Measurement of Mean Systemic Filling Pressure & Stressed Volume with CardioQ+® Oesophageal Doppler Measurement

Published: 20-12-2016
Last updated: 19-04-2024

Objectives1. To assess the sensitivity, specificity, negative and positive predictive value of Vs to predict fluid loading responsiveness (>12% increase in CO after 500 ml of fluids).2. To assess the accuracy of Vs to follow a 500 mL increase in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON47434

Source
ToetsingOnline

Brief title
Measurement of MSFP & stressed volume with CardioQ+®

Condition

- Other condition

Synonym
Hemodynamic instability, shock

Health condition

Geavanceerde hemodynamische monitoring bij hemodynamische instabiliteit obv verschillende oorzaken zoals cardiogene shock, etc.

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Mean Systemic Filling Pressure, Oesophageal Doppler, Stressed Volume, Systemic Vascular Compliance

Outcome measures

Primary outcome

In this study fluid loading responsiveness after 500 mL fluid, and stressed volume measurement before and after 500 mL fluid administration are the main outcome measures.

Secondary outcome

Stressed volume is calculated from mean systemic filling pressure (MSFP). Previous studies have shown it is possible to measure MSFP with the MSFParm method, However they describe limitations [Geerts] and it is not well established how accurate this method is. If the MSFParm method would be as reliable in assessing stressed volume as the MSFPhold method this would be clinically relevant since the MSFParm method is not restricted to mechanically ventilated sedated patients. The MSFParm method could potentially be used in all ICU patients with an arterial line.

In this study, aside from patient demographics and surgical procedure statistics we will document MAP, SBP, DBP, PPV, SV, SVV, COdoppler,

COpulsecontour, HR, central temperature, Vs, Csys and MSFP, as well as wave reflection parameters (augmentation index, reflection magnitude) determined using FloTrac/Vigileo (Edwards Lifesciences).

Paired measurement will be performed before and after the fluid challenge. At steady state, 1-2 minutes clean signal collection will be recorded, before and after the fluid challenge. Kinetic energy will be calculated from SV, Peak velocity and Mean acceleration (Peak velocity/ Flow time to peak velocity). Afterload parameters of elastance, resistance and inertia will be calculated from Flow time to peak, Pressure at peak flow, Flow time (FT), not corrected for HR, End systolic pressure (Pressure at FT), Diastolic pressure, Peak Velocity, Mean acceleration.

Study description

Background summary

Accurate assessment of the intravascular volume status of a hemodynamically unstable patient at the bedside or in the operating theatre is challenging but, if available, would be important for assessing the determinants of cardiovascular insufficiency and response to therapy. Clinical symptoms, like skin turgor, are notoriously unreliable to assess volume status. Static filling pressure, like central venous pressure (CVP) and mean arterial pressure (MAP), have not been of much help to the clinician either. Consequently, dynamic parameters have become a focus of interest. Stroke volume variation (SVV) and pulse pressure variation (PPV) perform much better. However, conditions that frequently occur in the operating theatre and in the ICU (atrial fibrillation or tidal volume ventilation below 8 ml/kg for instance) can make precise and accurate measurement troublesome. Challenges with PEEP, passive leg raising or a mini fluid challenge have been used as alternatives but often difficult to execute in clinical practice. Moreover, reliability is often an issue. We are still not able to define hypo-, hyper- or normovolaemia. We are still looking for a gold standard parameter to indicate volume status or even define it.

Intravascular volume can be divided into unstressed volume (the volume that is needed to fill the blood vessels, without creating a distending pressure) and stressed volume (Vs, the volume that stresses the vascular walls, resulting in a distending pressure). This distending pressure is referred to as mean systemic filling pressure (MSFP). MSFP is the pressure to which all intravascular pressures equilibrate during cardiac arrest and is the pressure that is determined by both systemic vascular compliance (Csys) and Vs [Guyton]. MSFP itself is a major determinant of venous return (VR), because it defines the upstream pressure, and relative to central venous pressure (CVP), is the driving pressure for venous return and thus cardiac output (CO):

CO = VR = (MSFP * CVP) / Rv
(Rv is resistance to venous return).

