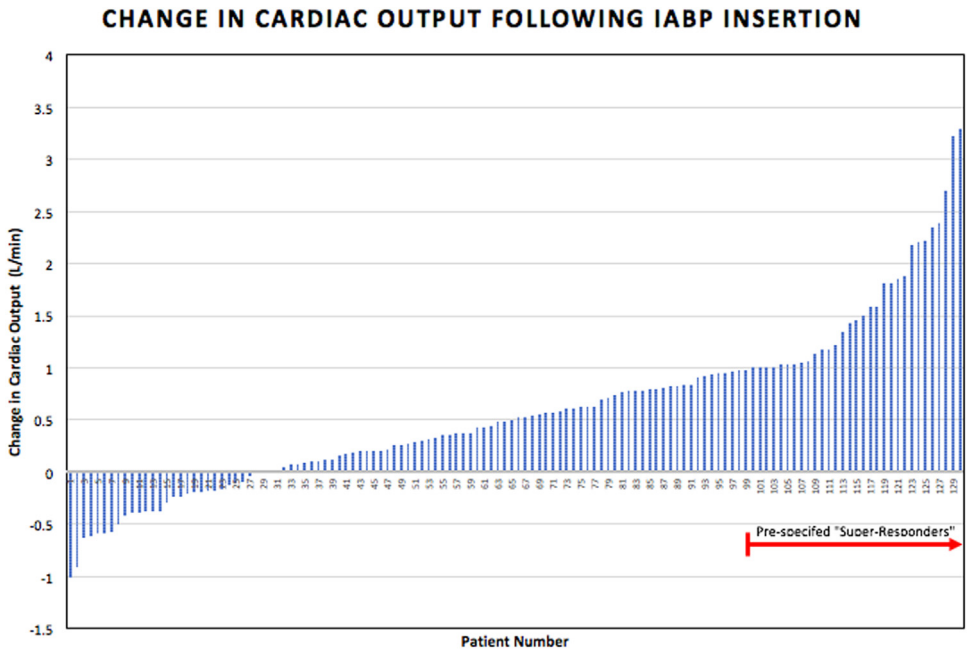

Figure 4 Change in cardiac output after IABP insertion. The top quartile of patients was pre-specified as "super-responders." IABP, intra-aortic balloon pump; L, liters; min, minute.

2.3%. Three patients required ≥2 units of PRBCs during IABP therapy, although only 1 was related to access-site bleeding. The same patient also had critical limb ischemia requiring device removal, and further evaluation diagnosed heparin-induced thrombocytopenia. The additional 2 bleeding events were not related to access site or directly linked to IABP therapy. No patient required endovascular or surgical intervention related to IABP, and no patient had a documented stroke while on IABP support. No pump malfunctions requiring catheter exchange occurred during the study period.

Discussion

In this study we have undertaken a large, in-depth examination of IABP use in chronic systolic HF patients with acute decompensation and CS. We described the clinical and hemodynamic response to IABP in this population and assessed the relative impact of pre-implant demographic, clinical, and hemodynamic parameters on clinical response. Our principal findings are: (1) IABP therapy in select chronic systolic HF patients with CS is associated with a high likelihood of bridge to HRT or discharge without the need for escalation to a more potent tMCSD; (2) poor right ventricular (RV) function, as measured by PAPi, and ICM are associated with clinical deterioration on IABP; and (3) hemodynamic response to IABP is variable in this population, but a robust hemodynamic response is associated with clinical stabilization after implantation.

Despite significant advances in percutaneous interventions and device technology, CS continues to carry short-term mortality rates as high as 30% to 50%, although the findings of the CardShock study suggest that those without

Table 3 Analysis of Potential Predictors of Robust Hemodynamic Response to IABP Therapy

	Univariable analysis		Multivariable analysis	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age	1.02 (0.99 to 1.05)	0.15	1.03 (0.99 to 1.08)	0.07
Male	0.80 (0.28 to 2.28)	0.68	1.40 (0.37 to 5.18)	0.61
Diabetes	0.45 (0.18 to 1.14)	0.09	0.44 (0.15 to 1.32)	0.14
Ischemic cardiomyopathy	0.62 (0.26 to 1.50)	0.30	0.34 (0.11 to 1.07)	0.07
Mean arterial pressure (mm Hg)	1.00 (0.97 to 1.04)	0.841		
Heart rate (beats/min)	0.99 (0.98 to 1.02)	0.876	0.99 (0.96 to 1.02)	0.42
Central venous pressure (mm Hg)	1.03 (0.97 to 1.09)	0.414		
Mean PA pressure (mm Hg)	1.05 (1.00 to 1.10)	0.03	1.07 (1.01 to 1.13)	0.008
Multiple inotropes (≥ 2)	1.12 (0.51 to 2.49)	0.76		
Pressors (≥1)	1.16 (0.49 to 2.75)	0.74		
Baseline eGFR (ml/min/1.73 m^2)	0.99 (0.98 to 1.01)	0.99		
Mitral regurgitation (moderate–severe)	0.76 (0.33 to 1.74)	0.518		

