Clinical Investigation

Right Ventricular Dysfunction in Acute Myocardial Infarction Complicated by Cardiogenic Shock: A Hemodynamic Analysis of the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) Trial and Registry

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ABSTRACT

Background: The prevalence and significance of right ventricular dysfunction (RVD) in patients with cardiogenic shock due to acute myocardial infarction (AMI-CS) have not been well characterized. We hypothesized that RVD is common in AMI-CS and associated with worse clinical outcomes.

Methods and Results: We retrospectively analyzed patients with available hemodynamics enrolled in the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial (n = 139) and registry (n = 258) to identify RVD in AMI-CS. RVD was defined by an elevated central venous pressure (CVP), elevated CVP–pulmonary capillary wedge pressure (PCWP) ratio, decreased pulmonary artery pulsatility index, and decreased right ventricular stroke work index. A *P* value of <.01 was used to infer significance. In the SHOCK trial and registry, respectively, 38% and 37% of patients had RVD, but RVD was not associated with 30-day or 6-month survival (hazard ratio [HR] 1.51, (99% CI 0.92–2.49; *P* = .10). RV failure with the use of inclusion criteria from the Recover Right Trial for RV Failure (RR-RVF) requiring percutaneous mechanical circulatory support included elevated CVP and CVP/PCWP and a low cardiac index despite ≥1 inotrope or vasopressor. In the SHOCK trial and registry, respectively, 45% (n = 63/139) and 38% (n = 98/258) of patients met RR-RVF criteria. The RR-RVF criteria were not significantly associated with 30-day mortality in the registry cohort (HR 1.44, 99% CI 1.01–2.04; *P* = .04), or in the trial cohort (HR 1.51, 99% CI 0.92–2.49; *P* = .10).

Conclusions: Hemodynamically defined RVD is common in AMI-CS. Routine assessment with pulmonary artery catherization allows detection of RVD; however, further work is needed to identify interventions that will result in improved outcomes for these patients. (*J Cardiac Fail 2018;24:148–156*)

Key Words: hemodynamics, cardiogenic shock, acute myocardial infarction, right ventricular dysfunction.

Cardiogenic shock remains a major clinical problem and complicates nearly 5%–10% of all acute myocardial infarctions (AMI-CS).[1–3] Despite therapeutic advances, AMI-CS is associated with in-hospital mortality risk of 33%–50%.[4] While AMI-CS due to right ventricular myocardial infarction (RVMI) is known to be associated with high in-hospital mortality rates,[5] the prevalence and prognostic importance of right ventricular dysfunction (RVD) or failure (RVF) in AMI-CS have not been well characterized.

Over the past decade, management of RVD in AMI-CS has evolved to include consideration of acute mechanical circulatory support (MCS) devices specifically designed for the right ventricle (RV-MCS).[6,7] Several studies have reported that early treatment of RVD was associated with less in-hospital

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mortality.[7–9] Recently, the Recover Right Trial evaluated the safety and potential benefit of the Impella RP axial-flow catheter in 30 patients with RVF refractory to medical therapy after cardiac surgery, left ventricular assist device (LVAD) implantation, or in AMI-CS.[6] The Impella RP improved cardiac output (CO) and cardiac filling pressures with 73% overall survival at 30 days and all discharged patients surviving to 180 days. These studies call attention to the importance of early RVD identification in AMI-CS patients by evaluating novel approaches of medical and device therapy directed at the RV and/or RV-MCS to restore end-organ perfusion.

In contrast to left ventricular (LV) dysfunction, which is readily detected by the presence of wall motion abnormalities and diminished ejection fraction, RVD is not easily discerned by clinical imaging and physical examination findings in AMI-CS patients. The assessement of hemodynamic parameters obtained by pulmonary artery (PA) catheterization is essential to the recognition of RVD, but hemodynamic evaluation is not uniformly performed in the AMI-CS setting. Although several clinical, hemodynamic, and imaging criteria have been proposed to characterize RVD after durable MCS implantation and heart transplantation, those criteria have not been consistently associated with clinical outcomes across cardiovascular disease populations.[10,11]

No study has applied existing criteria for RVD to characterize the prevalence and prognostic importance of RVD in patients with AMI-CS. We hypothesized that RVD is commonly associated with AMI-CS regardless of culprit coronary artery, and that RVD, when present, is associated with worse clinical outcomes.

