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HEMODYNAMIC RESUSCITATION CHARACTERISTICS ASSOCIATED WITH IMPROVED SURVIVAL AND SHOCK RESOLUTION AFTER CARDIAC ARREST

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Abstract

Purpose—To determine which strategy of early post-cardiac arrest hemodynamic resuscitation was associated with best clinical outcomes. We hypothesized that higher mean arterial pressure (MAP) achieved using IV fluids over vasopressors would yield better outcomes.

Methods—Retrospective cohort study of post-cardiac arrest patients between March 2011 and June 2012. Patients successfully resuscitated from cardiac arrest, admitted to an ICU and surviving at least 24 hours were included. Patients missing data for >2 hours after ROSC were excluded. The institutional standard for post-resuscitation MAP was 65 mmHg with no guidelines on how MAP was supported. We examined the association between early (6h) average MAP, vasopressor use summarized as cumulative vasopressor index (CVI) and fluid intake with outcomes including survival to discharge, favorable neurologic outcome based on Cerebral Performance Category (CPC) 1 or 2, and the surrogate outcome measure of lactate clearance using Pearson correlation and multivariable regression.

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Results—Of 118 patients, 55 (46%) survived to hospital discharge, 21 (18%) with favorable neurologic outcome. Higher 6h mean CVI was independently associated with worsened survival (OR 0.67; 95% CI 0.53, 0.85; $p = 0.001$). Resuscitation subgroups receiving higher than median vasopressors had worsened survival to hospital discharge regardless of fluid intake. In addition, higher MAP-6h correlated with increased lactate clearance ($r=0.29$; $p= 0.011$)

Conclusions—Early post-ROSC hemodynamic resuscitation achieving higher MAP using fluid preferentially over vasopressors is associated with improved survival to hospital discharge as well as better lactate clearance.

Keywords

Cardiac Arrest; Shock; Resuscitation; Post-Cardiac Arrest Syndrome; Hemodynamics; Vasopressors; Fluid Administration

Introduction

Shock, a component of the post-cardiac arrest syndrome, is prevalent after resuscitation from cardiac arrest (1). This state of hemodynamic compromise often persists after return of spontaneous circulation (ROSC), and is associated with both increased in-hospital mortality and diminished functional outcome (2). This post-ROSC shock state may be secondary to myocardial dysfunction (2-4), a sepsis-like state (5), or both. Prior reports have noted an association between vasopressor use and mortality (1, 6, 7), even though higher blood pressure is also associated with improved outcomes (6). While some post-ROSC patients preserve adequate mean arterial pressure (MAP) without any hemodynamic intervention, many require significant resuscitation to achieve an appropriate MAP. It is unknown whether volume resuscitation or vasopressor administration is preferable for the shock state post-ROSC.

After ROSC, hemodynamic dysfunction is the major extracerebral injury associated with in-hospital mortality (1). Given the parallels between cardiac arrest and sepsis (cytokine storm and myocardial dysfunction)(5), the International Liaison Committee on Resuscitation (ILCOR) and American Heart Association (AHA) have adopted similar goal-directed hemodynamic treatment recommendations as those used for sepsis (8) but little direct evidence supports MAP targets or the optimal means to achieve MAP (9). Improved outcomes have been noted with MAP of 65-75 mmHg (10), 80-100 mmHg (11), and >100 mmHg (12) compared to historical controls with lower MAP. However, the ideal MAP after ROSC is unknown, and hemodynamic management is rarely explicitly defined in post-resuscitation care observational studies (13). Optimization of cardiac output using fluids may improve tissue perfusion (14) over merely achieving MAP targets using vasopressors. This leaves considerable uncertainty surrounding the optimal post-cardiac arrest resuscitation strategy.

To better define the various strategies for early post-ROSC resuscitation, we ascertained MAP, the volume of resuscitative fluid used, and the amount of vasopressor used for a cohort of post-cardiac arrest patients at our institution. We then tested the associations between resuscitation strategy and clinical outcomes, and in a subset examined the

association with lactate clearance (7, 15-17). We hypothesized that achieving higher MAP using volume resuscitation preferentially to vasopressors would be associated with improved outcomes which may also manifest as faster lactate clearance.