CI, confidence interval; eGFR, estimated glomerular filtration rate; IABP, intra-aortic balloon pump; OR, odds ratio; PA, pulmonary artery.

an acute ischemic etiology of CS have a better prognosis.[11,12] Most studies have focused on patients who develop CS after AMI, and there is a paucity of data among chronic HF patients who develop CS after acute HF decompensation. Although randomized data suggest that the IABP is neither beneficial nor harmful for patients with CS after AMI,[7] our data demonstrate that the IABP may have utility in the treatment of patients with ADHF. Although our data are not randomized, the outcomes of our population are nonetheless encouraging. Despite a lower cardiac power index than patients in the SHOCK trial,[13] we found a 30-day survival of 84.1%, with 78.0% of patients successfully bridged to HRT or discharged without need for escalation to another tMCSD. This finding is consistent with those of the CardShock study, where patients without an ischemia-related etiology of CS had lower mortality rates than acute coronary syndrome patients despite similar clinical presentation and severity.[12] It is, however, important to note that, unlike studies of circulatory support devices in the setting of AMI, the majority of "favorable" clinical outcomes in our study included bridge to HRT as opposed to ventricular "recovery."

CS is not a single clinical entity but rather a condition that exists as a spectrum with varying phenotypes and degrees of severity. Importantly, our cohort of patients met hemodynamic criteria for CS, although they would not be considered severe refractory shock patients (i.e., INTERMACS Profile 1). Tailoring medical- and device-based therapies to the patient and clinical scenario is paramount to improving CS outcomes. The modest immediate hemodynamic response to IABP observed in our study was comparable to findings from earlier reports with this device.[14] Although the IABP may not be sufficient support for an AMI CS patient previously healthy until a catastrophic ischemic insult, it may be sufficient to stabilize many chronic HF patients who have decompensated into CS but had previously adapted to a chronic low-output state. Furthermore, medical therapies aimed to do the same for those with CS pose additional threats to the patient (e.g., arrhythmia) not seen with IABP.

Although the response to IABP therapy may be more pronounced in chronic HF patients, it is important to note that the IABP relies on intrinsic pulsatility to achieve a desired response and is unlikely to be effective in the most severe CS cases, regardless of etiology. For patients with severe refractory shock (INTERMACS Profile 1), other short-term tMCSDs, such as percutaneous LVADs or ventricular assist ECMO, are more appropriate, as they are able to provide a greater degree of hemodynamic support (including biventricular support for some devices/configurations). These devices, however, carry a higher risk of adverse events and their use should be limited to clinical scenarios in which full or nearly full hemodynamic support is required.[15] Our findings are consistent with earlier observations that the IABP carries a relatively low risk of such complications.[7,16] Indeed, even long-term IABP use has been shown to have very low complication rates.[17] Although the number of patients in this study requiring escalation to a more powerful device in attempts to stabilize them is limited, the outcomes of this subset appear inferior to those of the remainder of the cohort. It is unknown whether earlier implantation of such a device or bypassing IABP altogether may have improved these outcomes, but it should be a focus of future research so that patient selection for this and other devices can be optimized.

Our study has identified several predictors of clinical deterioration on IABP, notably low PAPi and ICM. The importance of right ventricular performance in predicting IABP response is consistent with findings from recent retrospective studies on IABP use in chronic HF patients.[18,19] In a cohort of 54 patients bridged to LVAD using IABP, Sintek et al observed that intrinsic contractile reserve, as defined by higher left and right ventricular cardiac power indices, was associated with clinical stabilization on IABP therapy. Similarly, in a retrospective analysis of 107 patients treated with IABP therapy for CS, Krishnamoorthy et al found a higher incidence of unplanned tMCSD escalation in patients with biventricular failure when compared with isolated left ventricular failure (21% vs 2%; $p < 0.001$).[19]

The observation that ICM was associated with clinical deterioration on IABP therapy is notable because the IABP is frequently used in patients with active myocardial ischemia. The tendency of ICM patients to have additional comorbidities like intrinsic renal disease and peripheral vascular disease may in part explain the increase in risk observed relative to their non-ischemic counterparts; however, additional studies are needed to validate and further explore this finding. Importantly, our findings challenge the notion that IABP is largely a therapy for ICM patients; instead, IABP may be considered as first-line device support for patients with ADHF in shock, particularly for those with non-ischemic cardiomyopathy and higher PAPi.