Methods

The SHOCK Trial and Registry

The present analysis used data from the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) Trial and Registry (NCT00000552). The design and results of both trial and registry have been published previously.[2,12,13] Briefly, eligibility criteria entailed myocardial infarction (MI) complicated by shock due to predominant LV dysfunction. A majority of patients enrolled in the trial (95%) and the registry (66%) had placement of a PA catheter for hemodynamic evaluation; the remaining patients with anterior infarction and evidence of pulmonary congestion on radiography did not require PA catheterization for randomization. Criteria for cardiogenic shock were hypotension (systolic blood pressure <90 mm Hg), end-organ hypoperfusion, cardiac index <2.2 $L \cdot min^{-1} \cdot m^{-2}$ of body surface area and a pulmonary capillary wedge pressure (PCWP) ≥15 mm Hg.[2] Patients with "isolated" right ventricular myocardial infarction (RVMI), based on investigator assessment of clinical, electrocardiographic, hemodynamic, and echocardiographic findings, were excluded from enrollment in the trial.[5] The SHOCK trial was prospective, randomized, and controlled to compare the effects of emergent revascularization with angioplasty or coronary artery bypass grafting (n = 152) versus initial medical stabilization (n = 150) on mortality. There was no significant between-strategy difference noted in mortality at 30 days. However at 6 months, a survival advantage was observed in the subjects randomized to early revascularization. Patients with AMI-CS not randomized in the trial were entered into the SHOCK registry (n = 1189) and were assessed for in-hospital mortality only.

Patient Sample and Definitions

All available hemodynamic and medical treatment data for the 286/302 patients in the SHOCK trial and 790/1189 patients in the SHOCK registry who underwent PA catheterization were reviewed. Only patients for whom all of the following hemodynamic data points were available at the time of shock diagnosis were included in the present analysis: (1) central venous pressure (CVP), (2) PCWP, (3) pulmonary artery systolic (PASP) and diastolic (PADP) pressures, and (4) cardiac output/index (CO/CI). The pulmonary artery pulsatility index (PAPi) was defined as PA pulse pressure/CVP.[14–16] The right ventricular stroke work index (RVSWI) was defined as (mean PA pressure − CVP) × stroke volume index (SVI). With the use of these hemodynamic variables, RVD, severe RVD (S-RVD), and the Recover Right Trial[6] criteria for RVF (RR-RVF) were defined based on earlier reports establishing cutoff values for CVP, CVP/PCWP, PAPI, and RVSWI (Table 1).[6,11,14–19] All 4 hemodynamic cutoffs were required to meet criteria for RVD or S-RVD.

Outcome

The primary clinical outcome analyzed was death at 30 days.

Table 1. Hemodynamic Variables For Detection of Right Ventricular (RV) Function

Variable	RV Dysfunction (RVD)	Severe RVD	Recover Right Trial Criteria for RV Failure (RR-RVF)	
CVP	>10 mm Hg	>15 mm Hg	CVP >15 mm Hg OR	
CVP/PCWP	>0.63	>0.8	CVP/PCWP >0.63	
PAPi	<2.0	<1.5	Cardiac index	<2.2 $L \cdot min^{-1} \cdot m^{-2}$
RVSWI	<450 g-m/m^2	<300 g-m/m^2	Inotrope/pressor	≥1

CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure; PAPi, pulmonary artery pressure index; RVSWI, right ventricular stroke work index.

Statistical Analysis

Baseline characteristics are presented as mean ± SD for patients who died compared with those alive at 30 days and compared with the use of Wilcoxon rank sum tests for continuous variables. Categoric variables are presented as percentages and compared with the use of chi-square tests. Variables included the clinical covariates of age, sex, previous MI, hypertension, diabetes mellitus (DM), renal insufficiency, hematocrit, creatinine, and culprit artery. To assess the risk of death across different hemodynamic groups, Cox proportional hazard regression model was used, and hazard ratios (HRs) with 99% confidence intervals (CIs) are reported. Adjusted Cox regression models were also reported in the secondary analysis, with adjustment for age, previous MI, DM, blood urea nitrogen, and culprit artery location in the trial cohort and for age, previous MI, DM, and blood urea nitrogen in the registry cohort. All statistical tests were 2 sided and a P value of ≤.01 was considered to be statistically significant. This more stringent value for significance was chosen to account for multiple hypothesis testing because many previous analyses have been conducted from the SHOCK trial and registry. SAS version 9.4 (Cary, North Carolina) was used for all analyses. Patients with missing data for CVP, PASP, PADP, PCWP, CO, or CI were not considered for analysis.