Materials and Methods

Data from all patients at UPMC Mercy Hospital who received chest compressions or defibrillation, either in the hospital or prior to arrival, are entered into a quality improvement (QI) registry. The University of Pittsburgh Institutional Review Board approved retrospective analysis of this data as exempt and waived the requirement for informed consent to permit acquisition of additional data to address our study hypotheses.

Study Setting and Population

Data are from a single university-affiliated hospital with 59 critical care beds staffed by a single intensivist group providing 24/7 coverage. During the study period the institutional target for post-resuscitation MAP was 65 mmHg. No protocol existed to assess volume status or to direct fluid intake vs. vasopressors to achieve goal MAP. Hypothermia (target temperature 33°C) was provided for 24h using intravascular cooling (Thermoguard XP, Zoll, Chelmsford, MA) to all comatose patients regardless of presenting rhythm. EEG use was at the discretion of the provider but is only available for episodic not continuous monitoring and from quality assurance data is generally used in ~50% of comatose patients at days 2-3. There are no institutional guidelines on neuroprognostication and this is left to the judgement of the critical care provider. Sedation is targeted in all critically ill patients to Riker 3-4 with occasional rare exceptions. Our ICUs employ daily sedation interruptions to minimize over-sedation. Recently we reported that for cardiac arrest patients admitted to this center during a time period inclusive of the study dates (18) the rate of survival to discharge was 41% and the rate of good neurologic outcome was 19%.

Study Design

This retrospective cohort study included all adult (age ≥ 18 years) patients successfully resuscitated from out of hospital cardiac arrest (OHCA) or in hospital cardiac arrest (IHCA) from March, 2011 to June, 2012 and admitted to the ICU. We excluded patients who did not survive 24 hours beyond hospital admission. Most of these excluded early deaths resulted from limitation of care (withdrawal of life support or limited resuscitation), which significantly impacted the aggressiveness of early resuscitation.

Study Definitions and Outcome Measures

We collected vital signs, vasopressor and inotrope infusion rates, fluid intake, output and balance from the electronic health record for each patient during the initial 6 hours after ICU admission with “baseline” corresponding to the initial values at ICU admission. Echocardiogram data was also collected, however this was not available for all patients. Vasopressor use was summarized hourly using the cumulative vasopressor index (CVI), which yields a numeric score that represents the dose and number of vasopressor agents used (19). CVI ≥ 2 represents a moderate vasopressor requirement and values > 4 represent high doses. Inodilators (milrinone and dobutamine) are not included in this index.

Clinical outcomes were survival to hospital discharge and favorable neurologic outcome defined as a discharge cerebral performance category (CPC) 1 or 2. Both outcomes were binary. To assess the association between MAP and shock resolution, we used the surrogate lactate clearance (mmol/L/day) which in prior cardiac arrest studies has been associated with outcome. We extrapolated 24h clearance using the first two measures obtained in the ICU provided they were drawn at least two hours apart (four cases used first and third measures). Lactate values were a median of 6.5 hours apart (IQR 4.5 – 12 hours), the first value generally obtained within 1h of ICU admission.

We defined “early” resuscitation as the first 6h of ICU care. We calculated the mean of the initial 6h ICU MAP (MAP-6h) and CVI (CVI-6h) as well as the sum of fluid intake in the first 6h. To delineate resuscitation groups based on management differences, we created dichotomized groups of high vs. low fluid intake and CVI based on the median distributions in the entire cohort. This resulted in four resuscitation subgroups:

1. Low fluids/low pressors: 6h fluid intake $\leq$ 700 ml, CVI $\leq$ 1
2. High fluids/low pressors: 6h fluid intake $>$ 700 ml, CVI $\leq$ 1
3. Low fluids/high pressors: 6h fluid intake $\leq$ 700 ml, CVI $>$ 1
4. High fluid/high pressors: 6h fluid intake $>$ 700 ml, CVI $>$ 1

Fluid intake=700 ml and average CVI=1 cutoffs approximated the cohort medians.

