COMPARISON OF FLUID RESPONSIVENESS USING TRANSESOPHAGEAL ECHOCARDIOGRAPHY IN PATIENTS WITHOUT CORONARY ARTERY DISEASE UNDERGOING NEUROSURGICAL PROCEDURES VERSUS PATIENTS WITH CORONARY ARTERY DISEASE UNDERGOING CORONARY ARTERY BYPASS GRAFT SURGERY

THESIS

SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

D.M (NEURO-ANAESTHESIA)

OF THE
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, THIRUVANANTHAPURAM, KERALA, 695011, INDIA

JULY 2018

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DECLARATION

I hereby declare that this thesis titled "**Comparison of fluid responsiveness using Transesophageal echocardiography in patients without coronary artery disease undergoing neurosurgical procedures versus patients with coronary artery disease undergoing coronary artery bypass graft surgery**"has been done and prepared by me under the capable supervision and guidance of Dr. Thomas Koshy, Professor, Division of Cardiac-Anesthesia, Department of Anesthesiology, SCTIMST, Thiruvananthapuram; and Dr S Manikandan, Professor, Division of Neuro-Anesthesia and Critical Care, Department of Anesthesiology, SCTIMST, Thiruvananthapuram, Kerala.

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CERTIFICATE BY GUIDES

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ACKNOWLEDGEMENTS

It is indeed a privilege as well as pleasant duty to express my gratitude to all those who have made it possible for me to complete this project.

It is my proud privilege to acknowledge with respectful gratitude, the invaluable guidance extended to me by my guide ***Dr. Thomas Koshy****, Professor, Dept. of Anesthesiology, SCTIMST, Thiruvananthapuram. Sir has always been a motivator and taken pain to make this study as good as this. He is a noble man who has devoted his lifetime for establishing a stronghold for this institute in India. I am thankful for his supervision, timely suggestions and continuous constructive criticism during the course of this study.*

I express my sincere thanks to my research guide and Head of the Division of Neuro-Anesthesia, SCTIMST, ***Dr. S Manikandan*** *for his guidance and supervision throughout the conduct of this study and preparation of report. Sir is an unquestionable authority and well acclaimed expert in the field of Neuro-Anesthesia and Critical care. His valuable observations have gone a long way in coming out with this work. I acknowledge my heartfelt gratitude to him.*

I would take this opportunity to thank my other teachers, colleagues, senior residents and support staff who helped me during the study period.

I express my sincere regards to all the patients who participated in this study.

Dr. Varun. S

Contents

LIST OF ABBREVIATIONS

ABP :	Arterial Blood Pressure
ACC:	American College of Cardiology
AHA :	American Heart Association
ASA:	American Society of Anesthesiologists
IBP:	Invasive Blood Pressure
AUC:	Area Under Curve
AUROC:	Area Under Receiver Operating Characteristic Curve
AV :	Aortic Valve
BBB :	Blood Brain Barrier
BMI :	Body Mass Index
BSA :	Body Surface Area
CABG:	Coronary Artery Bypass Graft
CAD:	Coronary Artery Disease
CBF :	Cerebral Blood Flow
CBV :	Cerebral Blood Volume
CI :	Cardiac Index
CIV :	Cardiac Index Variation
CO :	Cardiac Output
CPB:	Cardio-Pulmonary Bypass
CPP :	Cerebral Perfusion Pressure
CSA :	Cross Sectional Area
CSF :	Cerebro-Spinal Fluid
CVP :	Central Venous pressure

DBP:	Diastolic Blood Pressure
DD :	Delta Down
DSMB:	Data Safety Monitoring Board
EF :	Ejection Fraction
ESA :	End Systolic Area of Left Ventricle
Et :	End Tidal
FL :	Fluid Loading
FR:	Fluid Responsiveness
GA:	General Anaesthesia
GEDV :	Global End Diastolic Volume
GI:	Gastro-Intestinal
HR :	Heart Rate
ICP :	Intra Cranial Pressure
ICU:	Intensive Care Unit
IEC:	Institutional Ethics Committee
ITBV :	Intra Thoracic Blood Volume
IVC:	Inferior Vena Cava
IVCD :	Inferior Vena Cava Diameter
IVC-DI:	Inferior Venacava Distensibility Index
LAP :	Left Atrial Pressure
LV :	Left Ventricle
LVEDA:	Left Ventricular End Diastolic Area
LVEDV :	Left Ventricular End Diastolic Volume
LVEDVV:	Left Ventricular End Diastolic Volume Variability
LVOT :	Left Ventricular Outflow Tract

LVSV:	Left Ventricular Stroke Volume
MAC:	Minimum Alveolar Concentration
MAP :	Mean Arterial Pressure
MV :	Mitral Valve
PAC :	Pulmonary Artery Catheter
PAOP :	Pulmonary Artery Occlusion Pressure
PEEP:	Positive End Expiratory Pressure
PIP :	Peak Inspiratory Pressure
PLR:	Passive Leg Raising
PP:	Pulse Pressure
PPV :	Pulse Pressure Variation
PVI :	Pleth Variability Index
RAP :	Right Atrial Pressure
RCT :	Randomized Control Trial
ROC:	Receiver Operating Characteristic Curve
RR :	Respiratory Rate
RV :	Right Ventricle
RVEDP :	Right Ventricular End Diastolic Pressure
RVEDV :	Right Ventricular End Diastolic Volume
SAH :	Sub-Arachnoid Haemorrhage
SBP :	Systolic Blood Pressure
SPV :	Systolic Pressure Variation
SV :	Stroke Volume
SVC :	Superior Vena Cava
SVCCI :	Superior Vena Cava Collapsibility Index

SVR : Systemic Vascular Resistance

TEE : Trans-Esophageal Echocardiography

TTE : Trans-Thoracic Echocardiography

UO : Urine Output

Vpeak-CA: Carotid Artery Peak Velocity Variation

VTIAo : Aortic Velocity Time Integral

VTIAoV : Aortic VTI variation

INTRODUCTION

Hemodynamic stability is one of the key concept of perioperative management in patients undergoing major surgical procedures like neurosurgery. Among the many methods the anesthesiologist target optimising intravascular volume to achieve hemodynamic stability. The clinical determination of the intravascular volume can be extremely difficult in those undergoing major surgery. This becomes more difficult if the patient has underlying cardiac disease like coronary artery disease. The concept of fluid responsiveness attains relevance in maintaining optimal homeostasis, in the context that fluid loading is the first step in the resuscitation of hemodynamically unstable patients.

Hypovolemia is a common complication encountered perioperatively in patients who undergo major surgery. In neurosurgical practice hypovolemia is compounded by the use of aggressive measures to reduce the raised intracranial pressure, e.g:- osmotic therapy using drugs like mannitol which induce a phase of hypervolemia, followed by hypovolemia or as in the case of uncompensated diuresis. [1] This pharmacologic cerebral decompression leads to volume loss with resultant fall in blood pressure and loss of neuro-autoregulatory mechanism which increases the risk of the dreaded complication of cerebral ischemia. Prior studies have proven that a careful fluid management strategy in patients undergoing neurologic surgery resulted in better outcome. [2] It has been proven that the mainstay of management of hypovolemic patients is nevertheless intravenous fluids. Hence, calculation of dosage parameters of intravenous fluids is of paramount importance. Inadequate volume replenishment leads to hypoperfusion of tissues and thereby worsens organ dysfunction which may be further compounded by uncorrected hypovolemia, resulting in the use of inappropriate infusions of vasopressor agents, thus worsening

the viscous cycle of ischemia. [3, 4] However, fluid overloading also impedes oxygen delivery and compromise patient outcome especially in patients with associated cardiac dysfunction. Overzealous fluid resuscitation results in increased rate of complications the most common being pulmonary edema and cardiac failure thereby resulting in poor outcome represented as increased duration of hospitalisation in ICU setting; and increased morbidity and mortality. [5, 6]

Recent studies have put forth the concept of timely and aggressive resuscitation of critically ill patients which may limit and/or revert tissue hypoxia and thereby improve the outcome. [7] The landmark study by Rivers et al concluded that early goal-directed therapy driven protocols, will prevent organ dysfunction and improve overall survival rate in patients with severe sepsis and prevent subsequent septic shock. [8] Likewise protocols which optimize the preload and resultant cardiac output improvement in patients undergoing surgery have significantly reduced postoperative morbidity and duration of hospital stay. [9, 10, 11] Various indices are described in the literature for assessment of fluid status in critically ill and perioperative patients. [12, 13] They are classified as static and dynamic indices. Static indices are simple to measure; however various studies have found them unreliable to guide therapy. Hence dynamic indices are usually the preferred guide to assess the responsiveness of fluid challenge and requirement. [14, 15, 16]