Results

The Shock Trial

Baseline Characteristics. Data were available for all 4 hemodynamic parameters of the RVD definition in 139/302 patients in the SHOCK trial (Fig. 1). CVP was the most common variable missing for assessment of RVD, resulting in the exclusion of 150 patients. Baseline characteristics and hemodynamic data for survivors versus nonsurvivors at 30 days are presented in Table 2. The mean age of patients was 67 ± 10 years, 32% were female, and 81% were white. These demographics were similar to the overall SHOCK trial cohort.[2]

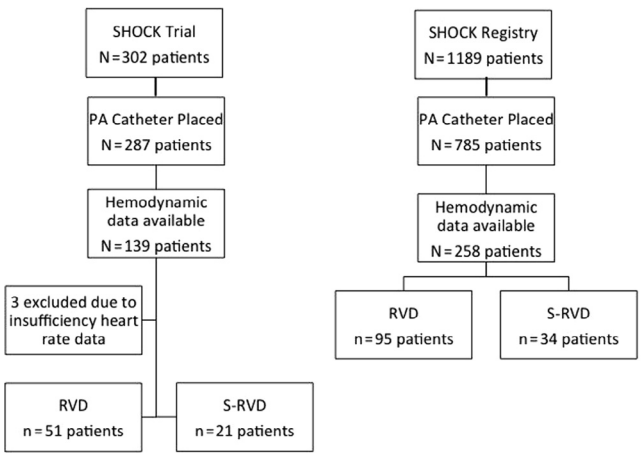

Fig. 1. Flow chart of patient selection in the SHOCK trial and registry cohorts. PA, pulmonary artery; RVD, right ventricular dysfunction.

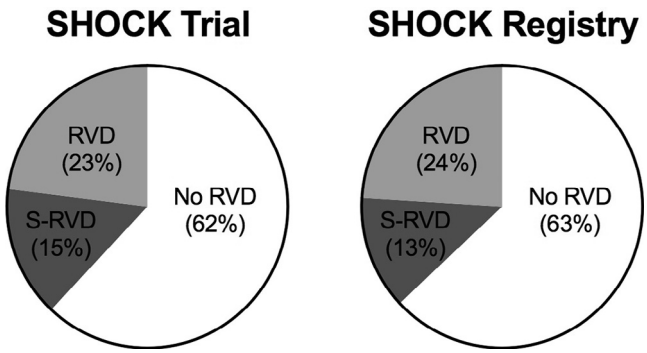

Fig. 2. The prevalence of right ventricular dysfunction (RVD) and severe RVD (s-RVD) in the SHOCK trial and registry cohorts.

Furthermore, baseline characteristics did not differ in patients included for analysis and patients excluded due to missing hemodynamic data (Supplemental Table S3a).

Prevalence of RV Dysfunction

Of the 139 patients included in the analysis, 3 were missing heart rate data, prohibiting calculation of RVSWI, leaving 136 with complete data for assessment of RVD. Based on the prespecified definitions of RVD and S-RVD, 38% (n = 51/136) of AMI-CS patients had evidence of abnormal RV function (RVD 23% and S-RVD 15%; Fig. 2; Table 3). Culprit artery location was significantly different ($P < .01$) between survivors and nonsurvivors 1.9 ± 0.7 versus 1.7 ± 0.5 $L \cdot min^{-1} \cdot m^{-2}$ (Table 2), because nonsurvivors were more likely to have involvement of the left anterior descending artery (LAD). Baseline characteristics for patients with RVD compared with those without RVD are presented in Table 4. Compared with patients without RVD, patients with any RVD were less likely to have had an anterior index MI.

When stratified by CVP and PCWP, 38% of patients (n = 53/139) had severely elevated biventricular filling pressures, defined as a CVP >15 mm Hg and PCWP >18 mm Hg. The profile of isolated elevated LV filling pressures, defined as CVP ≤15 mm Hg and PCWP >18 mm Hg, was observed in 42% (n = 58/139), whereas dominant elevations in RV filling pressures, defined as CVP >15 mm Hg and PCWP ≤18 mm Hg were seen in 3.6% (n = 5/139). More than one-half of patients (55%) demonstrated the presence of elevated biventricular filling pressures, and this profile was common regardless of treatment strategy (early revascularization or initial medical therapy; Fig. 3).

Analysis by Culprit Vessel

Angiography was performed in 97% of the early revascularization treatment arm but only 67% in the medical therapy arm and as such, analysis by culprit vessel was possible for 108/139 (78%) trial patients. The LAD was the culprit vessel in a 51 (47%) of cases and the right coronary artery (RCA) was involved in 34 (31%), followed by the left circumflex artery in 13 (12%). Left main (LM) coronary artery

Table 2. Baseline Characteristics and Hemodynamic Parameters for All 139 Subjects with Complete Hemodynamic Data and Subjects Grouped by Survival Status at 30 Days in the SHOCK Trial