Missing Data

Data was complete for all variables except the hourly heart rate (HR) and MAP. For MAP, we preferentially used invasive arterial MAP as recorded or by calculating the value from the arterial systolic and diastolic blood pressures using the equation $MAP = [(systolic + 2 * diastolic) / 3]$. If this was missing or an arterial line was not placed, values were obtained from cuff measurements. If no hourly value was available for MAP or HR, we used the average value obtained from the hour before and after. We were missing 38/826 (4.6%) of HR and 56/826 (6.8%) of MAP values in 28/118 (24.7%) and 35/118 (29.7%) of subjects, respectively. HR and MAP missingness were correlated to one another (i.e., both data elements missing at same time; Spearman rho = 0.662, $p < 0.001$) but there was no association between missing data and shock severity (baseline MAP or CVI), injury severity (PCAC) or outcomes.

Statistical Analyses

Analyses were performed with SPSS v.22 (IBM, Armonk, NY) by the team statistician (DW) independent of the investigators. R version 3.0.0 (R Foundation for Statistical Computing, Vienna, Austria) was used along with the user-written package “rms” to assess regression diagnostics and test the assumption of linear relationships via restricted cubic splines (20). Analyses involving lactate clearance were restricted to the subset with complete lactate clearance data (n=79). All other analyses were completed within the full cohort (n=118).

Multivariable logistic regression tested the association of MAP-6h, IVF-6h, and CVI-6h with survival. We adjusted for all three of these variables simultaneously. Potential candidate covariates for the model included age, sex, OHCA, initial rhythm dichotomized as shockable (VF/VT) or not, PCAC (Pittsburgh Post-Cardiac Arrest Category) score, initial MAP and initial CVI dichotomized as not needing vasopressors (CVI=0; 78% of population) or needing vasopressors. In our model, we utilized PCAC, baseline MAP, and baseline vasopressor requirement, since these were felt to be the most clinically significant. The PCAC is a validated injury severity score based on early neurologic exam and SOFA respiratory and cardiovascular subscales. PCAC 1 is a patient who is following commands (best prognosis) and PCAC 4 is a deeply comatose patient (worst prognosis)(19). The Hosmer-Lemeshow test confirmed goodness-of-fit in adjusted logistic models. Similar multivariable regression could not be employed for good neurologic outcome due to limited good outcomes (n=21). In this multivariable model we therefore only included the most significant covariate (PCAC).

In a pre-specified analysis aimed at identifying a potential “optimal” resuscitation strategy, we compared clinical outcomes among the four resuscitation groups described above. We compared the proportion of patients surviving to hospital discharge across groups using the Fisher’s exact test. We used logistic regression to assess the association between resuscitation subgroup and clinical outcomes. The low fluid/low vasopressor subgroup was considered the reference group as it had the best outcomes and appeared to be the group with the lowest degree of shock. Due to the small sample size, further covariate adjustments could not be made.

We tested the correlation of MAP-6h, IVF-6h, and CVI-6h with lactate clearance as a surrogate for shock resolution. After using restricted cubic splines to confirm that the assumption of a linear relationship was not violated between these three variables and lactate clearance, we reported Pearson r correlations for these relationships. We compared mean lactate clearance by ANOVA using clinically relevant cut-points of < 65mmHg, 65-80 mmHg (10), and > 80 mmHg (11, 12). After using variance inflation factor (VIF) to rule out multicollinearity problems among MAP-6h, CVI-6h, and IVF-6h, we tested the association between these variables and lactate clearance by linear regression. We adjusted for these three variables simultaneously, as well as initial lactate, initial CVI, and initial MAP to account for shock severity. This model did not present major collinearity diagnostic issues (VIF or residuals), and the assumption of a linear relationship was confirmed to be acceptable through the use of restricted cubic splines in diagnostic testing.

We compared ejection fraction between our 4 resuscitation groups using one-way ANOVA. Comparison of SpO₂:FiO₂ ratios over time was made using repeated measures ANOVA for the two intermediate subgroups (low fluids/high pressors and high fluids/low pressors).