We observed significant variability in the hemodynamic response to IABP insertion. Although our results are consistent with those of previous studies demonstrating an average augmentation of CO of 0.5 liter/min, it is notable that some patients had a more robust improvement in CO that was accompanied by a larger reduction in PA pressures. These patients may be considered "IABP super-responders," akin to those considered super-responders to cardiac resynchronization therapy; therefore, it is not surprising that they had improved clinical outcomes compared with the rest of our cohort. However, it is important to recognize that clinical stabilization and super-response were not perfectly aligned and lack of super-response does not preclude clinical stabilization. Importantly, we found that defining super-response by augmentation of CO (as opposed to other favorable hemodynamic response to IABP) provided the greatest ability to differentiate between those with favorable vs unfavorable clinical outcomes. As with any therapy, a variable response to a hemodynamic support device should be expected. However, given the invasive nature of counterpulsation, clinicians would ideally be able to predict which patients would derive the greatest benefit. Further study of this variability in hemodynamic response is an important next step in advancing the understanding of counterpulsation in decompensated heart failure.

Identification of potential super-responders may be particularly important in the future, given several

developments in this field. First, anticipated changes to heart transplant allocation guidelines in the United States that may prioritize IABP-supported patients will likely take effect shortly.[20] In addition, a larger mega-IABP is now available, although it is not well characterized how this device may affect hemodynamics when compared with smaller IABPs. A retrospective analysis of 150 patients who received this device demonstrated clinical efficacy with 72.7% of patients surviving to hospital discharge, yet 34 required another tMCSD.[21] Finally, the development of fully implantable counterpulsation devices capable of supporting patients out of the hospital for longer periods of time offers exciting opportunities for patients with advanced HF and hemodynamic compromise while awaiting heart transplant.[22]

Limitations

Our study has several notable limitations. The main limitation is its single-center, retrospective design. Although our sample size is among the largest in-depth examinations of IABP use in chronic HF patients, a smaller proportion of patients either required escalation to a more powerful device or were weaned off IABP and discharged without durable LVAD. Furthermore, the decision to escalate to another device was not strictly protocolized. The timing of pre- and post-implantation hemodynamics and laboratory measurements were not uniform nor were vasoactive medications held constant in all cases, limiting our ability to make conclusions regarding immediate hemodynamic response to IABP. Although all patients had CVP, PA pressure, and CO measured before and after IABP insertion, pulmonary capillary wedge pressure was not measured in all instances, potentially preventing us from recognizing the power of this parameter to predict response to this therapy. As such, we also examined the clinical response of IABP therapy in these patients, although we recognize that clinical outcomes may be influenced by additional factors not measured in our study. Importantly, candidacy for advanced therapies was not a prerequisite for enrollment, as has been the case in similar studies of this patient population. Furthermore, all patients received an IABP and the lack of a control group introduces the possibility of selection bias. However, our study population was selected based on perceived clinical need and represents a "real-world" population of chronic HF patients who underwent IABP placement for CS.

In conclusion, in selected chronic HF patients with decompensation into CS, IABP insertion is associated with a high likelihood of clinical stabilization and survival, particularly when used as a bridge to durable LVAD. Preserved RV function may predict a favorable response to this therapy. Hemodynamic response to IABP insertion was highly variable; some patients had a robust response to this therapy with augmentation of CO of at least 1 liter/min, and these "super-responders" had a higher likelihood of favorable clinical outcome. Further study is required to validate these findings and identify predictors of hemodynamic response.

Disclosure statement

A.R.G. has received honoraria from Abiomed. Y.N. has received consulting fees from Abbott Vascular/St. Jude Medical. D.M. has received honoraria from Abbott Vascular and Boston Scientific. A. K. has received institutional grant support from Abbott Vascular, Medtronic, Boston Scientific, Abiomed, CSI, Siemens, Philips, and ReCor Medical. D.B. has received institutional grant support from Abiomed. P.C.C. has received institutional grant support from Abbott Vascular. The remaining authors have no conflicts of interest to disclose.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.healun.2018.03.011.

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