Variable	Overall Cohort (n = 139)	Survivors at 30 Days (n = 77)	Nonsurvivors at 30 Days (n = 62)	*P* Value, Survivors vs Nonsurvivors
Age (y)	67 ± 10	66 ± 10	68 ± 9	.22
Female	32%	35%	29%	.45
Height (in)	66.4 ± 3.9	66.4 ± 3.6	66.3 ± 4.2	.89
Weight (lb)	170 ± 38.9	173.2 ± 40.3	166.0 ± 37.2	.28
BMI (kg/m^2)	27.2 ± 6.3	27.9 ± 6.8	26.4 ± 5.5	.18
Race, n (%)				.24
White	112 (81%)	58 (75%)	54 (87%)	
Black	6 (4%)	3 (4%)	3 (5%)	
Asian	12 (9%)	9 (12%)	3 (5%)	
Other	9 (6%)	7 (9%)	2 (3%)	
Smoking	50%	48%	53%	.59
History				
Previous MI	27%	26%	27%	.85
Hypertension	43%	40%	47%	.39
DM	30%	32%	27%	.50
Renal insufficiency	7%	9%	5%	.51
CHF	4%	5%	3%	.69
CABG	4%	3%	5%	.66
PTCA	6%	8%	5%	.73
Anterior index MI	56%	49%	65%	.07
Laboratory values				
Hematocrit (%)	39 ± 9	39 ± 10	40 ± 9	.33
Creatinine (mg/dL)	1.8 ± 2	1.8 ± 2.4	1.7 ± 1.5	.79
Blood urea nitrogen (mg/dL)	28 ± 23	29 ± 27	27 ± 15	.57
SBP before IABP (mmHg)	87 ± 20	87 ± 189	86 ± 20	.78
DBP after IABP (mmHg)	56 ± 15	55.58 ± 15	56 ± 16	.91
Hemodynamic parameters				
CVP	15 ± 7	15 ± 6	15 ± 7	.88
CVP/PCWP	0.63 ± 0.3	0.66 ± 0.3	0.59 ± 0.3	.16
PASP	42 ± 12	42 ± 11	43 ± 12	.64
PADP	25 ± 8	24 ± 7	27 ± 9	.11
mPAP	31 ± 8	30 ± 8	32 ± 9	.23
Cardiac index	1.8 ± 0.6	1.9 ± 0.7	1.7 ± 0.5	.04
RVSWI (n = 136)	308 ± 168	312 ± 176	302 ± 160	.73
PAPi	1.5 ± 1.2	1.4 ± 0.9	1.6 ± 1.5	.42
Culprit artery location				.01
LM	7 (6%)	4 (6%)	3 (7%)	
LAD	51 (47%)	24 (38%)	27 (61%)	
RCA	34 (31%)	28 (44%)	6 (14%)	
LCX	13 (12%)	7 (11%)	6 (14%)	
SVG	3 (3%)	1 (2%)	2 (5%)	

BMI, body mass index; MI, myocardial infarction; DM, diabetes mellitus; CHF, congestive heart failure; CABG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty; SBP, systolic blood pressure; IABP, intra-aortic balloon pump; DBP, diastolic blood pressure; CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure; PASP, pulmonary artery systolic pressure; PADP, pulmonary artery diastolic pressure; mPAP, mean pulmonary artery pressure; RVSWI, right ventricular stroke work index; PAPi, pulmonary artery pressure index; LM, left main; LAD, left anterior descending; RCA, right coronary artery; LCX, left circumflex; SVG, saphenous vein graft.

Table 3. Hemodynamic Variables of Right Ventricular (RV) Function in SHOCK Trial and Registry Patients, n (%)

Any RV Dysfunction		Severe RV Dysfunction		Recover Right Trial Criteria	
SHOCK Trial Patients (n = 139)					
CVP >10	99 (71%)	CVP >15	58 (42%)	CVP >15 or CVP/PCWP >0.63	58 (42%)
CVP/PCWP >0.63	62 (45%)	CVP/PCWP >0.8	29 (21%)		62 (45%)
PAPi <2.0	109 (78%)	PAPi <1.5	83 (60%)	Cardiac index <2.2	116 (83%)
RVSWI <450	110 (81%)	RVSWI <300	76 (56%)	Inotrope/pressor ≥1	136 (98%)
All criteria	51 (38%)	All criteria	21 (15%)	All criteria	63 (45%)
SHOCK Registry Patients (n = 258)					
CVP >10	176 (68%)	CVP >15	92 (36%)	CVP >15 or CVP/PCWP >0.63	92 (36%)
CVP/PCWP >0.63	118 (46%)	CVP/PCWP >0.8	56 (22%)		118 (46%)
PAPi <2.0	193 (75%)	PAPi <1.5	145 (56%)	Cardiac index <2.2	165 (64%)
RVSWI <450	190 (77%)	RVSWI <300	111 (45%)	Inotrope/pressor ≥1	251 (97%)
All criteria	95 (37%)	All criteria	34 (13%)	All criteria	98 (38%)

Abbreviations as in Table 2.