Results

183 subjects were admitted to our ICUs within 2 hours of ROSC. 65 subjects died within the first 24 hours due to limitation of care or recurrent arrest without ROSC leaving 118 subjects in the final cohort (Fig. 1). A subset of the final cohort (n=79) had complete lactate

clearance data available. Clinical features of the full cohort (n=118) are presented in Table 1. Compared to the full cohort, the lactate subset had more severe injury based on trends towards more vasopressor and inotrope use and worsened PCAC (21, 22) scores indicating more severe post-cardiac arrest illness.

Clinical Outcomes

55/118 patients (46%) survived to hospital discharge and 21/118 (18%) had favorable neurologic outcome. Adjusting for shockable initial rhythm, OHCA, and PCAC score ($p < 0.05$ in forward stepwise regression), we found that CVI-6h was associated with survival to hospital discharge (OR 0.68; 95% CI 0.53, 0.87; $p = 0.002$) (Fig. 2a). No exposure variable assessed was associated with neurologic outcome (Fig. 2b). Both models had acceptable fit.

Different Resuscitation Strategies

All four groups displayed similar distributions of baseline MAP and 6h average MAP (Fig. 3a). There were 38 patients in the low fluid/vasopressor group, 21 in the low fluid/high vasopressor group, 19 in the high fluid/low vasopressor group, and 40 in the high fluid/vasopressor group. Only one patient received any dobutamine in the first 6 hours and none received milrinone. There was a trend towards higher baseline heart rate and CVI in the high fluid/vasopressor group and higher MAP in the low fluid/vasopressor group (Table 1). Compared to the low vasopressor group (6h mean CVI $\pm$ SD = 0.08 ± 0.23), the high vasopressor group received on average significantly greater exposure to pressors (6h mean CVI $\pm$ SD = 4.23 ± 3.27 ; $p < 0.001$) during the initial 6h of resuscitation. Likewise, compared to the low fluid intake group, (6h mean intake $\pm$ SD = 270.3 ± 222.1 ml), the high fluid intake group received on average significantly greater volume (6h mean intake $\pm$ SD = 1195.1 ± 1163.5 ml; $p < 0.001$).

The number of survivors to hospital discharge for each subgroup is shown in Figure 3b. Survival significantly differed between the four groups ($p = 0.001$). The baseline variables suggested that the high fluid/vasopressor group had the most severe degree of shock and the low fluid/vasopressor group had the least degree of shock. Within the two intermediate groups (similar baseline characteristics; Table 1) we noted significantly greater survival in the high fluid/low vasopressor group (14/19; 74%) compared to the low fluid/high vasopressor group (6/21; 29%) by post-hoc pairwise comparison (Bonferroni adjusted $p = 0.024$). Independent of fluid intake, above-median vasopressor use was associated with worsened survival to hospital discharge (low fluids: OR [95%CI] = 0.261 [0.083, 0.823]; high fluids: OR [95%CI] = 0.247 [0.096, 0.640]; (Fig. 3c).

To examine whether differences in resuscitation strategy could be accounted for by differences in cardiopulmonary function, we compared the ejection fraction (EF) derived from ECHO performed within 48h of ROSC and the hourly SpO₂:FiO₂ ratio during the first 6h of resuscitation by group. No difference ($p = 0.214$) was observed between the hourly mean SpO₂:FiO₂ of the low vasopressor/high fluid intake group (n=19) and the high vasopressor/low fluid intake group (n=21) (Fig. 4a) nor in the first EF recorded post-ROSC (mean difference of -3.3 [95% CI: -14.3 to 7.7]) (Fig. 4b).

Lactate Clearance

Higher MAP-6h correlated with increased lactate clearance ($r=0.29$; $p=0.011$) (Fig. 5a). Lactate clearance increased across ascending MAP ranges ($p=0.022$) (Fig. 5b). There was no evidence of multicollinearity between MAP-6h, IVF-6h, and CVI-6h. Adjusting for all three simultaneously, MAP-6h ($\rho=0.233$; $p=0.045$), and IVF-6h ($\rho=0.004$; $p=0.001$) were associated with increasing lactate clearance whereas CVI-6h ($\rho=-1.007$; $p=0.039$) was associated with decreasing lactate clearance. These associations persisted after controlling for shock severity by adding initial lactate, CVI and MAP into our models.

