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Response to Fluid Boluses in the Fluid and Catheter Treatment Trial

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BACKGROUND: Recent emphasis has been placed on methods to predict fluid responsiveness, but the usefulness of using fluid boluses to increase cardiac index in critically ill patients with ineffective circulation or oliguria remains unclear.

METHODS: This retrospective analysis investigated hemodynamic responses of critically ill patients in the ARDS Network Fluid and Catheter Treatment Trial (FACTT) who were given protocol-based fluid boluses. Fluid responsiveness was defined as ≥ 15% increase in cardiac index after a 15 mL/kg fluid bolus.

RESULTS: A convenience sample of 127 critically ill patients enrolled in FACTT was analyzed for physiologic responses to 569 protocolized crystalloid or albumin boluses given for shock, low urine output (UOP), or low pulmonary artery occlusion pressure (PAOP). There were significant increases in mean central venous pressure (9.9 ± 4.5 to 11.1 ± 4.8 mm Hg, $P < .0001$) and mean PAOP (11.6 ± 3.6 to 13.3 ± 4.3 mm Hg, $P < .0001$) following fluid boluses. However, there were no significant changes in UOP, and there were clinically small changes in heart rate, mean arterial pressure, and cardiac index. Only 23% of fluid boluses led to a ≥ 15% change in cardiac index. There was no significant difference in the frequency of fluid responsiveness between boluses given for shock or oliguria vs boluses given only for low PAOP (24.0% vs 21.8%, $P = .59$). There were no significant differences in 90-day survival, need for hemodialysis, or return to unassisted breathing between patients defined as fluid responders and fluid nonresponders.

CONCLUSIONS: In this cohort of critically ill patients with ARDS who were previously resuscitated, the rate of fluid responsiveness was low, and fluid boluses only led to small hemodynamic changes.

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ABBREVIATIONS: APACHE = Acute Physiology and Chronic Health Evaluation; CVP = central venous pressure; FACTT = Fluid and Catheter Treatment Trial; HR = heart rate; MAP = mean arterial pressure; PAC = pulmonary artery catheter; PAOP = pulmonary artery occlusion pressure; UOP = urine output

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Positive fluid balance is associated with worse outcomes in critically ill patients.[1-3] Consequently, some experts have recommended that fluid administration be restricted to patients with commonly accepted indications (eg, oliguria, hypotension) who are "fluid responsive."[4] Between 40% to 70% of patients who are ventilated are deemed fluid responsive[5,6] when defined as a 10% to 15% increase in cardiac output following a crystalloid challenge ≥ 500 mL.[7] Noninvasive techniques to quantify fluid responsiveness may be difficult to interpret in many critically ill patients[8]; therefore, further study into the clinical relevance of fluid responsiveness is needed. The relationship between fluid responsiveness and near-term physiologic improvements (eg, heart rate [HR], urine output [UOP], BP) as well as longer-term clinical outcomes (eg, survival) is not well described.[9,10]

The National Heart, Lung, and Blood Institute ARDSNet Fluid and Catheter Treatment Trial (FACTT) was a factorialized, randomized, protocolized study of fluid management in patients with acute lung injury/ARDS. One-half of patients received a pulmonary artery catheter (PAC) that provided cardiac output measurements.[1] Hence, the FACTT dataset offers the opportunity to evaluate short-term physiologic effects of fluids and longer-term outcomes among fluid responsive and non-fluid-responsive patients. As most of these patients received fluids prior to study enrollment, we hypothesized that rates of fluid responsiveness would be < 25% and that additional fluid administration would not lead to durable improvements in hemodynamic parameters. Since the ability to increase cardiac output after a fluid bolus might indicate a more adaptable cardiovascular system, and cardiovascular adaptability has been linked to improved outcomes in other conditions,[11-13] we also hypothesized that clinical outcomes would be better in patients who were fluid responsive.

Materials and Methods

Patient Selection

Deidentified bedside flow sheets from 127 patients with ARDS enrolled in FACTT were collected from the coordinating center and participating sites; this was an unselected sample of available flow sheets. All patients had been previously resuscitated with IV fluids as clinically indicated prior to enrollment. Eligible patients for this study were those randomized to receive a PAC who had received one or more fluid boluses and had complete hemodynamic data available before and after the fluid bolus. Institutional review board approval (LSUHSC #8114) was obtained to conduct these analyses.

Data Collection

Hemodynamic variables were collected before ("pre") and 1 to 4 h after ("post") protocol-directed 15 mL/kg normal saline or 25-g albumin boluses; the fluid bolus could occur at any time during the patient's enrollment. The FACTT protocol dictated reassessment at 1 h if the indication for fluids was shock, ineffective circulation, or low UOP and 4 h if the indication was only low filling pressure.[1] Variables of interest were mean arterial pressure (MAP), HR, UOP, central venous pressure (CVP), cardiac index, and pulmonary artery occlusion pressure (PAOP). To control for unmeasured confounding factors that may have influenced hemodynamic changes, the same variables were also collected from the same patients during periods when fluids had not been administered (Fig 1).

Definitions

We defined fluid responsiveness as an increase in cardiac index of ≥ 15% following a single fluid bolus of 15 mL/kg crystalloid or 25 g albumin. Shock was defined as an MAP < 60 mm Hg or the need for vasopressors to maintain MAP ≥ 60 (except dopamine < 5 μg/kg/min), and oliguria was defined as a UOP < 0.5 mL/kg/h.

Data Analysis

Data are reported as mean ± SD or proportions where appropriate. Pearson correlations were calculated between prebolus hemodynamics and change in cardiac index. Changes in hemodynamic variables after a fluid bolus were compared using paired *t* tests. To control factors that may influence fluid responsiveness rates, the proportions of boluses leading to a ≥ 15% increase in cardiac index were compared using Fisher exact test for the following comparisons: (1) boluses that caused a CVP increase of ≥ 2 mm Hg vs boluses that did not cause a CVP increase of ≥ 2 mm Hg, as it has been postulated that if a fluid bolus does not increase the CVP there is not expected to be a cardiac index change[14]; (2) boluses that had repeat measurements 1 or 4 h later, as time from bolus to cardiac index measurement may affect fluid responsiveness

Fluid bolus
pre post

Time	1000	1100	1500	1900	2300
MAP	69	68	69	69	79
HR	117	109	111	113	91
UOP	0.42	0.76	0.38	0.54	0.66
CVP	6	7	8	15	8
CI	2.0	2.6	2.8	2.8	3.4
PAOP	9	9	12	18	11
Fluid bolus	1000mL	-	-	-	-
Furosemide	-	-	-	-	-

No fluid bolus or diuretic for more than 6 hours
pre
post
No fluids

Figure 1 – *Sample bedside flow sheet. To be included in this "no fluids" analysis, variables were collected at a time point at least 6 h after a fluid bolus or diuretic dose; these same variables were then collected 1 to 4 h later. At the top, "pre" (time 1000) represents hemodynamic variables prior to a fluid bolus, and "post" (1100) refers to hemodynamic variables 1 h after the fluid bolus was started. No fluid bolus or diuretic was given for > 6 h from 1100 to 1900; therefore, variables measured at 1900 are "pre" and at 2300 are "post" for the "no fluids" analysis, as described in the Materials and Methods section. CI = cardiac index; CVP = central venous pressure; HR = heart rate; MAP = mean arterial pressure; PAOP = pulmonary artery occlusion pressure; UOP = urine output.*