Table 4. Baseline Characteristics for Patients With Right Ventricular (RV) Dysfunction Compared with Those Without RV Dysfunction in the SHOCK Trial

Variable	Any RV Dysfunction (n = 51)	No RV Dysfunction (n = 85)	*P* Value
Age (y)	68 ± 10	66 ± 9	.22
Female	35%	31%	.57
Height (in)	66.1 ± 4.2	66.6 ± 3.7	.49
Weight (lb)	175.5 ± 46.8	166.5 ± 33.7	.25
BMI (kg/m^2)	28.3 ± 7.1	26.6 ± 5.8	.16
Race			.13
White	45 (88%)	65 (76%)	
Black	1 (2%)	5 (6%)	
Asian	1 (2%)	10 (12%)	
Other	4 (8%)	5 (6%)	
Smoking history	55%	48%	.49
History			
Previous MI	16%	34%	.02
Hypertension	37%	48%	.23
DM	31%	31%	.97
Renal insufficiency	6%	8%	.74
CHF	4%	5%	1.00
CABG	0%	6%	.16
PCI	4%	8%	.48
Anterior index MI	41%	66%	.004
Laboratory values			
Hematocrit (%)	39 ± 8	40 ± 10	.58
Creatinine (mg/dL)	1.6 ± 1.6	1.9 ± 2.3	.45
Blood urea nitrogen (mg/dL)	28 ± 31	28 ± 16	.96
Culprit artery location			.0004
LM	1 (3%)	6 (9%)	
LAD	13 (33%)	37 (55%)	
RCA	23 (58%)	11 (16%)	<.001
LCX	3 (8%)	10 (15%)	.36
SVG	0 (0%)	3 (4%)	

PCI, percutaneous coronary intervention; other abbreviations as in Table 2.

lesions constituted less than 7% and vein graft culprit lesions were even less common. The likelihood of having elevated biventricular filling pressures (as defined by CVP>10 mm Hg and PCWP>18 mm Hg) if the culprit lesion was the RCA versus LAD/LM did not differ (HR 1.47 (0.1–3.57) *P* = .39). However, patients with the RCA as the culprit vessel were three times more likely (HR 3.23 (1.32–3.33)) to have severely elevated biventricular filling pressures (CVP>15 mm Hg and PCWP>18 mm Hg, *P* = .01). Patients with evidence of RVD were more likely to have the RCA as the culprit artery compared to those without RVD (Table 4).

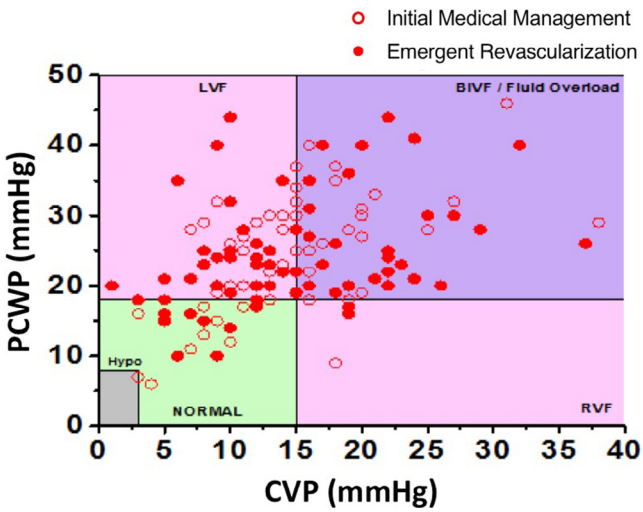

Fig. 3. Scatter plot of central venous pressure (CVP) versus pulmonary capillary wedge pressure (PCWP) according to revascularization status in the SHOCK trial. LVF, left ventricular failure; BIVF, biventricular failure; RVF, right ventricular failure.

The Shock Registry

Data for the baseline hemodynamic variables were available for 258 of the 790 patients enrolled in the registry (Fig. 1). Baseline characteristics stratified by in-hospital survivors versus nonsurvivors are presented in Table 5. Survivors were younger, were less likely to have had a history of MI and DM, and had lower levels of blood urea nitrogen than nonsurvivors. They also had lower mean pulmonary artery (PA) pressure (28 ± 8 mm Hg compared with 30 ± 8 mm Hg; *P* = .01) and higher mean CI (2.3 ± 0.9 compared with 2.0 ± 0.7; *P* = .001). Patients with higher left ventricular stroke work index (LVSWI) and cardiac power output (CPO) were more likely to be alive at 30 days. This was similar to the overall reported registry characteristics and subsequent analyses.[13,20] Baseline characteristics for patients with RVD compared with those without RVD were similar in this cohort of registry patients to the trial cohort (Supplemental Table S1). A majority of patients had CVP >10 mm Hg (68%), PAPi <2.0 (75%), and RVSWI <450 L/min/m^2 (77%), and 37% patients satisfied criteria for RVD, with 13% meeting criteria for S-RVD (Fig. 2; Table 3). Patients included in the present analysis were less likely to have renal insufficiency and distinct culprit artery involvement compared with patients excluded due to missing hemodynamic data (Supplemental Table S3b).