Passive leg raising is a form of reversible auto-transfusion, which transfers approximately 150-300 ml of blood from the lower limbs to the central circulation, thereby serves as an immediate method of resuscitation in hypovolemia. Apart from treatment of hypovolemia this method also serves as test to determine fluid responsiveness without administering a single drop of fluid; and thereby determine the position of each patient in the Frank-Starling curve. This way overzealous fluid

resuscitation can be avoided in fluid unresponsive patients avoiding the adverse effects of excess intravenous fluids. Transoesophageal echocardiography (TEE) is a semi invasive dynamic imaging modality which rapidly gained credence and popularity in the cardiothoracic centers worldwide by mid 1990s. It has also been found to be useful in some non cardiac surgical procedures, in particular in the management of neurosurgical patients and haemodynamically unstable patients in intensive care units (ICUs). TEE has been validated in monitoring cardiac output (CO) and changes in diameter of caval veins or left ventricular stroke volume (LVSV). [17]

TEE is a far more specific and objective method of assessment as well as monitoring the response to therapy when compared to impedance plethysmography especially in terms of measuring stroke volume, cardiac output and cardiac index. Moreover, TEE has got very little inherent risk, in comparison to invasive methods of measuring such indices like pulmonary artery catheter. [18, 19, 20] Further, as per ACC/AHA guidelines, TEE ought to be routinely used in neurosurgical procedures where there are anticipated risks of major fluid shifts, and hemodynamic perturbations (Class IIa indication).

The present evidence on PLR assessed fluid responsiveness is predominantly limited to Intensive care unit setting. Multitude of co-morbid conditions like sepsis, acute kidney injury, cardiac dysfunction, ionotropic therapy etc can confound fluid dynamics in critically ill patients. In this background, we proposed the present study to compare fluid responsiveness using clinical and TEE derived parameters in two groups of patients - Group 1:- Patients (without coronary artery disease) undergoing neurosurgical procedures; and Group 2:- Patients with coronary artery disease undergoing coronary artery bypass graft procedure under general anaesthesia (GA).

REVIEW OF LITERATURE

Fluidresponsiveness (FR) is the ability of stroke volume and thereby cardiac output to increase in response to a fluid infusion. SV is the amount of blood ejected from the heart with each beat and is dependent on preload (end-diastolic wall tension), contractility and afterload (end-systolic wall tension). When myocytes are stretched, they contract more forcefully and so SV increases as venous return increases. This concept is depicted by the Frank–Starling law. As well this is the foundation for the concept of fluid responsiveness. However, when stretched beyond a certain level, they are unable to contract more forcefully and so SV does not increase further (fluid 'unresponsiveness').The ultimate goal of resuscitation with fluids, vasopressors and inotropes is to ensure adequate oxygen delivery (DO2) to prevent or treat organ dysfunction.

Static and dynamic physiologic parameters have been described to quantify fluid responsiveness. Traditionally the central venous pressure (CVP) has been the main static physiologic parameter to guide fluid management. A European survey of intensivists/anesthesiologists reported that more than 90% used the CVP to guide fluid management. [21] A Canadian survey also reported that 90% of intensivists use the CVP to monitor fluid resuscitation in patients with septic shock. [22] The CVP is a good approximation of right atrial pressure, which is a major determinant of right ventricular (RV) filling. It has been assumed that the CVP is a good indicator of RV preload. Furthermore, because RV stroke volume determines LV filling, the CVP is assumed to be an indirect measure of LV preload.

However, due to the changes in venous tone, intrathoracic pressures, LV and RV compliance, and geometry that occur in critically ill patients, there is a poor relationship between the CVP and RV end-diastolic volume. Furthermore, the RV

end-diastolic volume may not reflect the patients' position on the Frank-Starling curve and therefore his/her preload reserve. More than 100 studies have been published to date that have demonstrated no relationship between the CVP (or change in CVP) and fluid responsiveness in various clinical settings. [23] Based on this information, it has been ascertained that the CVP should no longer be routinely used for guiding fluid management in the ICU, operating room, or emergency room.

With the advancement in technology, many other invasive methods to determine the fluid status of a patient were postulated. One of these being the pulmonary artery occlusion pressure (PAOP), which was suggested to be a reliable index to predict the volume status in patients who were critically ill. Tousignant and Diebel, after extensive research on PAOP, came to the final conclusion that the PAOP had a lower baseline value in patients who were responders in comparison with those who were not responsive. Furthermore, studies conducted by Wagner and Leatherman brought to the notice of all that, patients who had an increase in the LV stroke volume after fluid therapy had a co-relation with the baseline PAOP in a linear manner. Inspite of this linear relationship, no single PAOP cut off value has been determined to gauge the hemodynamic response to volume expansion prior to giving fluid infusion to the patient.[24]

Since there was no consensus on the cut-off value which was found to be the baseline to initiate fluid administration, it was concluded that though the PAOP showed values that were significant statistically, and they could not be used to discriminate between patients who were responders or non-responders. Many other studies came to prove a fact that the baseline values of PAOP were comparable between the responder and the non-responder groups of patients. Studies also came to the conclusion that there was absolutely no co-relation when cardiac filling pressures

were compared before volume expansion and also the hemodynamic response to volume expansion. [25, 26, 27]

During the past decade a number of dynamic tests of volume responsiveness have been reported. These tests dynamically monitor the change in stroke volume after a maneuver that increases or decreases venous return (preload). These tests allow the clinician to determine the individual patient's position on his/her Frank-Starling curve, and thus determine whether the patient is likely to be fluid-responsive. These techniques use the change in stroke volume during mechanical ventilation or after a passive leg raising (PLR) maneuver to assess fluid responsiveness. Different dynamic tests have diverse applicability in spontaneous breathing patient versus in a patient on mechanical ventilation.

An impressive number of studies have demonstrated that the pulse pressure variation (PPV) derived from analysis of the arterial waveform, the stroke volume variation (SVV) derived from pulse contour analysis, and the variation of the amplitude of the pulse oximeter plethysmographic waveform to be highly predictive of fluid responsiveness. [28] These three tests have applicability in patients on mechanical ventilation. It should be appreciated that both arrhythmias and spontaneous breathing activity will lead to misinterpretations of the respiratory variations in pulse pressure/ stroke volume. Heart – Lung interactions during mechanical ventilation attain importance in this context. Intermittent positive-pressure ventilation induces cyclic changes in the loading conditions of the left and right ventricles. Mechanical insufflation decreases preload and increases afterload of the right ventricle. The RV preload reduction is due to the decrease in the venous return pressure gradient that is related to the inspiratory increase in pleural pressure. [29] The increase in RV afterload is related to the inspiratory increase in transpulmonary

pressure. The reduction in RV preload and increase in RV afterload both lead to a decrease in RV stroke volume, which is at a minimum at the end of the inspiratory period. [30] The inspiratory reduction in RV ejection leads to a decrease in LV filling after a phase lag of two or three heart beats because of the long blood pulmonary transit time. Thus, the LV preload reduction may induce a decrease in LV stroke volume, which is at its minimum during the expiratory period when conventional mechanical ventilation is used. The magnitude of the respiratory changes in LV strokevolume is an indicator of biventricular preload dependence. With remarkable consistency, a variation of greater than 12% to 13% has been reported to be highly predictive of volume responsiveness.

The pulse oximeter plethysmographic waveform differs from the arterial pressure waveform by measuring volume rather than pressure changes in both arterial and venous vessels. The dynamic changes of the plethysmographic waveform with positive pressure ventilation have shown a significant correlation and good agreement with the PPV and have accurately predicted fluid responsiveness in both the operating room and ICU setting. [31, 32, 33] The "Pleth Variability Index" (PVI) is an automated measure of the dynamic change in the "Perfusion Index" that occurs during a respiratory cycle (Masimo Corporation, Irvine, CA).The "Perfusion Index" is the infrared pulsatile signal indexed against the nonpulsatile signal and reflects the amplitude of the pulse oximeter waveform. The PVI correlates closely with the respiratory induced variation in the plethysmographic and arterial pressure waveforms and can predict fluid responsiveness noninvasively in mechanically ventilated patients. [34, 35]

Echocardiography is an essential tool for guiding resuscitation in critically ill patients. The question of whether the patient improves with fluid, additional

vasopressors or inotropes can be difficult to answer. Echocardiography is an evidence-based dynamic approach and ideally suited to address this problem. Echocardiography provides much more information on the causes of shock than just FR and is increasingly considered the first-line monitoring tool of choice in hemodynamically compromised patients. Both static and dynamic parameters may be assessed to build a picture of the circulatory state.

