COMPARISON OF THE ACCURACY OF MONITORING DEVICES IN PREDICTION OF FLUID RESPONSIVENESS IN SEVERE SEPSIS AND SEPTIC SHOCK

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VERSION 3

BACKGROUND

One of the most challenging problems in critical care is determination of whether patients have adequate intravascular volume, and whether they would benefit from additional intravenous fluids. Giving too much fluid to patients with adequate intravascular volume could lead to fluid overload, congestive heart failure and subsequent respiratory failure. Not giving enough fluid to

patients, risks leaving them under-resuscitated and worsening their shock state, leading to organ failures, such as kidney failure. Clinically, it is very difficult to determine this "intravascular volume status", and predict which patients would benefit from more fluid. One of the ways we currently determine this, is to measure cardiac output and one of its main components, stroke volume (how much blood is pumped by the heart each beat) and see whether these increase in response to a passive leg raise (PLR) maneuver[1]. The maneuver is simple, quick, with essentially no risk. The maneuver involves measuring baseline cardiac output and stroke volume with the patient's head up at 45 degrees and legs flat for 3 minutes. Subsequently, the head is placed flat and the legs are raised to 45 degrees for 3 minutes. If the cardiac output and stroke volume increase in response to this maneuver, there is a high probability that the patient will have a good response to giving intravenous fluid.

Currently there are multiple FDA approved devices which can be used to measure cardiac output and stroke volume, ranging from very invasive (pulmonary artery catheter), to minimally invasive (requiring arterial catheter +/- central venous catheter- Flotrac, PICCO)[3,4] to a newer, completely non- invasive device, called the NICOM (Cheetah). The FloTrac is a commonly used device for assessment of fluid status in the ICU, but to date has not been validated in predicting volume responsiveness of patients with sepsis or septic shock, although it has been validated in a number of other clinical settings. The monitor is able to determine stroke volume, heart rate, cardiac output, and other hemodynamic information.

OBJECTIVES

The most commonly used device for hemodynamic monitoring at Cottage is the Edwards FloTrac monitor, which requires arterial catheterization. Use of this device is our standard practice in treating patients with septic shock, with virtually all of our patients requiring the device both for continuous arterial pressure monitoring, as well as determination of cardiac output and stroke volume, and prediction of fluid responsiveness as described above. Unfortunately, it is well known that use of the FloTrac in septic patients is problematic, due to the state of their blood vessels from the disease state, as well as the effect of medications we use to treat their low blood pressure. We would like to test the accuracy of the FloTrac device in septic patients.

This study is designed to test the ability of the Flotrac device to predict the need for fluid administration in septic shock patients, requiring medications (vasopressors) to support their blood pressure. We will be using the measurements of cardiac output and stroke volume derived from the FloTrac, in conjunction with the passive leg raise test described above. Patients whose measurements suggest a need for more fluid with one or both devices, will receive a standard intravenous fluid bolus. Additionally, any patient who the treating clinician feels a fluid bolus is clinically indicated, regardless of the results of the PLR, will receive a fluid bolus. Clinicians may use ultrasound imaging of the inferior vena cava, or any other clinical information they routinely use, to make this determination. In this way false positives and false negatives will be apparent with both devices.

STUDY POPULATION

50 patients will be studied. Patients may have one or multiple assessments during their ICU stay as clinically indicated.

Inclusion Criteria:

- All adult patients with severe sepsis with hypotension, or septic shock, who have an arterial catheter with Flotrac monitor, with or without a central venous catheter, will be eligible for inclusion in the study.

Exclusion Criteria:

- Patient or legally authorized representative (LAR) decline consent.
- Pregnancy.
- Contraindication to raising legs or head to 45 degrees for 3 minute intervals.

Withdrawal and termination criteria:

- Patients may ask to withdraw from the study at any time.
- Termination criteria would include removal or malfunctioning of arterial catheter or Flotrac device. Resolution of hypotension or shock state, and discharge or transfer from the ICU.

STUDY METHODS AND PROCEDURES

This will be a prospective, non-blinded, non-randomized study. Identification of appropriate patients meeting inclusion criteria, will be made by house staff and medical attending staff. Patients or their LAR will be asked to participate and sign consent, if in agreement.