Recover Right Trial Inclusion Criteria

To explore how many AMI-CS patients in the SHOCK trial and registry may have been considered as candidates for a RV-MCS device, we applied the RR-RVF definition[6] to these cohorts (Table 1). Of the SHOCK trial and registry patients studied, 45% (n = 63/139) and 38% (n = 98/258), respectively, satisfied the trial definition of RR-RVF.

Hemodynamic-Clinical Outcome Correlations

The various individual hemodynamic parameters were assessed in relation to the outcome of mortality at 30 days. Although previous studies identified hemodynamic variables associated with clinical outcomes such as CPO in the registry cohort,[20] in the present analysis of the trial cohort there was no association between the assessed hemodynamic variables representing RV function (individually or in sum) and mortality. The presence of severely elevated biventricular filling pressures as defined above was not associated with increased mortality (Table 6; Supplemental Fig. S1). Similar results were seen for 6-month mortality in the trial cohort (Supplemental Table S2). Analyses adjusted for relevant variables including age, previous MI, DM, blood urea nitrogen,

Table 5. Baseline Characteristics and Hemodynamic Parameters for Survivors Versus Nonsurvivors at 30 Days in the SHOCK Registry

Variables	Overall Cohort (n = 258)	Survivors at 30 Days (n = 131)	Nonsurvivors at 30 Days (n = 127)	*P* Value, Survivors vs Nonsurvivors
Age (y)	68 ± 12	65 ± 12	71 ± 11	.0001
Female	43%	37%	49%	.06
Height (in)	66.1 ± 4.1	66.4 ± 4.1	65.7 ± 4.2	.22
Weight (lb)	166.0 ± 36.8	171.2 ± 39.7	160.0 ± 32.4	.02
BMI (kg/m^2)	26.7 ± 4.7	27.2 ± 5.2	26.1 ± 4.1	.10
Race				.87
White	86%	86%	87%	
Black	4%	4%	3%	
Asian	6%	7%	5%	
Other	4%	3%	5%	
Smoking	47%	51%	43%	.21
History				
Previous MI	34%	26%	43%	.005
Hypertension	57%	59%	55%	.48
DM	33%	25%	41%	.004
Renal insufficiency	7%	7%	7%	.9
Laboratory values				
Hematocrit (%)	38 ± 8	38 ± 7	38 ± 8	.72
Creatinine (mg/dL)	1.7 ± 1.5	1.6 ± 1.3	1.8 ± 1.6	.3
Blood urea nitrogen (mg/dL)	29 ± 21	25 ± 19	32 ± 22	.01
Hemodynamic parameters				
CVP	14 ± 6	14 ± 6	15 ± 6	.25
CVP/PCWP ratio	0.64 ± 0.27	0.63 ± 0.25	0.65 ± 0.29	.57
PASP	41 ± 11	39 ± 11	43 ± 11	.01
PADP	23.2 ± 7	22.6 ± 6.44	23.82 ± 7.02	.15
mPAP	29 ± 8	28 ± 8	30 ± 8	.04
Cardiac index	2.1 ± 0.8	2.3 ± 0.9	2.0 ± 0.7	.001
RVSWI	339 ± 199	363 ± 218	315 ± 174	.06
PAPi	1.6 ± 1.2	1.6 ± 1.3	1.6 ± 1.2	.86
LVSWI	1.23 ± 0.67	1.37 ± 0.71	1.02 ± 0.56	.002
CPO	0.58 ± 0.28	0.64 ± 0.30	0.49 ± 0.22	.001
Culprit artery location				.2
LM	2%	1%	3%	
LAD	33%	39%	26%	
RCA	23%	24%	21%	
LCX	10%	7%	13%	
Unspecified	32%	29%	38%	

LVSWI, left ventricular stroke work index; CPO, cardiac power output; other abbreviations as in Table 2.