Echocardiography derived left ventricular (LV) dimensions, LV outflow variations and great vein diameter variations have been used to assess fluid responsiveness. Changes in LV size as assessed by TEE reflect changes in preload. However, increasing preload does not necessarily increase SV, and LV size is not always a predictor of fluid responsiveness. LV outflow variation parameters commonly studied include – stroke volume variation (SVV), aortic peak velocity (aortic velocity time integral or aortic VTI) and aortic VTI variation. The left ventricular outflow tract (LVOT) diameter can be assumed not to change in size over the respiratory and cardiac cycle and so changes in aortic blood flow reflect changes in stroke volume. Measuring the VTI (measurement of all the velocities of RBCs for each contraction at a certain point) can be done by tracing the spectral Doppler envelope. Tracing the largest and smallest VTI over a respiratory cycle allows the percentage change to be calculated.

Certain facts need be remembered while using LV outflow variation. The patient must be in sinus rhythm otherwise stroke volume may vary because of the arrhythmia. There must be no spontaneous respiratory effort, which would alter preload and SV and make variations a reflection of work of breathing rather than FR. Tidal volumes should be around 8 mL/kg. Lower tidal volumes, although now desirable in critical illness, cause small amplitude changes in intravascular pressure

and have been shown to cause false negatives. Intra-abdominal pressure should also be normal.

The size and variation in size over the respiratory cycle of both the inferior venacava (IVC) and superior venacava (SVC) also give information about volume status. IVC size, measured just distal to the hepatic vein, in spontaneously breathing patients correlates with RAP. [36] Ventilated patients demonstrate a low correlation between IVC size and right atrial pressure (RAP); however, an RAP of less than 10 mm of mercury can be assumed if the IVC is less than 12 mm. [37] Invasively ventilated patients often have a dilated IVC because of increased intrathoracic pressure rather than as a reflection of their intravascular volume status.IVC diameter variation can reliably predict fluid responsiveness even in patients on mechanical ventilation. A diameter 'variability' cut-off value of more than 12% identifies responders. [38] A variation threshold of 18% is used if 'IVC distensibility index' is used.IVC diameter variation has also been studied in spontaneously breathing patients without respiratory support; however, the evidence to support its use is weak and cannot be advocated at this time. [39] The superior venacaval (SVC) diameter changes are opposite of the IVC in mechanical ventilation. The collapsibility index of the SVC has been shown to be predictive of fluid responsiveness with a variation in SVC size of 36%, being an appropriate cut-off value using the equation 100 × (Dmax – Dmin/Dmin). [40]

Right ventricle (RV) size can also be used to titrate fluid administration. An increase in RV size with no increase in SV is a definite stopping point for fluid administration. Paradoxical septal wall motion demonstrating very high RV pressure may be a contraindication to IV fluids.

Echocardiography also allows titrating fluid therapy based on fluid tolerance. In both spontaneously breathing and ventilated patients, a small IVC that varies in

size with respiration, non-dilated right heart chambers, a non-displaced inter-ventricular septum, absence of right and left ventricular systolic failure and absence of markers of raised LVEDP all suggest that fluid administration will not cause acute harm. Fluid administration should stop when aortic velocity time integral (VTIAo) no longer significantly increases with a fluid bolus.

Passive leg raising (PLR) is a reversible maneuver that mimics rapid fluid loading by shifting venous blood from the legs [41] toward the intra-thoracic compartment and by increasing right and left ventricular preloads, thereby increasing LV SV and CO. [42, 43] It has been demonstrated that up to 300 ml of blood is transferred into the central circulation with this method, but it may vary depending on anthropometric features, venous valve competency, and the use of compression stockings or devices. The volume is likely diminished during conditions of severe vasoconstriction, such as cardiogenic or hypovolaemic shock or use of high dose vasopressors. The increase in CO and/or arterial pressure after PLR could predict the corresponding response after a fluid infusion. Hence, PLR may be considered a reversible auto-transfusion, the effects of which mostly vanish after one minute. An increment of 10% or more in SV or aortic VTI after one minute of PLR is suggestive of fluid responsiveness.

The concept of detecting preload responsiveness by using PLR emerged from a study in mechanically ventilated patients, where the increase in thermodilution stroke volume after a fluid infusion correlated with the increase in arterial pulse pressure produced by PLR.[44] Since then the ability of PLR to serve as a test of preload responsiveness has been confirmed in additional studies performed in critically ill patients. [45, 46, 47, 48, 49, 50, 51]

Monnet X et al [52] have provided a succinct summary of performing the PLR test which importantly should be performed by tilting the bed rather than lifting the patient's legs. PLR should start from the semi-recumbent and not the supine position. Adding trunk lowering to leg raising should mobilize venous blood from the large splanchnic compartment, thus magnifying the increasing effects of leg elevation on cardiac preload and increasing the test's sensitivity. Therefore starting PLR from a semi-recumbent position induces a large increase in cardiac preload because it induces the shift of venous blood not only from both the legs but also from the abdominal compartment. The PLR effects must be assessed by a direct measurement of cardiac output and not by the simple measurement of blood pressure. Indeed, reliability of PLR is poorer when assessed by using arterial pulse pressure compared with cardiac output.[53] Although the peripheral arterial pulse pressure is positively correlated with stroke volume, it also depends on arterial compliance and pulse wave amplification. The latter phenomenon could be altered during PLR, impeding the use of pulse pressure as a surrogate of stroke volume to assess PLR effects.

The technique used to measure cardiac output during PLR must be able to detect short-term and transient changes since the PLR effects may vanish after1 minute. Techniques monitoring cardiac output in 'real time', such as arterial pulse contour analysis, echocardiography, esophageal Doppler, or contour analysis of the volume clamp-derived arterial pressure, should be used. [54] Conflicting results have been reported for bio-reactance method. [55, 56] The hemodynamic response to PLR can even be assessed by the changes in end-tidal exhaled carbondioxide, which reflect the changes in cardiac output in the case of constant minute ventilation. Pain, cough, discomfort, and awakening could provoke adrenergic stimulation, resulting in mistaken interpretation of cardiac output changes. Some simple precautions must be

taken to avoid these confounding factors. PLR must be performed by adjusting the bed and not by manually raising the patient's legs. Bronchial secretions must be carefully aspirated before PLR in an intensive care scenario. It has been suggested that PLR is unreliable in the case of intra-abdominal hypertension. [57] Nevertheless, the single study investigating this issue did not confirm the hypothesis since intra-abdominal pressure was not measured during PLR.

Because it has no side effects, PLR should be considered as replacement for the classic fluid challenge. [58] The main drawback of the fluid challenge is that, if it is negative, fluid has nonetheless been irreversibly administered to the patient. Repeated fluid challenges therefore can lead to fluid overload. In this regard, PLR is an attractive method of challenging preload without administering one drop of fluid. Importantly, it should be remembered that detection of preload responsiveness by a positive PLR test should not routinely lead to fluid administration. Indeed, the decision to administer fluid must always be made individually on the basis of the mandatory presence of the three following situations: hemodynamic instability or signs of circulatory shock (or both), preload responsiveness (positive PLR test), and limited risks of fluid overload. Also, a negative PLR test should contribute mainly to the decision to stop or discontinue fluid infusion, in order to avoid fluid overload, suggesting that hemodynamic instability should be corrected by means other than fluid administration.