Discussion

In our cohort, we observed that higher use of vasopressors was independently associated with mortality. Perhaps most interesting, lower fluid resuscitation (<700 mL) and high vasopressor use ($CVI > 1$) resulting in similar MAP as the opposite strategy was associated with increased inpatient mortality despite no observable differences in baseline characteristics between the patients in these two subgroups or differences in cardiopulmonary physiology to explain the chosen strategy. Finally, lactate clearance was correlated with higher MAP, and we noted a step-wise increase in lactate clearance at progressively higher MAP bands (MAP <65 , 65-80 and >80 mmHg). In multivariable regressions including all three resuscitation variables (MAP, CVI and fluid intake) the use of increasing vasopressors was inversely associated with lactate clearance whereas higher MAP and fluid intake both had positive associations.

Higher MAP has been associated with improved survival in post-cardiac arrest patients in several other studies (6, 11, 12) and likely speaks to improved perfusion pressures and less myocardial dysfunction. Elevated admission lactate levels have been associated with duration of ischemia and neurological impairment (23). Other studies have shown that lactate clearance or lower serum lactate levels correlate with improved survival (15, 24, 25). Admittedly, this is only a surrogate for effectiveness of resuscitation, but it was the one most readily available in this retrospective study and does have some association with outcomes in prior work performed in cardiac arrest. Although higher MAP translates into higher afterload and increased myocardial work, it is ultimately neurologic injury that most often dictates clinical outcomes after cardiac arrest (26). Targeting higher MAP may be beneficial for cerebral perfusion, due to impaired autoregulation post-cardiac arrest (27). Ultimately, we cannot elucidate in this cohort whether higher MAP was the direct result of resuscitation or the degree of post-cardiac arrest injury such that higher MAP in many cases may be just a marker of reduced ischemic injury, not the result of therapy (6, 11, 12).

Our data address some limitations of previous work by examining how MAP was attained (fluid intake vs. vasopressors). Our findings suggest that high vasopressor use to achieve higher MAP may be detrimental. Figure 2b demonstrates the independent association between increased CVI and worsened survival, while Figure 3 highlights the same association irrespective of the amount of fluids given. Several recent studies have also identified associations between vasopressors and poor outcomes (7, 28). It may be that pharmacologic vasoconstriction, intended to improve vital organ perfusion, reduces microvascular perfusion of those same vital tissues. The exact mechanism for the adverse

effect of vasopressors is unknown. Increased vasopressor requirements may reflect poor peripheral vascular responsiveness or just severe underlying shock.

The stratification and comparison of different resuscitation therapies focusing on the use of fluids or vasopressors is a novel feature of this study. It is important to look at both fluids and vasopressors since the use of vasopressors may merely be a marker of shock severity and thus predicts poor outcomes. Indeed, when comparing the low fluid/vasopressor (least shock) and high fluid/vasopressor (most shock) groups (Fig. 3b) clear mortality differences exist. However, the middle groups where patients had similar MAP, the use of liberal fluid resuscitation over vasopressors was associated with better survival. This suggests that some of the mortality benefit may be attributed to improved shock resolution based on the resuscitation strategy selected. An important limitation of this retrospective study is that it is unclear what parameters guided the decision to use fluids over pressors. Examination of pulmonary ($\text{SpO}_2\text{:FiO}_2$) and cardiac function (EF) did not show differences which could explain physicians' desire to withhold or liberally provide fluids (Fig. 4). We are unable to comment further on why difference exist in the management of these patients who otherwise appear fairly similar at the outset. The use of early invasive monitoring including pulmonary artery catheters or central venous oximetry was low in our cohort (<20%), but nearly all patients in our cohort had arterial catheters. Thus, clinicians could have estimated fluid responsiveness by bedside pulse pressure variability assessment, (29) but this data did not appear in the medical record. Likewise echocardiogram data was only available for 75 of the 118 patients (63.6%).