Table 6. Hemodynamic Variables and Mortality in the SHOCK Trial and Registry Cohorts, Hazard Ratio (99% Confidence Interval)

Variable	Mortality at 30 Days*	*P* Value	Mortality at Discharge	*P* Value
Trial Cohort				
CVP >15 vs ≤15	1.08 (0.56–2.09)	.77	1.06 (0.55–2.04)	.83
PCWP >18 vs ≤18	1.36 (0.56–3.32)	.37	1.28 (0.55–3.02)	.45
CVP/PCWP >0.8 vs ≤.08	0.82 (0.35–1.93)	.55	0.84 (0.36–1.97)	.59
PAPI <1.5 vs ≥1.5	1.19 (0.61–2.32)	.51	1.17 (0.6–2.29)	.54
RVSWI <300 vs ≥300	1.09 (0.56–2.13)	.74	1.01 (0.52–1.97)	.96
All criteria	0.98 (0.39–2.48)	.95	0.99 (0.39–2.5)	.97
Recover Right Trial criteria	1.51 (0.79–2.91)	.10	1.43 (0.75–2.74)	.16
SHOCK Registry Cohort				
CVP >15 vs ≤15	1.39 (0.87–2.21)	.07	1.38 (0.87–2.18)	.07
PCWP >18 vs ≤18	1.44 (0.86–2.4)	.07	1.47 (0.88–2.44)	.05
CVP/PCWP >0.8 vs ≤.08	1.01 (0.58–1.75)	.98	1.02 (0.59–1.76)	.93
PAPI <1.5 vs ≥1.5	0.82 (0.51–1.3)	.26	0.82 (0.52–1.3)	.26
RVSWI <300 vs ≥300	1.17 (0.73–1.88)	.38	1.12 (0.7–1.77)	.54
All criteria	1.15 (0.58–2.3)	.61	1.12 (0.56–2.23)	.68
Recover Right Trial criteria	1.44 (0.91–2.28)	.04	1.35 (0.86–2.13)	.09

Abbreviations as in Table 2.
*30-day and in-hospital mortalities were similar in the SHOCK trial.[2]

and culprit artery location also did not show any association with mortality at 30 days or at discharge (Supplemental Table S4).

Consistent with a previous report,[20] low LVSWI and CPO were associated with increased mortality in the registry cohort (Table 5). The 30-day mortality rate did not differ among registry patients with or without RR-RVF (HR 1.44, 99% CI 1.01–2.04; $P = .04$). A non–statistically significant HR for 30-day mortality was observed in the trial cohort (HR 1.51, 99% CI 0.92–2.49; $P = .10$). No significant association was observed between RR-RVF criteria and 6-month mortality in the trial cohort (HR 1.38, 99% CI 0.86–2.21; $P = .18$).

Discussion

Cardiogenic shock in the setting of acute MI remains a major cause of in-hospital mortality for patients worldwide. This is the 1st report to establish that hemodynamic evidence of RVD and elevated biventricular filling pressures are common in AMI-CS. First, using well established hemodynamic criteria, we identified that both RVD and S-RVD were common among patients in the SHOCK trial and registry despite exclusion of subjects with isolated RV shock from the SHOCK trial. Next, we stratified patients in the SHOCK trial based on cardiac filling pressures and identified that elevated biventricular congestion is common in AMI-CS. The presence of hemodynamically defined RVD according to established thresholds for CVP, CVP/PCWP, PAPi, and RVSWI was not associated with clinical outcome, although in patients with elevated CVP or CVP/PCWP and CS refractory to ≥1 inotropes, higher in-hospital mortality was suggested in both the trial and the registry cohorts. These observations demonstrate that regardless of the culprit coronary vessel, RV compromise is common in AMI-CS. Uniform hemodynamic assessment may allow for early identification of abnormal RV function and biventricular congestion in AMI-CS.

Contemporary management of cardiogenic shock focuses on early revascularization, pharmacologic therapy, or devices that target the failing LV. The role of RV dysfunction in AMI-CS remains poorly understood, but can be expected to be important for several reasons. First, as much as 40% of RV contractile force is derived from the interventricular septum.[21] As a result, occlusion of the left main coronary artery or LAD leads to septal ischemia and a loss of RV contractile force. Second, the RV is highly sensitive to acute increases in afterload.[11] In the setting of left heart failure, increased left atrial pressure will reduce PA compliance and increase PA resistance, thereby leading to an increase in RV afterload and a subsequent decline in RV stroke volume.[22] Finally, elevated right heart filling pressures can reduce LV coronary blood flow and myocardial perfusion,[23] thereby leading to a vicious cycle of worsening biventricular failure. For these reasons, abnormal RV function is likely to be a common occurrence in the setting of AMI-CS, regardless of the culprit coronary vessel.