Since its introduction, the diagnostic ability of PLR induced auto-transfusion in predicting fluid responsiveness has been studied by many authors. The predictive value of PLR-induced changes in CO or in other hemodynamic parameters having the same physiological meaning; such as cardiac index (CI), stroke volume (SV), aortic blood flow (ABF), aortic velocity–time integral (VTIAo); was the core concept in all

these studies. Cardiac output or its corroborative variables were derived from either of the many methods in these studies namely – esophageal Doppler, transthoracic echocardiography, transpulmonary thermodilution, pulse-contour analysis and bioreactance. The PiCCO™ system (Pulsion Medical Systems, Munich, Germany) uses transpulmonary thermodilution to calibrate the pulse-contour-derived stroke volume, whereas the stroke volume derived from the FloTrac-Vigileo™ (Edward Lifesciences, Irvine, CA) device is uncalibrated. Both of these devices may be useful to determine the hemodynamic response to PLR. In this regard, an increase in "pulse contour" cardiac output by more than 10% in response to PLR has been shown to accurately predict volume responsiveness in mechanically ventilated patients with spontaneous breathing activity. Although less invasive than pulmonary artery catheterization, these techniques are not ideally suited to resuscitation in the emergency room or ward or on initial presentation in the ICU. In these situations, the change in stoke volume after a PLR maneuver can be assessed noninvasively by bioreactance.

Bioreactance cardiac output measurement is based on an analysis of relative phase shifts of an oscillating current that occurs when this current traverses the thoracic cavity. It differs from traditional bioimpedance-based systems, which rely on measured changes in signal amplitude.[59] The NICOM™ (Cheetah Medical, Portland, OR, USA), based on bioreactance technique, is comprised of a high-frequency (75 kHz) sine wave generator and four dual electrode "stickers" that are used to establish electrical contact with the body. The cardiac output as measured by bioreactance has been shown to be highly correlated with that measured by thermodilution and pulse contour analysis. [60, 61] The NICOM™ system has an algorithm with user prompts and an interface that rapidly facilitates the performance of a PLR maneuver. Patient

ventilator status (spontaneous ventilation versus mechanical ventilation) and cardiac rhythm (sinus versus arrhythmia) were found to be confounding the effects of PLR induced changes since the original study. A few studies [44 46] enrolled only patients adapted to ventilator and in sinus rhythm to assess PLR induced changes in cardiac output, whereas, many other studies [45 47 51] also enrolled patients with spontaneous respiratory efforts and/ or arrhythmias to assess similar changes. However, almost all these studies are entirely limited to critical care/sepsis scenario. In 2010, Cavallaro F et al [62] systematically reviewed the published evidence on the ability of PLR induced changes in cardiac output (PLR-cCO) and in arterial pulse pressure (PLR-cPP) to predict fluid responsiveness and found – PLR induced changes in cardiac output reliably predict fluid responsiveness regardless of ventilation mode, underlying cardiac rhythm and technique of measurement; and can be recommended for routine assessment of fluid responsiveness in majority of ICU population. PLR-induced changes in pulse pressure can be a viable alternative with lower predictive ability, irrespective of ventilator status (spontaneous ventilation versus mechanical ventilation) and cardiac rhythm (sinus versus arrhythmia). These changes were also independent from the device used to measure CO: PiCCO (pulse contour cardiac output), Vigileo/FloTrac, esophageal Doppler, echocardiography. All studies included in this meta-analysis were conducted in ICU on patients in shock due to various etiologies. A further meta-analysis of 21 studies conducted in 991 adult patients, published recently by Monnet et al, [63] also demonstrated that the changes in CO during a PLR test predicted fluid responsiveness with excellent pooled sensitivity and specificity. The pooled area under the ROC curve in the meta-analysis was 0.95±0.01. The AUROC with a value of 0.805, in their study confirmed very good diagnostic accuracy of the test.

The clinical use of TEE in cardiac surgery has been a standard of care. The clinical use of TEE in non- cardiac surgery has been growing and is now a valuable tool in the anesthesiologist's perioperative diagnostic armamentarium. The use of TEE in cardiac surgery has been well established for a large variety of cardiac and aortic conditions.[64] In the non-cardiac surgical realm, the primary accepted indication has been 'suspected cardiovascular pathology that may result in hemodynamic, pulmonary, or neurologic compromise.[65] For intensivists, the use of TEE is recommended when it may change therapies and when other monitoring or less invasive diagnostic modalities are not expected to give the same timely information. TEE in the non-cardiac operating room has been associated with altering therapies in up to 60% of patients for over a decade, as long as the patients had appropriate indications for the TEE to be performed.[66] The commonly recognized benefit is the ability, with TEE, to assess left ventricular function and loading conditions, to recognize wall motion abnormalities, and in guiding vasopressor therapy.[67] In neuro-anaesthesia practice, the dreaded complication of venous air embolism in which non compressible venous cavities are open to the air, and frequently above the level of the heart, remains the published recommendation for the use of TEE in the peri-operative arena for this population. Sitting craniotomies are a subset of this field's patients in which TEE is frequently considered a very useful diagnostic tool, even to the extent that it has been considered a standard of care at certain institutions in this specific population subset.[68] TEE also has expanded use in the arenas of vascular surgery – for detection of myocardial dysfunction during aortic cross clamping and large fluid volume shifts; urological surgery – for detection of macroscopic embolism from renal cell carcinoma; and orthopaedic surgery – for detection of embolic material in hip or femoral intramedullary surgeries. In liver transplantation surgery TEE is used as a

real-time, biventricular tool for evaluating ventricular chamber size and function where in this type of surgery where rapid shifts in intravascular volume or electrolyte fluctuations can quickly change hemodynamics. Diastolic dysfunction in liver transplant patients has recently been associated with increased risk of allograft rejection, graft failure, and mortality.[69] It has been shown that grade 1 or 2 esophagealvarices, though considered a relative contraindication to placement, do not preclude the use of TEE when deemed clinically indicated.[70, 71] In the field of intensive care medicine TEE has established role in monitoring hemodynamic instability, monitoring during weaning from extracorporeal membrane oxygenation and for surveillance of circulatory status after return of spontaneous circulation post-cardiac arrest. The increased popularity of recently developed small, miniaturized, single use TEE probes (hTEE) need be asserted in this context.

Studies evaluating fluid responsiveness in patients with coronary artery disease undergoing coronary artery bypass surgery are scarce. Appropriate fluid management is one of the most important elements of early goal-directed therapy after cardiothoracic surgery [72, 73, 74] Cautious fluid management is usually advocated in patients suffering acute myocardial infarction, particularly when the left ventricle is affected, because of the risk for deleterious volume overload leading to venous congestion, pulmonary & tissue oedema; and increased strain on an acutely ischaemic, failing ventricle. Increased pre-load may still be beneficial, however, in the subset of patients in whom the left ventricle is still operating on the upward slope of the Frank– Starling pre-load to stroke volume relation. The clinical challenge lies in predicting the response to volume expansion in the individual patient, i.e. in which patient will stroke volume increase in response to fluid administration. In the critically ill coronary artery disease patient on mechanical ventilation, cyclic changes in intra-

thoracic pressure influence both cardiac pre and afterload, further contributing to the complexity of determining volume responsiveness.

Snygg J et al [75] studied the fluid responsiveness in a pig closed chest model of induced acute myocardial infarction. The authors anaesthetized fifteen mechanically ventilated pigs following acute left myocardial infarction by temporary coronary occlusion. Animals were instrumented to monitor central venous and pulmonary artery occlusion pressures; and systolic pressure variation and pulse pressure variations. The authors measured cardiac output using pulmonary artery catheter and the PiCCO ((PiCCO Plus, Version 6.0; Pulsion Medical Systems, AG, Munich, Germany) monitor was used for measuring stroke volume variation. Variations in the velocity time integral by pulsed-wave Doppler echocardiography were determined in the left (VTI LV) and right (VTIRV) ventricular outflow tracts. Consecutive boluses of 4 ml/kg hydroxyethyl starch were administered and volume responsiveness was defined as a 10% increase in CO. Receiver–operator characteristics (ROC) in this study demonstrated the largest area under the curve for VTIRV [0.81 (0.70–0.93)] followed by PPV [0.76 (0.64–0.88)] [mean (and 95% CI)]. SPV, VTILV and SVV did not change significantly during volume loading. CVP and PAOP increased but did not demonstrate significant ROC.

