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Introduction

Central venous pressure (CVP) measured invasively through a central venous catheter in the internal jugular vein or through a right atrial port of a pulmonary artery catheter is commonly used during liver transplant surgery. CVP measurements at the SVC-RA junction are a function of circulating blood volume, right ventricle function, intrathoracic pressure. (1) CVP measurements can also be affected by the presence of tricuspid regurgitation. Because central venous pressure measurements are determined by several factors and do not predict the response to subsequent fluid bolus administration, they are considered “static measures” and are poor indicators of fluid responsiveness. (2)

CVP measurements remain an important measurement during liver transplant surgery (3) since a rise in CVP especially during the postanhepatic phase can alert the perioperative team to worsening pulmonary artery elevations and/or a decline in RV function. (4)This in turn triggers several therapeutic interventions aimed at reducing an increasing afterload on the newly transplanted liver, which can otherwise result in disruption of liver anastomoses, increased bleeding and coagulopathy and liver failure of the transplanted liver.(5)

In spontaneously breathing patients, transthoracic echocardiographic measurements of the inferior vena caval diameter and its change with inspiration (sniff) is routinely used to estimate right atrial pressure measurements (Size <2.1 cm; collapses >50% during sniff = RAP 0–5 mm H; g Size > 2.1 cm; collapses >50% during sniff = 5–10 mm Hg Size > 2.1; collapses <50% during sniff = 10–20 mm Hg. This echocardiographic measurement allows noninvasive estimation of pulmonary artery systolic pressure based on the modified Bernoulli equation (PASP=RVSP= 4v2 + RA pressure). (6)

Due to its intraabdominal location, the IVC is less suited for estimation of right atrial pressure during mechanical ventilation; especially that positive pressure ventilation causes a dilation of IVC diameter. (7)

Given the entirely intrathoracic location of the superior vena cava (SVC), its diameter and collapsibility with positive pressure ventilation it is a potentially attractive method of non-invasively estimating CVP. (8)

SVC diameter and collapsibility index, dynamic measures of fluid responsiveness have been successfully utilized as echocardiographic indices for fluid responsiveness in ventilated septic patients. (9)Whether SVC collapsibility is correlated with CVP measurements in liver transplant patients is not known.

Significance:

While most centers utilize central venous catheters or pulmonary artery catheters during liver transplant surgery, (3) there are complications associated with central invasive catheter use. (10)

If SVC collapsibility index is correlated with CVP measurements, it would allow:

1- Less reliance on central invasive catheter use especially in select population of liver transplant recipients especially those with normal pulmonary artery pressures and normal right ventricle function. Large bore peripheral venous catheters that allow rapid administration of fluids and blood products would substitute central venous catheter use with transesophageal monitoring of SVC diameter and collapsibility for calculation of pulmonary artery systolic pressure (PASP).
2- Noninvasive measurement of PASP in mechanically ventilated patients with no central venous monitoring (not just in patients undergoing liver transplantation) especially that IVC measurement in mechanically ventilated patients may be inaccurate in identifying CVP. (7) Since the SVC is entirely located intrathoracic its collapsibility with positive pressure ventilation makes it an attractive method of non-invasively estimating CVP.(8)
3- There are no studies that identify the changes in SVC diameter and collapsibility index during IVC cross- clamping (during the anhepatic phase of liver transplant surgery). This study will provide insight to changes in SVC diameter and collapsibility index in response to IVC crossclamping during the anhepatic phase.

Hypothesis:

SVC diameter and SVC collapsibility index is correlated with CVP measurement in patients undergoing liver transplant surgery (liver transplant recipients)

Aim of the study:

1- To assess the correlation of SVC diameter and SVC collapsibility index measurements obtained intraoperatively by Transesophageal echocardiography (TEE) with simultaneous CVP measurements obtained and recorded electronically (via an automated intraoperative record keeping system) through a centrally inserted central venous catheter or a right atrial port of a pulmonary artery catheter
2- To identify the changes in SVC diameter and SVC collapsibility index that occur with inferior vena cava cross clamping during liver transplant cases performed using IVC cross clamping

Inclusion criteria:

Adult patients => 18 years of age undergoing liver transplantation surgery (cadaveric and living related)

Exclusion criteria:

Contraindication to Transesophageal echocardiography: Esophageal pathology (stricture, trauma, tumor, scleroderma, Mallory-Weiss tear, diverticulum), Active upper gastrointestinal bleed, perforated viscous, esophagogastrectomy, esophagectomy, recent upper gastrointestinal surgery. (11)

Methods:

Following RAC and IRB approval, consecutive patients undergoing liver transplant surgery will be included in the study. We will ask the IRB for informed consent waiver since both TEE and central venous monitoring are used routinely in liver transplant recipients.