Vs can be considered as reflecting the effective intravascular blood volume. Estimation of Vs would thus help the clinician in the decision of whether to choose volume resuscitation, diuresis, inotropic drugs, or vasoactive medication. In combination with a cardiac function curve, measuring MSFP and Vs should provide a powerful and basic tool to characterize the hemodynamic status of patients.
In recent years, it has been shown to be possible to measure mean systemic filling pressure in alive ICU patients at the bedside using multiple methods amongst others employing respiratory holds of 12 seconds at incremental airway pressures. When MSFP is measured before and after fluid administration, a pressure-volume relationship can be constructed, in which Csys is the slope of the relation (*volume/*MSFP). The measurement of MSFP has been repeated by other groups. Consequently, physiological principles that were first described by Arthur Guyton were used to estimate stressed volume in these patients:

Vs = Csys x MSFP

Using the inspiratory hold method to determine MSFP we can now determine total Csys, Vs, and cardiac function curves at the bedside. This model was validated earlier by Jansen and Vs values were found to be similar to those found by Magder and De Varennes who measured Vs and MSFP in arrested patients (i.e. of course the gold standard).
Vs has thus only been measured once in patients. In this study, we will use the CardioQ to measure MSFP in an automated way, and determine Csys and Vs to assess their reliability to assess fluid loading responsiveness to 500 mL fluid in 42 patients during elective CABG surgery. No clinical application of this useful parameter exists yet. This study can be the next step to make bedside stressed volume determination possible for the use in the operating theatre. It will allow us to directly determine an individual*s volume status.

Furthermore by comparing MSFP measured with inspiratory holds (MSFPhold) and with the arm pressure method (MSFParm) we are able to compare those two methods. The arm method is in theory applicable to a broad patient population.

Using the CardioQ, parameters of intrinsic cardiac contractility and afterload can be measured at the bedside. Ejection fraction, the gold standard for non-invasive contractility assessment, is proportional to mean blood flow velocity measured in the descending thoracic aorta with the CardioQ. Oesophageal doppler-derived indexes of blood flow velocity and acceleration, as well as force and kinetic energy, can be derived and used for continuous assessment of cardiac contractility at the bedside. Using oesophageal doppler-derived parameters, the different components of afterload: inertia, resistance and elastance, can also be individually determined.
The integration of these additional hemodynamic parameters can assist the clinician in optimising and individualising the haemodynamics of unstable patients in theatre and the ICU. However, these concepts remain largely non-validated in patients (i.e. no *normal* values have been defined and no knowledge of their real variation with common hemodynamic treatments is known). The current observational study allows characterising baseline values in a population of high risk surgical patients and study their variation in response to a fluid challenge.

Study objective

Objectives

1. To assess the sensitivity, specificity, negative and positive predictive value of Vs to predict fluid loading responsiveness (>12% increase in CO after 500 ml of fluids).

2. To assess the accuracy of Vs to follow a 500 mL increase in stressed volume.

3. To assess the sensitivity, specificity, negative and positive predictive value of HR, CO, CVP, MSFP, MAP, SV, SVV and PPV to predict fluid loading responsiveness.

4. To assess the reliability of the measurement of stressed volume with the arm method (MSFParm) compared to the inspiratory hold method (MSFPhold)

5. To determine the effect of a standardised fluid loading on parameters of intrinsic contractility and afterload.

Research hypothesis

1. Bedside-determined stressed volume using MSFP, Csys and CO measured with CardioQ+ can predict fluid responsiveness (>12% increase in CO) by at least 90% sensitivity and specificity.

2. Bedside-determined stressed volume pre- and post 500 mL infusion will correlate within 95% of the infused volume.

Study design

42 patients planned for elective CABG surgery, will be studied postoperatively at the Intensive Care Unit after approval by the university medical ethics committee and patient*s informed consent is obtained.