Sobczyk D et al [76]studied the usefulness of dynamic IVC-derived parameters (collapsibility index, distensibility index) in comparison to passive leg raising, in postoperative fluid management in 35 mechanically ventilated patients with left ventricular ejection fraction ≥30%, immediately after elective coronary artery bypass grafting. The IVC collapsibility index (IVC-CI) was defined as: IVC-CI = IVCmax -

IVCmin/IVCmax. The IVC distensibility index (IVC-DI) was calculated using the formula: IVC-DI = IVCmax - IVCmin/IVCmin. Both indices were expressed as a percentage. The authors assessed fluid responsiveness of the study population after fluid bolus administration and after passive leg raising. Among the study population 68.57% were fluid responders. Cardiac output was assessed using transthoracic echocardiography. A 15 % PLR-induced increase of cardiac output predicted a 15 % increase in cardiac output after fluid administration, with 79.17 % sensitivity and 81.82 % specificity. The diagnostic accuracy of PLR (area under ROC curve) was 0.805. Both dynamic IVC derivatives (IVC-CI, IVC-DI) were slightly higher in fluid responders when compared to non-responders, however this trend did not reach statistical significance. The authors concluded that ultrasonographic measurement of IVC respiratory variation did not reach statistical significance in differentiation between fluid responders and non-responders.

Song Y et al [77] studied respirophasic carotid artery peak velocity variation (Vpeak-CA) apart from pulse pressure variation as a predictor of fluid responsiveness in 40 mechanically ventilated patients with coronary artery disease undergoing elective coronary artery bypass surgery. In this study the authors found PPV and Vpeak-CA correlated significantly with an increase in stroke volume index after volume expansion. Area under the receiver-operator characteristic curve (AUROC) of PPV and Vpeak-CA were 0.75 [95% confidence interval (CI) 0.59–0.90] and 0.85 (95% CI 0.72– 0.97). The optimal cut-off values for fluid responsiveness of PPV and Vpeak-CA were 13% (sensitivity and specificity of 0.74 and 0.71) and 11% (sensitivity and specificity of 0.85 and 0.82), respectively. Further, in a subgroup analysis of 17 subjects having pulse pressure hypertension (≥ 60 mm Hg), PPV failed

to predict fluid responsiveness (AUROC 0.70, P = 0.163), whereas the predictability of Vpeak-CA remained unchanged (AUROC0.90, P = 0.006). The authors concluded that Doppler assessment of respirophasic Vpeak-CA to be a highly feasible and reliable method to predict fluid responsiveness in mechanically ventilated patients undergoing coronary revascularization.

At present the available evidence on PLR is limited mainly to the ICU, with investigations conducted in patients with hemodynamic instability of multiple etiology; most common being sepsis. Co-morbid conditions like acute kidney injury, cardiac dysfunction, pulmonary dysfunction and ionotropic infusions can confound fluid responsiveness in ICU patients. Evidence pertaining to evaluation of efficacy of PLR on fluid responsiveness in peri-operative scenario is limited. Moreover, the use of echocardiography as a method to assess such responsiveness is not widespread. [78] None of published studies have used transesophageal echocardiography (TEE) to evaluate such responsive changes in cardiac output. In this context TEE offers the distinct benefit of real time assessment of fluid responsiveness as compared to transthoracic echocardiography which may be methodologically cumbersome in the perioperative period.

HYPOTHESIS

We hypothesised that fluid responsiveness to a passive leg raising maneuver in patients without and with coronary artery disease under general anaesthesia and mechanical ventilation will be the same. Patients without any co-morbid illness presenting for elective major neurosurgery represented the non-coronary artery disease group; and patients undergoing coronary artery bypass graft surgery represented the cases with coronary artery disease in our study.

AIMS AND OBJECTIVES

Primary Objective:-

The primary aim of the study was to find the diagnostic accuracy of TEE assessed parameters in predicting fluid responsiveness to PLR in two groups of patients:– **Group (1)** Patients without coronary artery disease undergoing major elective neurosurgical procedures; and **Group (2)** Patients with coronary artery disease undergoing coronary artery bypass graft procedure under general anaesthesia (GA).

Secondary Objectives:-

The secondary objectives of our study were

(a) To describe and classify the study variables as clinical and TEE derived in both the groups, and to assess changes in each within stipulated time intervals after PLR.

(b) To study whether patients with and without coronary artery disease respond the same way or differently to a physiological fluid challenge induced by PLR.

(c) To study the consistency and duration of a hemodynamic response (clinical/TEE derived) to the PLR, provided there was a response.

(d) To compare across clinical and TEE derived parameters, and to find the best pair of either to predict a hemodynamic response to fluid challenge induced by PLR, provided there was a response in either of the groups

(e) To find the threshold raise/fall in each of the clinical and TEE derived parameter to predict responsiveness with the best sensitivity and specificity, provided there was a response.

MATERIALS AND METHODS

DESIGN

Prospective observational study

SETTING

Neurosurgery and cardiothoracic surgery operating rooms of the Sri Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, Kerala. Both the operating rooms of our institution are equipped with TEE system.

METHODOLOGY

We designed a prospective observational study to find the diagnostic accuracy of various clinical and TEE assessed parameters in predicting fluid responsiveness in two groups of patients – **Group 1:** Patients (without coronary artery disease) undergoing elective major neurosurgical procedures under general anesthesia; and - **Group 2:** Patients with coronary artery disease undergoing elective coronary artery bypass graft procedure under general anesthesia and cardiopulmonary bypass (CPB). The study was conducted at the neurosurgery and cardiothoracic surgery operating rooms of our hospital. Both the operating rooms of our institution are equipped with TEE ultrasound system.

Both the operating rooms of our institution are equipped with TEE system. Institute Technical Advisory committee approval was obtained prior to conduct of the study vide TAC Registration number: SCT/S/2016/524 dated 22.09.2016. Institutional ethics committee clearance was obtained prior to initiating the study vide approval number SCT/IEC/980/DECEMBER-2016 dated 06.01.2017. The study was registered with the Clinical Trial Registry of India vide reference number REF/2018/03/018851

and registration number CTRI/2018/05/013655 dated 03/05/2018. Written informed consent was obtained from all participants. A Data Safety Monitoring Board (DSMB) was constituted which included five faculty members of our institution who independently did periodic surveillance of the study conduct and adverse events if any. None of the members of DSMB were investigators of this study.

Patients were enrolled to the study from the elective operation list of the respective surgical department namely neurosurgery (Group 1) and cardiothoracic and vascular surgery (Group 2). The study was conducted between January 2017 and December 2017.

Written informed consent was obtained from patients willing to participate in the study.

The following are the inclusion criteria of each of the group of patients-

Group 1

a) Patients of age 19-65 years undergoing major elective neurosurgical procedures under GA and mechanical ventilation.

b) Patients in whom intraoperative TEE monitoring was required on account of their surgical or disease factors like risk of venous air embolism, surgery in semi-sitting posture, or anticipated occurrence of intraoperative hemodynamic instability.

Group 2

Patients with coronary artery disease, undergoing coronary artery bypass graft procedure (CABG) under GA and mechanical ventilation.

All patients undergoing CABG under GA are routinely monitored for intraoperative diagnosis of myocardial ischemia and hemodynamic instability as well as aid in therapeutic management with intraoperative TEE at our institute.

EXCLUSION CRITERIA

- Patient refusal.
- Age less than 18 years and more than 65 years.
- For Group-1: patients with documented coronary artery disease or regional wall motion abnormality seen in preoperative echocardiography
- Presence of heart block, cardiac rhythms other than sinus rhythm.
- Valvular heart disease, intracardiac shunts, peripheral vascular disease. pregnant or nursing woman
- Patients with left ventricular dysfunction as determined by preoperative echocardiography.
- Presence of esophageal pathologies like esophageal mass, stricture, tracheo-esophageal fistula, esophageal varices, history of previous esophageal/upper GI surgery.
- Cervical arthritis/Atlanto -axial joint disease with restricted neck mobility.
- Hip and Knee replacement or arthritis restricting the movements of leg.
- Pregnant and nursing women
- Patients undergoing emergency surgery

DETAILED DISCUSSION OF THE STUDY PROTOCOL

Patients in group 1 of our study required routine intraoperative TEE monitoring on account of their surgical/disease factors/risk for venous air embolism,

irrespective of the study requirement. All patients undergoing CABG are monitored with TEE intraoperatively in our institution.

During pre-anesthetic visit, patients were explained about the study protocol in detailed and written informed consent was obtained for study enrollment. On the day of surgery patients were shifted to the operation theatre suite and American Society of Anesthesiologists (ASA) standard monitors were connected. Baseline recordings of heart rate, non-invasive blood pressure and SpO2 were monitored using a bedside monitor (Philips Intellivue, MX700, Philips Medizin systems, Germany).Under local anaesthesia infiltration [Lignocaine (2%) skin infiltration] I.V access with 16 G /18 G venous cannula was obtained. An arterial access with 20 G arterial cannula was obtained in the non-dominant upper extremity radial artery and the pressure transducer was positioned at the mid-axillary level for beat to beat measurement of blood pressure.