Simultaneous measurements of SVC diameter, SVC collapsibility index, CVP (captured electronically through an automated record keeping system) will be recorded by experienced anesthesiologists with expertise and qualifications in Transesophageal Echocardiography. Simultaneous cardiac output measurements (thermodilution) will also be recorded.

Measurements of the SVC will be taken in the midesophageal bicaval view (90-110 degrees) using M-mode echocardiography, 1 to 2 cm away from the entry point into the right atrium. This technique is analogous to that recommended when measuring IVC diameter and collapsibility (7) and was previously described by Cowie et al. (8)

The maximum and minimal diameter of the SVC will be measured and recorded.

Collapsibility index of SVC, "SVC collapsibility index" which is a measure of the inspiratory decrease in SVC diameter will be determined based on the following formula

(Maximum diameter on expiration—minimum diameter on inspiration)/Maximum diameter on expiration, expressed as a percentage

Patients will be ventilated using Pressure Control Ventilation with a tidal volume of 6 to 8 ml/kg with a respiratory rate of 10-12/min and a positive end expiratory pressure of 5 to 8 cmH20.

Measurements will be recorded during the following time periods:

1- Before surgical incision (following induction of General Anesthesia and placement of invasive monitoring and TEE)
2- Preanhepatic phase
3- Anhepatic phase
4- Postanhepatic phase (following reperfusion)
5- Following closure of the deep fascial layer of the anterior abdominal wall

Simultaneously, CVP will recorded from the right atrial port of the pulmonary artery catheter or from the proximal port of a CVC inserted in the internal jugular vein

Patients will be placed in the supine position with pressure transducers zeroed to atmospheric pressure and located at the mid-thoracic position, half-way between the sternum and bed, as recommended in recent guidelines. (12)

Statistical methods

Demographics and perioperative characteristics of this cohort will be summarized using the standard summary statistics.

We will use a linear mixed effect model with repeated measures to estimate the correlation between (1) SVC diameter and (2) SVC collapsibility index and simultaneously measured CVP across over the five measurement times, including before surgical incision, start of preanhepatic phase, start of anhepatic phase, start of postanhepatic phase, and after closure of deep fascial layer of the anterior abdominal wall (13). In the mixed model, an unstructured covariance matrix will be used to account for within-patient correlation. The significance criterion will be 0.025 for each analysis; thus 97.5% CI will be reported (i.e., 0.05/2, Bonferroni correction).

In addition, we will assess whether the correlation between SVC diameter and SVC collapsibility index and CVP differs over measurement time (time interaction) using a separate linear mixed effect model with a time interaction term. Regardless of the significance of the interaction, we will repot the correlation coefficient at each of the five measurement times along with 99.5% confidence interval (i.e., 0.025/5, Bonferroni correction) for information purpose.

Secondly, we will also assess whether the correlation between SVC diameter and SVC collapsibility index and CVP differs between patients with and without normal pulmonary artery pressures and normal right ventricle function. If the above interaction exists, we will repot the correlation separately.

The changes in SVC diameter and SVC collapsibility index that occur with inferior vena cava cross clamping during liver transplant will be summarized.

Sample Size Considerations

With 100 patients and 5 pairs of measurement per patients we will provide enough data to adequately study the accuracy. For example, the width of our 97.5% CI for Pearson correlation will range from 0.19 to 0.15 for correlations ranging from 0.2 to 0.5, respectively, assuming a within-subject correlation of 0 (i.e., equivalent to 500 independent patients). In the other of the extreme scenario (i.e., within-subject correlation of 1), the width of our 97.5% CI for Pearson correlation will range from 0.43 to 0.34 for correlations ranging from 0.2 to 0.5, respectively. Approximately 10 liver transplant cases per month are conducted at the Cleveland Clinic main campus. Thus, a plan of 100 patients is feasible within 1 year. SAS software version 9.4 for Windows (SAS Institute, Cary, NC, USA) will be used for all analyses.

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