When the clinical team feels assessment of intravascular volume status is appropriate, a passive leg raise maneuver(PLR) (see figure 1) will be performed, and clinical and hemodynamic variables (see data collection sheet- figure 2) will be recorded by the physicians and/or critical care nurse performing the maneuver. All patients will get a single fluid challenge after the initial PLR assessment, regardless of the result of the PLR. This fluid challenge can be cancelled by the treating physician based on clinical judgement. A physician may wish to cancel this fluid challenge if there is a risk of fluid overload with the patient. This fluid challenge will help us determine a false negative rate. After the first PLR, subsequent fluid challenges will only be given if the patient has greater than or equal to 10% increase in any of the 3 listed parameters, SVI, CI, or PP. PLRs will be done every 6 hours routinely (Figure 3), and additionally, if ordered by the physician. A physician can also order a fluid challenge at any time, based on clinical judgement regardless of PLR result. The fluid challenge will consist of intravenous administration of 500 ml of crystalloid solution (either saline or plasmalyte) given as rapidly as possible via a pressure bag, as is standard practice. If in the judgment of the treating physician, a smaller amount would be safer, the patient can be given a 250 ml bolus. Alternatively, the

patient may be given a bolus of either 250, or 500 ml of 5% albumin administered at the maximum IV infusion pump rate of 1200 ml/hr.

The type of fluid, volume, and duration of infusion of the fluid challenge will be recorded. Following the fluid challenge, the patient's hemodynamic response will be recorded, with the patient in the semi-upright 45 degree head up position.

During the above maneuvers, in accordance with standard practice, doses of vasopressors and mechanical ventilation settings (if on a ventilator) will be recorded and maintained constant, so as not to effect the measurements.

RISKS AND BENEFITS

We do not anticipate any significant risks to the patient from the study. There is a remote risk of excessive fluid administration with the Flotrac device, but this risk is routinely present outside of the study. However, while the Flotrac device is routinely used with PLR for assessing fluid responsiveness in our ICU, it also has not been adequately studied in septic patients. It should be kept in mind that fluid challenges are routinely given in this patient population based on clinical factors other than indicated by these devices.These clinical factors include central venous pressure, respiratory variation of inferior vena cava caliber by ultrasound, fluid balance, clinician "gestalt", etc. Such fluid challenges are considered diagnostic, potentially therapeutic and generally safe, and may be given during this study, if the treating physician feels they are indicated. Therefore, we do not feel there is any additional risk posed by this study.

CLINICAL DATA MANAGEMENT

See the attached data collection tool. In addition to the data sheet, routine data collected on all septic patients as part of the IRB approved SBCH Sepsis registry will be collected. We will also collect information on comorbidities which could impact the results, such as presence of heart failure. Echocardiogram results, if any, will also be collected as part of this process.
The data will be transferred from the data collection tools to Redcap database management system. The original data sheets will be kept on the SBCH premises in a locked cabinet.
All data will be reported in a collective fashion, without any unique patient identification.

STATISTICAL ANALYSIS

The predictive value of fluid responsiveness by the Flotrac device will be compared in the primary assessment. Other data accumulated during the trial, such as CVP, blood pressures (including MAP and pulse pressure), ultrasound assessment of IVC for fluid responsiveness will also be analyzed, secondarily. The ability of Flotrac to assess fluid responsiveness will be analyzed using the Receiver Operating Characteristic paradigm.

REFERENCES

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Comparison of cardiac output measurements by arterial trans-cardiopulmonary and pulmonary arterial thermodilution with direct Fick in septic shock.
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Figure 1.