Baseline infusion of crystalloid intravenous fluids was initiated as per standard operating protocol and treatment decision of the attending anaesthesiologist. Intravenous fluid administration dosage was not altered for study purpose. The patients were pre-oxygenated with oxygen at 6 L/min for three to five minutes after which they were premeditated with fentanyl 2-3mcg/kg and induced with propofol 1-2mg/kg. Further endotracheal intubation was facilitated with an intermediate acting muscle relaxant vecuronium, dosed at 0.1mg/kg. Post induction maintenance was achieved with an air: oxygen mixture of the ratio 1:1 and sevoflurane at a MAC of 0.5-1.0.Intravenous maintenance of anaesthesia was done with an infusion of fentanyl with atracurium at an infusion rate of 1mcg/kg /hr of fentanyl and 0.01 to 0.02 mg/kg/hr of atracurium. Mechanical ventilation was instituted in volume-controlled mode (Aestiva /5, Datex Ohmeda) with a square wave (constant inspiratory flow)

adjusted to obtain a PaCO2 of 35- 40 mm Hg during surgery. Positive end expiratory pressure (PEEP) was not applied.If necessary, the ventilator protocol was changed to achieve a PaCO2 of 35- 40 mm Hg. A blanket and a warming system using forced air (Bair Hugger Warming system, Augustine Medical, USA) were applied in order to avoid hypothermia. Body temperature was measured using temperature probe placed in the nasopharynx. Post-optimization of ventilatory settings and final positioning, the Peak Inspiratory Pressure (PIP) was recorded.

The TEE probe (GE Vivid 7 with 9T 4, 0-10.0 MHz multiplane TEE probe, GE Healthcare, Wauwatosa, WI 53226, USA) was inserted after insertion of a bite block and adequate lubrication with lubricant jelly in neurosurgical patients. The probe was inserted before the patient was positioned for surgery.TEE derived variables were recorded as per standard American Society of Echocardiography guidelines. For cardiac surgical patients iE33, RT3D TEE ultrasound machine (Philips Ultrasound USA) and matrix array TEE transducer (X7-2t) was used.

Clinical and TEE measurements were obtained at three time intervals – baseline, 1 minute after PLR and 10 minutes after PLR. The clinical and TEE variables studied were entered manually into a proforma. TEE variables were obtained using mid-esophageal four chamber view,mid-esophageal bicaval view,mid-esophageal aortic valve long-axis view, trans-gastric mid-papillary short axis view and deep trans-gastric long axis view. The TEE study protocol used in this study is as follows.

Echocardiographic (TEE) based evaluation and measurements

(1) Mid-esophageal four chamber view (ME 4C):-

The probe was advanced to a depth of 30 to 35cm until it was immediately posterior to the left atrium. With the imaging angle at 0 to 10 degrees, sector depth at 12-14 cms and with the TEE probe in neutral position, the four chamber view was obtained. The probe was turned to the left (counter clockwise rotation of the probe) to center the mitral valve (MV). Clockwise rotation of the probe (turning it to the right) would center the left ventricle in the sector display. The key structures observed here were the left atrium, the left ventricle, the right atrium, right ventricle, tricuspid and mitral valves; and the septal and lateral walls of the myocardium.

In this view we measured left ventricular end diastolic volume (LVEDV) and left ventricular end systolic volume (LVESV). In the ME four chamber view, short loops were saved and end -systolic and end diastolic frames were identified. End-diastole was defined as the largest left ventricular cross sectional area immediately after R-wave peak in the echocardiogram. End-systole was defined as the smallest left ventricular cross-sectional area immediately after the end of the T wave. The endocardial borders were traced, starting at the medial or anterior mitral annulus and finishing at the lateral or posterior mitral annulus. We obtained non-foreshortened views of the left ventricle so as to visualize the true apex and prevent underestimation of volumes. Left ventricular volume was calculated using modified Simpsons method. In this method, the LV is described as a series of 20 discs from the base to the apex of the left ventricle, like a stack of coins with decreasing size. The computer software package calculated the volume of each disc as area multiplied by height and the volumes were summated to give total left ventricular volume.

(2) Midesophageal aortic valve long -axis view:-

This view was obtained by rotating the imaging angle to approximately 110 to 130 degrees and a sector depth of 8 to 10 cm with the probe in neutral position. The

important structures seen here are the left ventricular outflow tract (LVOT), aortic valve (AV) and the ascending aorta. The stroke volume (SV), cardiac output (CO) and stroke volume variation (SVV) were calculated using LVOT diameter measured from this view during systole.

(3) Midesophageal Bicaval View:-

This view was obtained by turning the probe further to the patient's right at an angle of 105 to 120 degrees and a sector depth of 8 to 10 cms with the probe neutral. Structures visualized in this view include the left atrium, the right atrium, right atrial appendage, inter-atrial septum, superior venae cava and inferior venae cava. Anatomical M-mode was used to measure the diameters of the superior venae cava (SVC) by adjusting the probe position cranially or caudally. The SVC diameters measured were the maximum diameter on expiration (SVC max) and minimum diameter on inspiration (SVC min). The measurements were done during the same respiratory cycle.

(4) Trans-gastric mid-papillary short axis view:-

This view was obtained with the probe of the TEE at an angle of 0 degrees and a sector depth of 12 cm with the probe in the ante-flexed position inside the stomach. This view shows the left ventricular walls, the left ventricular cavity and the papillary muscles.

(5) Deep trans-gastric long axis view:-

The probe was pushed into the deep transgastric position and the tip of the probe was anteflexed further to bring the above mentioned view. The pulse wave Doppler cursor was placed 5 mm above the level of aortic valve inside the LVOT. The Doppler recordings were obtained with low speed to depict both the high and low

height of the wave tracing in the same respiratory cycle consisting of both inspiration and expiration. The stroke volume was calculated from multiplying the LVOT cross sectional area with the velocity time integral (VTI) by tracing the Doppler waves at the high and low waves. The stroke volume and cardiac output were calculated using the software provided in the TEE machine.

After obtaining baseline TEE readings, both groups of patients underwent PLR from semi-recumbent position, as per standard protocol using movements of the electronic position adjustable operating table. Patients were first made semi-recumbent using the electronic adjustments of the operating table. Following this head end of the operating table was lowered and simultaneously PLR was introduced using electronic adjustments of the operating table. Real-time assessment of clinical and TEE based parameters were done at 1 minute and 10 minutes after PLR. The clinical parameters studied included heart rate, systolic blood pressure, diastolic pressure, pulse pressure, systolic pressure variability and pulse pressure variability. The TEE derived parameters studied included left ventricular end diastolic volume, aortic VTI, aortic VTI variability, stroke volume, superior venae cava diameter, superior venacava collapsibility index, cardiac output and cardiac index. Averages of three readings for each measurement at – baseline, 1 minute after PLR and 10 minutes after PLR - were taken for all the clinical and TEE derived recordings. Patients were watched for any adverse events following PLR. In case of any adverse event in the form of hemodynamic instability or compromise in mechanical ventilation, patients were returned to supine position and excluded from study. Patients were returned to supine position after recording the observations following which surgical procedure was continued as planned by the surgical team.

STATISTICAL ANALYSIS

Sample size calculation:- Assuming an equivalence margin of 2% and standard deviation of 2.6% for fluid responsiveness measured by TEE, to achieve 80% power with alpha error of 5%, minimum sample size required in each of the two groups is estimated to be 21. We recruited 29 patients to group 1 and 25 patients to group 2 (age 19-65years in both groups), to compensate for the outliers and confounders.

Analysis of data:- Data collected during the study were compiled using Microsoft Office Excel. Normality of data was tested with Kolmogorov–Smirnov one-sample test. Variates were presented as mean±SD for continuous variates with normal distribution. Hemodynamic parameters were classified as clinical and echocardiographic variables and analysed at paired intervals. Repeated measure ANOVA was used for paired comparison of hemodynamic data in both groups at 3 intervals - baseline versus hemodynamic response at 1 minute after PLR; baseline versus 10 minutes after PLR; and 1 minute versus 10 minute PLR response. The correlation between significant clinical and echocardiographic variables was assessed using Karl Pearson correlation coefficient. Bland-Altman analysis was performed to evaluate the agreement between significant clinical and echocardiographic variables. Receiver operating characteristic (ROC) curves were generated separately for significant clinical and echocardiographic variables and area under curves was calculated. Sensitivity, specificity and corresponding likelihood ratios of each hemodynamic variable in predicting a response was calculated from the ROC curves data. A P value <0.05 was considered as statistically significant. All statistical analyses were carried out with IBM SPSS Statistics for Windows, version 21.0 (IBM Corp, USA.