It is physiologically plausible that increasing intravascular volume using fluids could increase cardiac output and tissue perfusion without constricting arteriolar beds and avoiding shunting (as occurs with vasopressors)(30). Our findings suggest the early use of fluids preferentially over vasopressors, assuming volume responsiveness, could improve outcomes in cardiac arrest patients in the ICU. The initial liberal use of fluids (30 ml/kg) and subsequent titration (based on fluid responsiveness) is already advocated by international committees for resuscitation from septic shock (31). Although pre-hospital use of aggressive fluid resuscitation may have adverse effects after ROSC (32), our definition of "early" was the ICU course which began often an hour after ROSC. As one gets further from ROSC and the effects of drugs given for resuscitation and mechanical compressions are more distant, the heart may better tolerate an increase in preload without precipitating heart failure. Our findings at least provide equipoise when considering liberal fluid resuscitation in the early post-ROSC hours despite probable post-arrest myocardial dysfunction (2-4).

Our results do not support the indiscriminate use of IV fluids as the primary means of sustaining a target MAP. Aggressive fluid resuscitation carries risks, including both pulmonary edema and even re-arrest (33). Furthermore, use of liberal fluid resuscitation in patients unlikely to be fluid responsive can worsen outcomes (34). Cardiac arrest patients with a significant component of systemic inflammation-mediated distributive shock (5) would likely have vasoplegia and require some degree of vasopressors in order maintain vascular tone independent of the impact of fluids on cardiac output. Exactly what that balance should be has not been defined, but may be guided by frequent assessment of fluid responsiveness. Practically speaking, ICU nurses are often allowed to titrate vasopressors to

a target MAP, but are not given similar liberty to administer fluids. Thus, increasing vasopressor dosage to maintain MAP may get priority over fluid boluses for practical rather than physiologic reasons. Our data suggest that the singular use of vasopressors to target MAP levels post-cardiac arrest may be less beneficial than a matched fluid-and-vasopressor approach, which should prompt clinicians to design protocols aimed at optimizing the complex hemodynamics of post-cardiac arrest syndrome (9).

Limitations

Our retrospective study design and the size of our data set both limit the conclusions we can draw. The decision to target higher MAP and whether to use fluids or vasopressors was at the discretion of individual physicians and nurses, so we cannot know all of the variables that influenced treatment decisions. A formal, prospective assessment comparing resuscitation strategies is needed to define optimal MAP, fluid and vasopressor targets, and the utility of a tailored approach to account for the clinical heterogeneity encountered in post-arrest patients. Our work does provide some suggestion of what constitutes an “optimal” MAP, and the consistency of the findings through differing analytic approaches provides some strength. The use of a summary scoring system such as CVI as a measure of vasopressor dependence is a limitation since it does not reflect subtle differences among patients with similar CVI. Our use of lactate clearance as a measure of shock resolution was somewhat limited by the smaller number of patients in whom serial lactate levels were measured, and it is unclear how well our calculation of lactate clearance approximates shock resolution. It should be noted that in our own data set, lactate clearance did not associate with better outcome (data not shown) although it has in other groups’ prior work (15-17, 24, 25). CPC was utilized in this study as a measure of neurologic outcome due to its universal availability among these patients. However, CPC does not correlate well with other measures of neurologic outcome such as discharge location or modified Rankin Scale. Neurologic outcome improves over time with ongoing rehabilitation or therapy (35). This work addresses an important gap in the present literature by evaluating the impact of MAP, vasopressor use, and fluid use on shock resolution and clinical outcomes.

Conclusions

Early resuscitation achieving higher MAP using fluid preferentially over vasopressors is associated with improved survival to hospital discharge. Prospective evaluation of a strategy assessing fluid responsiveness and prioritizing fluid resuscitation over vasopressor use to resolve post-resuscitation shock is warranted.

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Figure 1. Consort diagram of patient flow

Of the 183 patients admitted to the hospital with cardiac arrest in the study period, only 118 met the inclusion criteria of survival at least 24 hours. Only 79 of these had the required data to be included in the lactate clearance analysis.