Anaesthesia:
Anaesthesia is induced with propofol, sufentanil and rocuronium. Anaesthesia is maintained with sufentanil, sevoflurane and rocuronium over a peripheral venous cannula (18, 16 or 14G). Patients are treated in line with routine CABG anaesthesia care, i.e. a radial artery line is introduced prior to induction, and a central line is placed immediately after induction. Patients are ventilated in a volume controlled ventilation mode adjusted to achieve normocapnia (etCO2 between 35 and 50 mmHg) with tidal volumes of 6*8 mL·kg-1 IBW and a respiratory rate of 12*14 breaths·min-1. Fraction of inspired oxygen (FiO2) is 0.4 and a positive end-expiratory pressure (PEEP) of 5 cmH2O will be applied. Relative hemodynamic stability is achieved using fluids and catecholamines at the discretion of the treating anaesthesiologist. At the end of the surgery the standard transoesophageal echocardiography (TOE) probe is removed and replaced by a smaller CardioQ transoesophageal doppler probe (ODM). This ODM probe is fixed to the mouth and remains in situ for measurements at the ICU.

Measurements:
Patient age, height, weight, and gender is recorded. Arterial blood pressure (Prad) is monitored via a 20G, 3.8-cm long radial arterial catheter inserted by Seldinger technique (Arrow AK-04220, Teleflex Incorporated, Wayne, PA, United States of America) and connected to a pressure transducer. A central venous line is introduced thourgh a side port in the right inertnal jugular vein. The Prad and CVP transducer is referenced to the intersection of the anterior axillary line and the fifth intercostal space. The arterial blood pressure is looped to the CardioQ+ device (Deltex Medical, Chichester, United Kingdom) and MAP, CVP, SBP, DBP, PPV, SV, SVV, CO and CI are registered. Standard electrocardiogram leads are used to monitor heart rate. SpO2 is monitored with pulse oximetry on the index finger of either right or left hand. Beat-to-beat CO, SV and SVV is also obtained by CardioQ+ via the oesophageal Doppler probe. The probe inserted orally according to device guidelines. The signal is optimized and the probe is fixed to the mouth with tape consequently.

Experimental Protocol:
MAP must be at least 55 mmHg and CI above 1.5 L·min-1 to allow start of the study measurements. Central temperature is kept between 35.5 and 37.5 ºC.After the surgery,when the patient is in the Intensive Care Unit (ICU), when the above conditions are met and there is no contra-indication for fluid

administration, the rapid cuff inflator is attached around the upper arm and study measurements are performed. These measurements are performed in the first hour postoperatively. According to standard care anaesthesia is maintained for at least the first 2,5 hours after surgery, so the patient will be sedated and mechanically ventilated. First, a baseline measurement is performed (MAP, SBP, CVP, DBP, PPV, SV, SVV, COdoppler, COpulsecontour, HR, core temperature. Hb levels will be measured using arterial blood gas analysis.Radial artery pressure and COdoppler are logged on the Deltex CardioQ+ device at a sample frequency of 100 Hz and 0.2 mmHg resolution. From the steady-state over the final three seconds of a set of four 12-second inspiratory-hold manoeuvres at Pvent plateau pressures of 5, 15, 25 and 35 cmH2O, mean arterial pressure and cardiac output are recorded. From these values cardiac output is extrapolated to zero and the concomitant MAP is calculated. This value is equal to MSFP. The hold procedures are marked in the CardioQ device to allow post-hoc analysis, and to allow a new algorithm to be created for the device to automate this procedure. The inspiratory-hold manoeuvres are separated by one-minute intervals to re-establish the initial hemodynamic steady state. When Pvent increases, CO and MAP decrease with a delay of three-four beats, reaching a steady state between 7 and 12 seconds after start of inflation.

Consequently, a 100 mL fluid bolus is given in 30 seconds via the peripheral venous cannula using a 50 mL Syringe (Baxter Nederland BV, Utrecht, the Netherlands). MSFP (2) is measured again. Hereafter, 500 mL of fluid is administered within 10 minutes. A second round of overall measurements is done (MAP, CVP, SBP, DBP, PPV, SV, SVV, COdoppler, COpulsecontour, HR, central temperature). MSFP (3) is measured, a 100 mL fluid bolus is given after two minutes within 30 seconds. During the last round of measurements, MSFP (4) is measured again. The total duration of the measurements will be around 30 minutes. After the study measurements the CardioQ oesophageal doppler monitor probe (ODM) will be removed.