RESULTS AND OBSERVATIONS

Patients undergoing major elective neurosurgery were classified as Group 1 and patients undergoing elective CABG were classified as Group 2 in our study. A total of 29 patients undergoing elective neurosurgery and 25 patients undergoing elective CABG were recruited into the study. The demographic characteristics, medical condition and baseline echocardiography characteristics of the recruited cases are depicted in **Table 1, 2 and 3.**. A total of 137 TEE examinations and measurements were obtained across both the groups. Study variables were classified as clinical and echocardiographic for the purpose of analysis. Measurements were recorded as baseline, 1 minute after PLR and 10 minutes after PLR. Paired comparison was done for clinical and echocardiographic parameters at baseline versus hemodynamic response at 1 minute after PLR; baseline versus 10 minutes after PLR; and 1 minute versus 10 minute PLR response. Percentage of change in each parameter at 1 and 10 minutes after PLR, from baseline and also change at 10 minutes with regard to 1 minute values were also calculated. A p value of <0.05 was considered significant. A 10% or more change in paired comparison of any clinical/echocardiographic variable was considered as hemodynamic response based on results from previous studies.

Table 1– Demographic parameters of the study population

(Group 1 – Non-coronary artery disease patients undergoing major elective neurosurgery

Group 2 - Coronary artery disease patients undergoing elective coronary artery bypass surgery)

Age in years	Group I*(n=29)*		Group II*(n=25)*		Total	
	n=	%	*n=*	%	*n=*	%
≤40	12	41.4	0	0.0	12	22.2
41 – 50	9	31.0	2	8.0	11	20.4
51 – 60	2	6.9	10	40.0	12	22.2
>60	6	20.7	13	52.0	19	35.2
Gender	Group I*(n=29)*		Group II(*n=25)*		Total	
Male	16	55.2	25	100.0	41	75.9
Female	13	44.8	0	0.0	13	24.1

Table 2: Baseline characteristics of Group 1 cases (non-cardiac disease patients undergoing elective major neuro-surgical procedures)

Parameter	***Values (%)****
Male	16 (55.17)
Female	13 (44.82)
Diagnosis (n=29)	
High grade glioma	11 (37.93)
Para-saggital meningioma	4 (13.79)
Para-falcine meningioma	3 (10.34)
Planumsphenoidale meningioma	2 (6.89)
Frontal ependymoma	1 (3.44)
Occipital meningioma	1 (3.44)
Recurrent meningioma	1 (3.44)
Cerebral metastasis	1 (3.44)
Choroid plexus papilloma	1 (3.44)
Frontal epidermoid tumor	1 (3.44)
Trigeminal neuralgia	1 (3.44)
Middle cerebral artery aneurysm	1 (3.44)
3^{rd} ventricular colloid cyst	1 (3.44)

(*Note- Percentages don't add up to hundred as values were approximated to the nearest decimal)

Table 3 – Demographic parameters and baseline echocardiographic parameters of the study population

Parameter	Group I		Group II		p value
	Mean	SD	Mean	SD	
Weight	63.8	11.9	67.4	12.2	0.283
Height	160.7	11.3	164.0	7.7	0.218
BSA	1.68	0.19	1.75	0.18	0.206
Heart rate	68.6	15.2	60.5	8.6	0.021
Systolic BP	111.6	17.5	108.6	15.2	0.509
Diastolic BP	65.0	10.2	62.1	9.0	0.281
Baseline LVOT	1.96	0.16	2.00	0.18	0.352
LVIDD	3.70	0.89	3.13	0.51	0.007
LVIDS	2.18	0.57	1.91	0.37	0.044
EF	66.7	8.3	71.0	7.1	0.045

We observed that baseline demographic parameters were comparable between two groups of patients.

Further to this, we analyzed the variation in clinical and echocardiographic parameters from baseline. Clinical parameters analyzed include – heart rate, systolic blood pressure (maximum and minimum), diastolic blood pressure (maximum and minimum), pulse pressure, systolic pressure variation and pulse pressure variation. Paired comparison was done for these clinical parameters at baseline versus hemodynamic response at 1 minute after PLR; baseline versus 10 minutes after PLR; and 1 minute versus 10 minute PLR response. Percentage of change in each parameter at 1 and 10 minutes after PLR, from baseline and also change at 10 minutes with regard to 1 minute values were also calculated. A p value of <0.05 was considered significant. A 10% or more change in paired comparison of any clinical/echocardiographic variable was considered as hemodynamic response based on results from previous studies.

Table 4 A –Heart rates at various intervals in group 1 and 2

HR	Group I		Group II		p value
	Mean	SD	mean	SD	
Baseline	68.6	15.2	60.5	8.6	0.021
1 minute PLR	67.2	14.6	59.4	8.9	0.024
10 minute PLR	66.7	14.7	59.1	9.0	0.030

Table 4 B – Paired comparison for heart rates across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		mean	SE		
Group I	Baseline vs 1 minute PLR	-1.414	0.766	-2.1	0.075
	Baseline vs 10 minute PLR	-1.948	0.834	-2.8	0.027
	1 minute PLR vs 10 minute PLR	-0.534	0.44	-0.8	0.235
Group II	Baseline vs 1 minute PLR	-1.06	0.837	-1.8	0.217
	Baseline vs 10 minute PLR	-1.34	0.786	-2.2	0.101
	1 minute PLR vs 10 minute PLR	-0.28	0.47	-0.5	0.557

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

Mean baseline heart rates were significantly lower in group 2 cases compared to group 1. We observed that there was no significant variation in heart rates after PLR **(Table 4B),** across both the groups at any of the paired comparison intervals. A 2.8% decrease in heart rate in group 1 cases after PLR though statistically significant (p=0.027) was not of hemodynamic relevance (only 10% or more change in any parameter after PLR was considered hemodynamic response). There was a decrease in heart rate in group 2 cases at rates of 1.8%, 2.2% and 0.5% at baseline versus 1 minute PLR, baseline versus 10 minute PLR and 1 minute PLR versus 10 minute PLR respectively. These changes were not significant.

Table 5 A – Systolic Blood Pressure at various intervals in group 1 and 2

SBP (Max)	Group I		Group II		p value
	Mean	SD	mean	SD	
Baseline	111.6	17.5	108.6	15.2	0.509
1 minute PLR	115.2	17.6	127.5	16.5	0.011
10 minute PLR	113.5	17.7	123.1	13.4	0.031

Table 5 B – Paired comparison for Systolic Blood Pressure across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		mean	SE		
Group I	Baseline vs 1 minute PLR	3.621	2.743	3.2	0.198
	Baseline vs 10 minute PLR	1.931	2.11	1.7	0.368
	1 minute PLR vs 10 minute PLR	-1.69	1.56	-1.5	0.288
Group II	Baseline vs 1 minute PLR	18.88	1.639	17.4	<0.001
	Baseline vs 10 minute PLR	14.48	1.835	13.3	<0.001
	1 minute PLR vs 10 minute PLR	-4.4	1.504	-3.5	0.007

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

We observed that in group 2 cases, there was significant increase in systolic blood pressure. **[Table 5]** at paired comparison intervals of baseline versus hemodynamic response at 1 minute after PLR and baseline versus 10 minutes after PLR. Systolic BP increased by 17.4% (18.88 +/- 1.639) and 13.3 % (14.48 +/- 1.835) at paired comparison intervals of baseline versus 1 minute after PLR and baseline versus 10 minutes after PLR respectively. A significant change in systolic BP at paired comparison interval of 1 minute versus 10 minutes after PLR was not of hemodynamic relevance (4.4% decrease). The changes in systolic blood pressure in group 1 cases were at the rates of 3.2%, 1.7% and -1.5% respectively at paired comparison intervals of baseline versus 1 minute PLR, baseline versus 10 minute PLR and 1 minute PLR versus 10 minute PLR. These changes were not significant.