Figure 2. Association between hemodynamics and outcomes

Adjusted associations between hemodynamic variables and survival to hospital discharge (a) or favorable neurologic survival (b). MAP: mean arterial pressure. CVI: cumulative vasopressor index.

Figure 3. Clinical outcomes stratified by resuscitation subgroup

(a) Baseline and 6 hour average MAP are shown for each resuscitation group with no significant differences. (b) The proportion of patients surviving to hospital discharge for each subgroup is shown with more (Exact $p=0.001$) survivors in the low vasopressor/high fluid intake group (14/19; 74%) compared to the high vasopressor/low fluid intake group (6/21; 29%). (c) The odds ratio and 95% CI of survival to hospital discharge for each subgroup indicates an association with worsened survival in both groups where higher vasopressor doses were used (*, $p<0.05$).

Figure 4. Cardiopulmonary factors associated with different resuscitation strategies

Hourly mean SpO₂:FiO₂ was used as a measure of oxygenation as an alternative to PaO₂:FiO₂ ratio (a). On comparison using ANOVA, no statistically significant difference ($p=0.214$) was observed between the low vasopressor/high fluid intake group ($n=19$) and the high vasopressor/low fluid intake group ($n=21$). There was no difference in Echocardiogram derived EF among the four subgroups (b). Comparison of low F/high VP vs. high F/low VP using Sidak's multiple comparison test yielded a non-significant mean difference of -3.3 (95% CI: -14.3 to 7.7).

Figure 5. Relationship between mean arterial pressure (MAP) and lactate clearance
Correlation between MAP and lactate clearance during the early post-cardiac arrest phase (a). Solid horizontal line represents no change in lactate, whereas vertical dashed lines represent MAP targets based on consensus guidelines (65 mm Hg) and/or conventional practice (80 mm Hg). Mean lactate clearance of patients stratified by MAP targets (b).

Table 1

Baseline characteristics of study population.

	Full Cohort (n=118)	Low pressor/fluid (n=38)	High pressor/low fluid (n=21)	Low pressor/high fluid (n=19)	High pressor/fluid (n=40)
Age (years)	63.6 ± 17.5	61.4 ± 17.5	65.4 ± 19.9	60.7 ± 15.7	66.0 ± 17.1
Male Sex	66 (56%)	18 (47%)	13 (61%)	11 (58%)	24 (60%)
Out of Hospital Arrest	58 (49%)	22 (57%)	9 (43%)	10 (53%)	17 (43%)
Presenting Rhythm					
Ventricular fibrillation or tachycardia	25 (21%)	9 (24%)	4 (19%)	3 (16%)	9 (23%)
Pulseless electrical activity	45 (38%)	11 (29%)	9 (43%)	7 (37%)	18 (45%)
Asystole	28 (24%)	10 (26%)	6 (29%)	5 (26%)	7 (18%)
Unknown	20 (17%)	8 (21%)	2 (10%)	4 (21%)	6 (15%)
Pittsburgh Cardiac Arrest Category					
I	40 (34%)	17 (45%)	5 (24%)	6 (32%)	12 (30%)
II	15 (13%)	5 (13%)	2 (10%)	7 (37%)	1 (3%)
III	21 (18%)	3 (8%)	5 (24%)	2 (11%)	11 (28%)
IV	42 (36%)	13 (34%)	9 (43%)	4 (21%)	16 (40%)
Initial HR	100.3 ± 28.7	100.8 ± 30.1	91.4 ± 33.4	90.0 ± 34.9	92.9 ± 32.2
Initial MAP	92.6 ± 32.2	96.5 ± 26.3	93.2 ± 20.5	98.2 ± 30.3	108.7 ± 32.5
Initial CVI	1.0 ± 2.3	0	0.4 ± 1.2	0.5 ± 1.9	2.4 ± 3.3
Inotrope Use	47 (40%)	5 (13%)	13 (62%)	4 (21%)	25 (63%)
Length of Stay	14.4 ± 19.8	15.6 ± 11.1	16.6 ± 31.7	12.9 ± 9.3	16.4 ± 30.7

Continuous data is presented with Mean ± Standard Deviation.