Previous studies have established that mortality associated with cardiogenic shock due to RVMI is high and equivalent to shock due to LV failure.[5] However, the role of less overt RVD in cardiogenic shock had not been studied. The SHOCK trial excluded patients with isolated RV shock as defined by individual investigators based on investigator assessment of clinical, electrocardiographic, hemodynamic, and echocardiographic findings. In the present analysis, we studied whether patients in the trial without isolated RV shock have evidence of abnormal RV function by first defining RVD and S-RVD according to readily available hemodynamic variables, including CVP, PCWP, PAPi, and RVSWI. Each of these variables has been independently studied and associated with abnormal RV function.[7,11,14–17,19,21,22] RVD defined by the presence of increased CVP and CVP/PCWP and low RVSWI and PAPi was commonly identified in both the SHOCK trial and the registry. Furthermore, with the use of more conservative hemodynamic cutoffs, 15% and 13% met the definition for S-RVD in the trial and registry, respectively. Stratifying patients by CVP and PCWP alone demonstrated that 38% of patients had evidence of increased biventricular filling pressures. These patients may have had greater volume overload (either total body sodium and water overload), increased thoracic volume due to splanchnic venoconstriction and/or biventricular compromise. Overall, these findings suggest that PA catheterizaation–based assessment of hemodynamics allows for the discovery of subclinical RVD and S-RVD in AMI-CS patients.

Next, we explored whether RVD or S-RVD was associated with increased mortality. No single hemodynamic variable nor the use of combined variables to define RVD or S-RVD was associated with clinical outcomes. Although this analysis was limited in that it represented a subset of the total trial population, the absence of association may be explained by variability in timing of hemodynamic assessment as well as by the possibility that factors beyond RV function, such as multiorgan failure, affect clinical outcomes. Furthermore, each hemodynamic parameter is highly dependent on cardiac loading conditions at the time of assessment. Data on volume management were not available, and it may be that many of the cases of RVD had improved hemodynamic parameters later in their clinical course. The inclusion of RVSWI, which, in addition to its dependence on preload, is derived from multiple measures and therefore more prone to error, may have limited the reliability of this variable as a determinant of RV function.

To further explore the association between RVD and mortality, we used the definition of RVF used in the Recover Right Trial, which studied the utility of an axial-flow catheter designed to pump blood from the right atrium into the PA, thereby bypassing a dysfunctional RV. That trial enrolled patients with cardiogenic shock due to RVF after surgical cardiotomy, LVAD implantation, or RVMI. Using the RR-RVF definition, we observed that patients meeting those criteria had a trend toward increased in-hospital mortality in the registry cohort, with a similar ratio observed in the trial cohort at 30 days, which did not reach statistical significance. The

similar HRs of 1.51 ($P = .04$) in the registry and 1.44 ($P = .10$) in the trial cohort suggest limited power to detect a statistically significant difference. To explore this, we performed a post hoc power calculation which revealed that with the use of a 2-sided log rank test with an overall sample of 139 subjects, we had 80% power at .01 significance level to detect an HR of 1.84. Further work is needed to understand an association of RVD with clinical outcome in the AMI-CS population.

Clinicians are challenged by the dilemma of whether placing MCS to improve hemodynamic parameters will translate to improvement in mortality. Although no percutaneous support device has significantly affected 6-month mortality in AMI-CS thus far, there are a number of reasons that this may be the case. A paradigm shift to unloading the heart with a door-to-unload strategy is under investigation.[24] Future prospective studies are required to establish uniform assessment of hemodynamics in the setting of AMI-CS and the clinical implications of RVD in determining which treatment approaches, including pharmacotherapy as well as RV circulatory support pumps, can improve outcomes.

Study Limitations

There are several caveats that limit interpretation of the present post hoc analysis of prospectively collected clinical trial and registry data. Incomplete hemodynamic data for all patients in the overall study cohort may have introduced selection bias in the sample. The main reason for missing data in this analysis was the fact that CVP was not recorded in nearly one-half of the trial patients with PA catheters in place (n = 150). Because the missing data was based on failure to record CVP rather than clinical decision making for placement of the PA catheter, missing data in this scenario is less likely to be due to systematic bias. Similar frequencies of RVD and S-RVD in the trial and registry cohorts with generally similar characteristics (Supplemental Table S3) support the conclusion that abnormal RV function is common in AMI-CS. Assessment of RV function was limited to standard hemodynamic variables because data from imaging studies were not available. Exclusion of subjects with missing hemodynamic data also reduced the power to detect an association between measures of RVD and clinical outcomes.

Conclusion

RV dysfunction, as defined by multiple clinically accepted indexes, is common in AMI-CS regardless of the culprit coronary vessel, even when isolated RV shock is excluded. Further prospective studies focused on defining RVD and evaluating its prevalence and the potential utility of the RR-RVF as a determinant of clinical outcomes in AMI-CS are warranted.

Disclosures

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Supplementary Data

Supplementary data related to this article can be found at doi:10.1016/j.cardfail.2017.10.009.

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