Compliance, Stressed Volume, and Fluid Responsiveness:
Compliance is calculated from the change in MSFP after the 100 mL fluid bolus. Csys = (*volume/*MSFP). Stressed volume is calculated as Vs = Csys x MSFP. Consequently Vs is described per kg body weight to correct for inter-individual differences. Fluid loading responsiveness is defined as an increase of >12% in cardiac output to a 500 mL fluid administration.

Study burden and risks

Potential study-associated side effects that can occur would be related to:

The total of 700 mL of fluid that is administered for study purposes. As 2000 to 4000 mL fluid is standard to be administred within the first 24 hours postoperatively, complications like decompensated heart failure seem very unlikely.

The introduction of the oesophageal probe for cardiac output measurement could theoretically lead to laceration of the oropharynx or oesophagus. This 4.8 - 7 mm probe is inserted orally. Reports of complications are rare despite its widespread use for this type of surgery in peri-operative goal-directed therapy protocols that are national standards in the UK, USA and France.

The inspiratory hold procedure will encompass a number of 12-second mechanical-breath holds at incremental pressures of 5, 15 and 25 cmH2O. These pressures are, however, within the normal airway pressure limits set for routine ventilation. The last inspiratory hold will be at 35 cmH2O. This airway pressure is above the standard ventilation pressures but well within the range of what is acceptable in clinical care. Earlier studies by Jansen et al. have used similar pressures and have not found any deleterious effects in their patients. During previous research on this topic in critically ill patients we did not encounter any pulmonary complications. We do not expect any complications during this study but to increase safety further we have ruled out inclusion of patients with lung emphysema and with right sided cardiac failure.

The use of the rapid cuff inflator (blood pressure cuff) will not lead to any additional risks for patients.

The measurements will be performed in the first postoperatively at the ICU. This implies that patients in this study will not receive additional anaesthesia since patients after a CABG are kept sedated and mechanically ventilated until at least 2,5 hours postoperatively.

To determine Kinetic Energy we will measure Hb levels. Since only a clinical indication for an arterial line will allow patients to participate in the study, drawing blood will be performed from the arterial line (i.e. no additional stabbing). We will use a closed arterial-line system as is the standard in our institution. This guarantees no loss of blood outside the blood needed for analysis. We will require to draw 4 ml of blood per participating subject for the study in total. This represents only a minute quantity of blood (approximately 0.01% of total blood volume of an adult) and will not cause harm to the patient.

The expected advantage from the development of this technique for future patients is large, as there is a demand for a sound method to measure intravascular volume status and response tot fluid loading in all hemodynamically compromised patients in the operating theatre and intensive care. There is considerable morbidity and mortality associated with hypovolemia and hypervolemia in these patients.

Risks and burdens for the study patients are minimal. The expected advantage of the development of a better method to ascertain volume status of patients outweighs the burden and risks for our study patients in our opinion. No

advantage is expected for the study subjects.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Patients planned for elective CABG surgery
- Aged 18 years and over
- Being able to give written informed consent prior to surgery

Exclusion criteria

- A contraindication for fluid loading (700ml) assessed by the treating ICU physician.

- Pregnancy
- Morbid obesity (BMI >40)
- Major hemodynamic instability with a mean arterial pressure (MAP) < 55 mmHg, a cardiac index < 1.5 L·min-1 or right heart failure
- Severe arrhythmias
- Intra-cardiac shunts
- Symptomatic peripheral vascular disease
- Symptomatic pulmonary disease
- Significant valvular regurgitation
- A poor left or right ventricular function
- Contra-indication for rapid cuff inflation, in case of:
* shunt-arm
* lymph-node excision
* skin laesions
- Contra-indication to oesophageal Doppler probe insertion, in case of:
* Nasal injuries
* Nasal polyps
* Facial trauma
* Intra-aortic balloon pump therapy
* Carcinoma of the pharynx, larynx or oesophagus
* Aneurysm of the thoracic aorta
* Severe coagulopathy or thrombocytopenia
* After oesophageal surgery
* (Suspected) oesophageal disease

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-05-2017
Enrollment:	42
Type:	Actual

Ethics review

Approved WMO Date:	20-12-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL55531.018.15