Standard Operating Procedure (SOP)

Management of intervention group patients
SOP 009

Scope

- To provide guidance on management of patients who have been allocated the intervention group in the Optimise Trial.
- The procedures for administering the intervention are described in detail below and a summary is provided on page 4.

Procedure

- The trial intervention period will commence at the start of general anaesthesia and continue for six hours after surgery is complete (maximum total duration: 24 hours).

Cardiac output monitoring

- Immediately following induction of anaesthesia, the LiDCOrapid system will be set up for monitoring of cardiac output.

General haemodynamic measures

Care for all patients has been loosely defined to avoid extremes of clinical practice but also for practice misalignment, as follows:
- Patients will receive 5% dextrose at 1 ml/kg/hr as maintenance fluid. An alternative maintenance fluid may be administered (using the same rate of 1ml/kg/hr) at the discretion of the treating clinician. Additional fluid will be administered at the discretion of the clinician, guided by the pulse rate, arterial pressure, urine output, core-peripheral temperature gradient, serum lactate and base deficit/excess.
- Blood will be transfused to maintain haemoglobin at greater than 8 g/dl.
- Oxygenation will be maintained at Sp0₂ 94% or greater.
- Heart rate will be maintained at less than 100 beats per minute.
- Core temperature will be maintained at 37°C.
Mean arterial pressure will be maintained between 60 and 100 mmHg using an alpha adrenoceptor agonist or vasodilator as required, although other measures such as adjustments to anaesthesia and analgesia should be considered first.

Post-operative analgesia and sedation

- Post-operative analgesia will be provided by epidural infusion (bupivicaine and fentanyl) or intravenous infusion (morphine or fentanyl).
- If required, post-operative sedation will be provided with propofol or midazolam.

Plasma potassium and glucose monitoring

- Monitoring of plasma potassium and glucose levels is recommended.

Administering fluid to a stroke volume end-point

- Currently, peri-operative intra-venous fluid is usually administered to subjective end-points. The use of stroke volume as a treatment end-point may significantly reduce but not eliminate this subjectivity. However, the measurement of stroke volume does not replace the discretion of the treating clinician in ensuring patient safety. The protocol allows for the treating clinician to adjust both the volume and type of fluid administered, e.g. if there is concern about persistent hypovolaemia or fluid overload. Such decisions may relate to clinical circumstances or physiological measurements (e.g. pulse rate, arterial pressure, urine output, serum lactate, base excess).

- Stroke volume will be determined by arterial waveform analysis (LiDCOrapid system). In order to ensure a standardised approach to fluid administration, no more than 500ml of intra-venous fluid will be administered prior to commencing cardiac output monitoring.

- Patients will receive 250ml fluid challenges, within duration of five minutes, with a colloid solution as required, aiming to maximise stroke volume. Maximal stroke volume is defined as the absence of a sustained rise in stroke volume of at least 10% sustained for 20 minutes or more in response to a fluid challenge.

- Once the maximal value of stroke volume is determined, this should be maintained throughout the intervention period with colloid boluses as required. Initial increases in stroke volume are often only transient. If stroke volume does not increase as defined above, it is likely that the heart is functioning on the horizontal part of the Starling curve (see figure). This suggests the patient is not hypovolaemic and fluid challenges should be stopped. If the stroke volume decreases, this is most likely due to ongoing fluid losses and a further fluid challenge is required.

- Many peri-operative physiological changes may alter the maximal value of stroke volume. These may be due to general and regional anaesthesia, surgical stimulation, endotracheal tube
removal, pain, fluid loss, etc. Further fluid challenges should be considered where there is reason to believe the maximal stroke volume may have changed. The most challenging situation is the patient who clearly remains stroke volume responsive despite large volumes of intra-venous fluid. This arises when an evolving severe fluid deficit has yet to become clinically apparent in any other respect. Experience from previous trials suggests that it is particularly important to continue to give fluid challenges in such patients to maintain maximal stroke volume. The small volume of each individual fluid challenge will minimise any potential adverse effects of confirming volume status in euvolemic patients. Data from previous studies confirm the safety of this approach.

**Figure: Starling’s curve**

The increase in venous return due to intra-venous fluid (red arrows) increases stroke volume in responsive patients. At maximal stroke volume (horizontal part of curve), the absence of a response indicates fluid is not required.

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**Dopexamine:**

- Patients in the intervention group will also receive dopexamine at a fixed rate of 0.5 $\mu$g/kg/min, to be commenced after the first fluid challenge and continued throughout the intervention period. Because of the vasodilator effects of dopexamine, correction of hypovolaemia (if present) should be initiated at least 30 minutes prior to commencement of the infusion. The dose of dopexamine should be reduced to 0.25 $\mu$g/kg/min if the heart rate increases to greater than 120% of the baseline value or to more than 100bpm (whichever is the greater) for more than 30 minutes despite adequate volume replacement, anaesthesia and analgesia. If, despite dose reduction, the heart rate does not decrease below this level, the dopexamine infusion should be discontinued.

**What if blood products or intravenous fluids are required for indications unrelated to changes in stroke volume?**

- Many patients will require blood products and, in some cases, additional intravenous fluid challenges may be requested by a clinician. Administration of colloid, blood or blood products under these circumstances should be guided by stroke volume monitoring and these data should be used to inform the need for subsequent fluid challenges.
General haemodynamic measures
1. 5% dextrose at 1 ml/kg/hr or an alternative maintenance fluid may be administered (using the same rate of 1ml/kg/hr) at the discretion of the treating clinician
2. Transfuse blood to maintain haemoglobin >8 g/dl
3. Clinician retains discretion to adjust therapy if concerned about risks of hypovolaemia or fluid overload
4. Mean arterial pressure 60-100 mmHg; SpO₂ ≥94%; core temperature 37°C;

Administering fluid to a stroke volume end-point
1. 250ml colloid boluses to achieve a maximal value of stroke volume
2. No more than 500ml fluid to be given before cardiac output monitor is attached
3. Fluid challenges should not be continued in patients who are not fluid responsive in terms of a stroke volume increase
4. Fluid responsiveness is defined as a stroke volume increase ≥10%
5. If stroke volume decreases further fluid challenge(s) are indicated
6. Persistent stroke volume responsiveness suggests continued fluid loss

Dopexamine
1. Start dopexamine infusion at fixed rate of 0.5 μg/kg/min after first colloid fluid challenge
2. Halve dose if heart rate rises to the greater of: (a) >120% of baseline value, or (b) >100bpm for more than 30 minutes.
3. Stop dopexamine if tachycardia persists

What if blood or IV fluid is required regardless of stroke volume?
1. If blood products or additional fluid challenges are required, then stroke volume should still be monitored to identify any change in maximal stroke volume