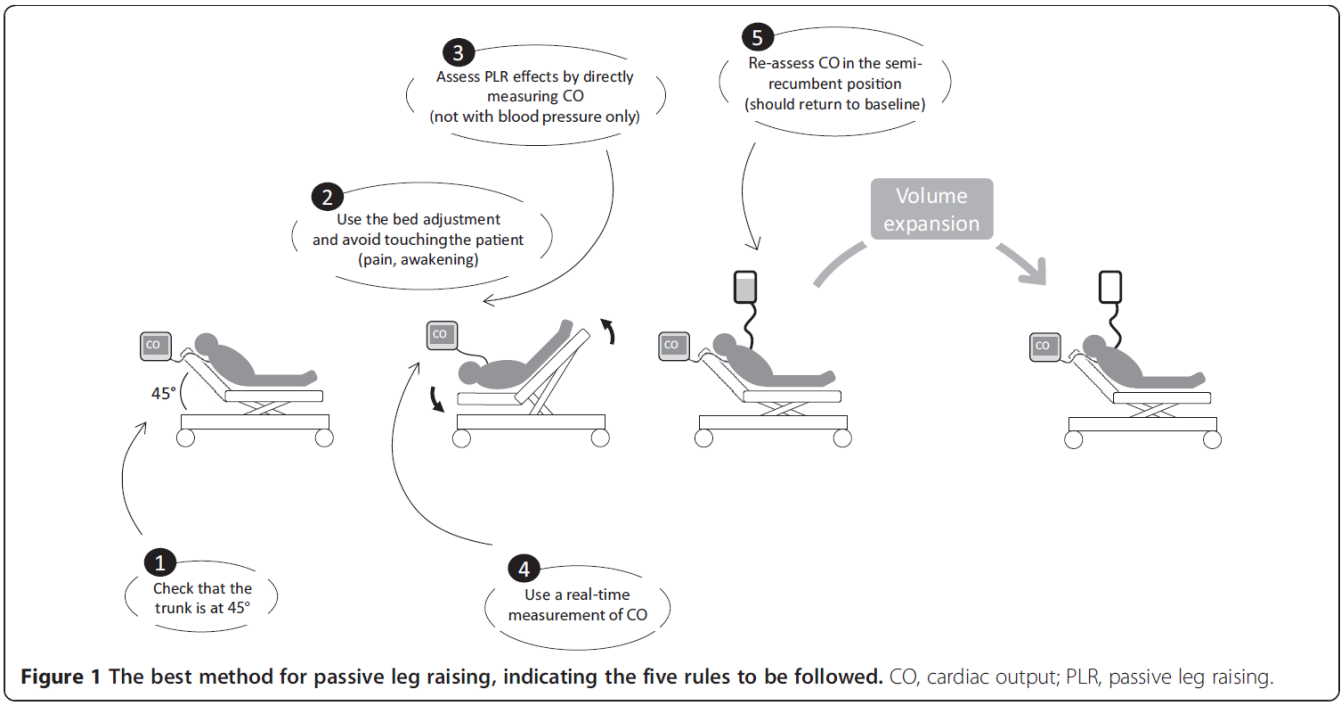


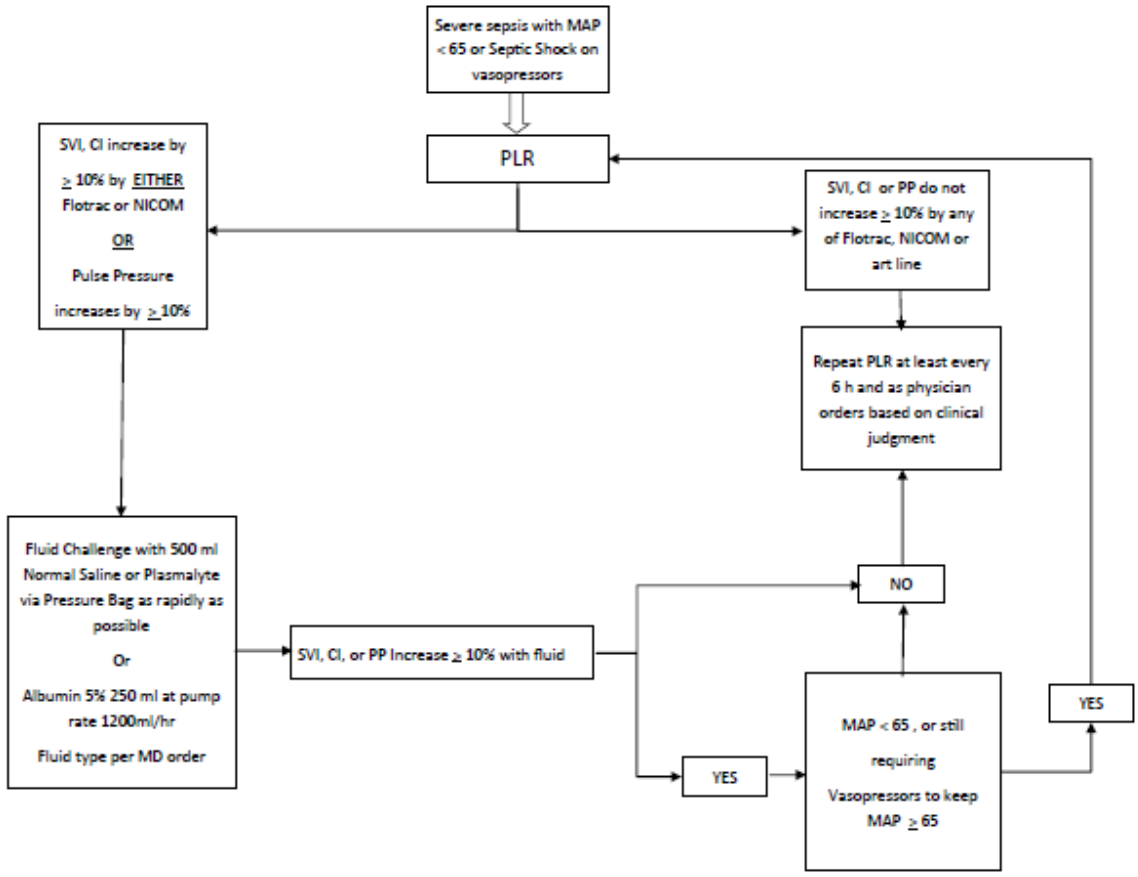
Figure 1 The best method for passive leg raising, indicating the five rules to be followed. CO, cardiac output; PLR, passive leg raising.

From Monnet and Teboul [1]

Figure 2.

DATE		NAME	MRN	ACCT	AGE	SEX	HT(CM)	WT(KG)	BSA	IBW (KG)
								BIPAP		
	VENT (y/n)	MODE	Pt. RATE	Vt	PEEP	PIP	Ppl	IPAP/EPAP		
	DOSE									
NE										
DA										
VP										
EPI										
PHEN										
DB										
		HEART RHYTHM:	HR	SBP	DBP	MAP	CVP	PAWP	SVI	CI
DATE	TIME	TRIAL #								
		PRE-PLR (HEAD UP 45- 3MIN)								
		FLOTRAC								
		NICOM								
		US IVC> 50% Resp var (Y/N/NA)								
	TIME									
		PLR (LEGS UP 45 - 3MIN)								
		FLOTRAC								
		NICOM								
	TIME									
		POST-PLR (HEAD UP 45- 3MIN)								
		FLOTRAC								
		NICOM								
	TIME									
		FLUID CHALLENGE (FC)								
		FLUID TYPE:								
		FLUID AMOUNT:								
		INFUSION TIME:								
	TIME	POST FC (HEAD UP 45)								
		FLOTRAC								
		NICOM								

Figure 3


Severe sepsis with MAP < 65 or Septic Shock on vasopressors
PLR
SVI, CI increase by ≥ 10% by EITHER Flotrac or NICOM
OR
Pulse Pressure increases by ≥ 10%
SVI, CI or PP do not increase ≥ 10% by any of Flotrac, NICOM or art line
Repeat PLR at least every 6 h and as physician orders based on clinical judgment
Fluid Challenge with 500 ml Normal Saline or Plasmalyte via Pressure Bag as rapidly as possible
Or
Albumin 5% 250 ml at pump rate 1200ml/hr
Fluid type per MD order
SVI, CI, or PP Increase ≥ 10% with fluid
NO
YES
MAP < 65 , or still requiring Vasopressors to keep MAP ≥ 65
YES