**Proposed Title:** *The hemodynamic and physiological effects of rapid versus slow fluid bolus therapy with 4% albumin in ICU patients with severe sepsis or septic shock*

**Study Type:** Interventional (Clinical Trial)

**Estimated Enrollment:** 68

**Study Design:** Single-Centre Randomized trial

**Masking:** Unblinded

**Estimated Start Date:** Early 2019

**Objectives**

Primary objective is to measure the effects and changes in stroke work following 4% albumin administered at different rates in ICU patients with sepsis.

Secondary objectives include measuring changes in other haemodynamic parameters following different rates of albumin administration, such as blood pressure, heart rate, urine output, stroke volume (by echocardiographic measurement), lactate, as well as plasma volume expansion and distribution using mathematical modelling of volume kinetics for two hours from albumin administration.

**Primary outcome measures:** Ventricular stroke work

**Secondary outcome measures:** Blood Pressure (SBP and MAP)

Heart Rate

Stroke Volume using bedside echo (LVOT VTI)

Lactate

Plasma Volume Expansion using volume kinetics model

(using frequent urine sampling)

**Expected outcomes**

In ICU patients with sepsis, slow fluid therapy with 4% albumin will lead to a greater increase in stroke work as well as more prolonged favourable changes in hemodynamic parameters compared to rapid bolus.

**Methods& Data Collection**

The patients who are admitted to ICU with diagnosis of severe sepsis or septic shock will be screened by ICU research nurses for eligibility for enrolment based on inclusion and exclusion criteria. Once enrolled and an appropriate informed consent has been obtained, the estimated target of 68 subjects will be randomly allocated to receive 10m/kg of albumin 4% run at either 100mL/min (rapid) or 10mL/min (slow) (see **Figure 1**). The baseline vital signs as well as other haemodynamic indicators of cardiac output will be measured prior to the administration of fluid bolus, and subsequently every 30 minutes min for a total of 2 hours observation period post-fluid bolus (except for urine output which will be taken every 15min for two hours and ABG obtained every 15min for the first hour, and every 30min for the rest).

Data collection will include patient characteristics (e.g., demographics, comorbidities, and mechanical ventilation status), followed by above mentioned outcome measures collected at baseline prior to intervention, and at every 30min intervals for 2 hours (with the exception as described above). This involves measurement of vital signs such as blood pressure and heart rate, bedside echocardiographic measurements, as well as lactate levels obtained from serial arterial blood gas sampling. All other data collection methods are non-invasive and does not interrupt standard care and monitoring in the intensive care.

Patients admitted to ICU with **severe sepsis or septic shock\*** are assessed for eligibility

**Excluded when:**

* Evidence of fluid overload or acute pulmonary edema
* Patient has contraindications to receiving albumin (e.g., allergic reaction or Jenovah’s Witness)
* Active bleeding requiring transfusion
* Haemoglobin level <70g/L
* Patients in whom death is considered imminent (within 24 hours)
* Receiving continuous renal replacement therapy (CRRT) or hemodialysis
* Pregnancy
* Expected discharge from ICU during 2 hour monitoring period
* Inability to give consent or refusing to consent
* Inability to obtain satisfactory echocardiographic images for cardiac output measurement

**Included when:**

* Admitted to ICU
* Age 18 years or older
* Meeting clinical criteria for fluid bolus administration (one of the following):
  + MAP <65mmHg
  + HR >100bpm
  + Urine output <0.5ml/kg/hr
  + Lactate levels of >3mmol/dL
  + Cardiac index <2.5L/min/m2

YES

NO

Enrolled patients (n=68) are randomized

10mL/kg of 4% Albumin given slowly at 10mL/min

10mL/kg of 4% Albumin given rapidly at 100mL/min

\*Definition of sepsis prior to SEPSIS-lll by ESICM-SCCM Sepsis Redefinitions Task Force was used

**Figure.1 Rapid vs Slow Fluid Therapy with 4% Albumin in Sepsis Trial Flow Diagram**