Table 6 A – Diastolic Blood Pressure at various intervals in group 1 and 2

DBP (Max)	Group I		Group II		p value
	Mean	SD	mean	SD	
Baseline	65.0	10.2	62.1	9.0	0.281
1 minute PLR	66.0	10.7	75.2	11.4	0.003
10 minute PLR	64.8	10.6	72.8	10.4	0.007

Table 6B – Paired comparison for Diastolic Blood Pressure across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		Mean	SE		
Group I	Baseline vs 1 minute PLR	1	1.62	1.5	0.542
	Baseline vs 10 minute PLR	-0.241	1.373	-0.4	0.862
	1 minute PLR vs 10 minute PLR	-1.241	1.303	-1.9	0.349
Group II	Baseline vs 1 minute PLR	13.12	1.087	21.1	<0.001
	Baseline vs 10 minute PLR	10.68	1.215	17.2	<0.001
	1 minute PLR vs 10 minute PLR	-2.44	1.02	-3.4	0.025

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

We observed that in group 2 cases, there was significant increase in diastolic blood pressure **[Table 6]** at paired comparison intervals of baseline versus hemodynamic response at 1 minute after PLR and baseline versus 10 minutes after PLR. Diastolic BP increased by 21.1% (13.12 +/- 1.087) and 17.2 % (10.68 +/- 1.215) at paired comparison intervals of baseline versus 1 minute after PLR and baseline versus 10 minutes after PLR respectively. A significant change in diastolic BP at paired comparison interval of 1 minute versus 10 minutes after PLR was not of hemodynamic relevance (3.4% decrease). The changes in diastolic blood pressure in group 1 cases were at the rates of 1.5%, -0.4% and -1.9% respectively at paired comparison intervals of baseline versus 1 minute PLR, baseline versus 10 minute PLR and 1 minute PLR versus 10 minute PLR. These changes were not significant.

Table 7 A – Mean Pulse Pressure at various intervals in group 1 and 2

PP (mean)	Group I		Group II		p value
	Mean	SD	Mean	SD	
Baseline	46.1	10.8	45.6	11.9	0.894
1 minute PLR	48.5	10.9	51.3	11.6	0.370
10 minute PLR	47.9	11.4	50.2	10.1	0.441

Table 7 B – Paired comparison for Mean Pulse Pressure across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		mean	SE		
Group I	Baseline vs 1 minute PLR	2.483	1.709	5.4	0.157
	Baseline vs 10 minute PLR	1.81	1.552	3.9	0.253
	1 minute PLR vs 10 minute PLR	-0.672	0.575	-1.4	0.252
Group II	Baseline vs 1 minute PLR	5.66	0.969	12.4	0
	Baseline vs 10 minute PLR	4.52	1.03	9.9	0
	1 minute PLR vs 10 minute PLR	-1.14	0.7	-2.2	0.116

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

We observed that in group 2 cases, there was significant increase in mean pulse pressure **[Table 7]** at paired comparison intervals of baseline versus hemodynamic response at 1 minute after PLR and baseline versus 10 minutes after PLR. Mean pulse pressure increased by 12.4% (5.66 +/- 0.969) and 9.9 % (4.52 +/- 1.03) at paired comparison intervals of baseline versus 1 minute after PLR and baseline versus 10 minutes after PLR respectively. The changes in mean pulse pressure in group 1 cases were at the rates of 5.4%, 3.9% and -1.4% respectively at paired comparison intervals of baseline versus 1 minute PLR, baseline versus 10 minute PLR and 1 minute PLR versus 10 minute PLR. These changes were not significant.

Further we analysed the variation in echocardiographic parameters from baseline.

Table 8 A – Maximum SVC diameter at various intervals in group 1 and 2

SVC (max)	Group I		Group II		p value
	Mean	SD	Mean	SD	
Baseline	1.44	0.27	1.45	0.31	0.911
1 minute PLR	1.49	0.27	1.50	0.23	0.806
10 minute PLR	1.43	0.23	1.54	0.26	0.133

Table 8 B – Paired comparison for maximum SVC diameter across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		Mean	SE		
Group I	Baseline vs 1 minute PLR	0.048	0.027	3.3	0.08
	Baseline vs 10 minute PLR	-0.003	0.03	-0.2	0.909
	1 minute PLR vs 10 minute PLR	-0.052	0.027	-3.5	0.061
Group II	Baseline vs 1 minute PLR	0.056	0.045	3.9	0.225
	Baseline vs 10 minute PLR	0.089	0.042	6.1	0.043
	1 minute PLR vs 10 minute PLR	-0.033	0.033	-2.2	0.334

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

It was observed that there was a significant increase in SVC diameter (p=0.043) at paired comparison interval of baseline versus 10 minutes after PLR in group 2 cases **(Table 8)**. This response was not of hemodynamic significance (6.1%).The changes of SVC diameter in group 1 cases were at the rates of 3.3%, -0.2% and -3.5% respectively at paired comparison intervals of baseline versus 1 minute PLR, baseline versus 10 minute PLR and 1 minute PLR versus 10 minute PLR.The SVC diameter variation at these intervals were not significant hemodynamically or statistically.

Table 9 A – Left ventricular end diastolic volume (LVEDV) at various intervals in group 1 and 2

LVEDV	Group I		Group II		
	Mean	SD	mean	SD	p value
Baseline	91.40	20.66	76.26	16.01	0.004
1 minute PLR	94.79	18.49	82.70	15.51	0.013
10 minute PLR	92.07	20.25	80.54	13.81	0.020

Table 9 B – Paired comparison for left ventricular end diastolic volume (LVEDV) across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		mean	SE		
Group I	Baseline vs 1 minute PLR	3.397	1.608	3.7	0.044
	Baseline vs 10 minute PLR	0.672	1.381	0.7	0.63
	1 minute PLR vs 10 minute PLR	-2.724	1.702	-2.9	0.121
Group II	Baseline vs 1 minute PLR	6.44	1.639	8.4	0.001
	Baseline vs 10 minute PLR	4.28	1.623	5.6	0.014
	1 minute PLR vs 10 minute PLR	-2.16	1.351	-2.6	0.123

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

We noticed that in group 2 cases LVEDV increased significantly at paired comparison intervals of baseline versus 1 minute after PLR and baseline versus 10 minutes after PLR with a 8.4% and 5.6% change respectively (p=0.001 and 0.014) **[Table 9]**. There was a 3.7% increase in LVEDV at paired comparison interval of baseline versus 1 minute after PLR among group 1 cases also (p=0.044). Neither of these changes in LVEDV was considered hemodynamic response to PLR (10% or more increase or decrease from baseline was considered response).

Table 10 A – Stroke volume at various intervals in group 1 and 2

SV	Group I		Group II		p value
	mean	SD	Mean	SD	
Baseline	64.8	23.9	54.9	17.1	0.090
1 minute PLR	67.1	20.1	61.0	18.1	0.253
10 minute PLR	65.9	21.2	57.9	19.4	0.160

Table 10 B – Paired comparison for stroke volume across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		Mean	SE		
Group I	Baseline vs 1 minute PLR	2.276	1.401	3.5	0.116
	Baseline vs 10 minute PLR	1.064	1.821	1.6	0.564
	1 minute PLR vs 10 minute PLR	-1.211	1.173	-1.8	0.311
Group II	Baseline vs 1 minute PLR	6.14	1.875	11.2	0.003
	Baseline vs 10 minute PLR	3.04	2.055	5.5	0.152
	1 minute PLR vs 10 minute PLR	-3.1	1.762	-5.1	0.091

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

We noticed that in group 2 cases there was a significant increase in stroke volume by 11.2% (p=0.003) at paired comparison interval of baseline to 1 minute after PLR **(Table 10)**. The responses at other paired comparison intervals were not significant hemodynamically or statistically in either of the groups.The changes of left ventricular stroke volume in group 1 cases were at the rates of 3.5%, 1.6% and -1.8% respectively at paired comparison intervals of baseline versus 1 minute PLR, baseline versus 10 minute PLR and 1 minute PLR versus 10 minute PLR. These changes were not significant.

Table 11 A – Average aortic velocity time integral (aortic VTI) at various intervals in group 1 and 2

Average VTI	Group I		Group II		p value
	Mean	SD	Mean	SD	
Baseline	21.7	5.4	17.6	4.8	0.005
1 minute PLR	22.8	4.5	19.4	4.3	0.007
10 minute PLR	22.3	5.0	18.7	5.0	0.011

Table 11 B – Paired comparison for average aortic velocity time integral (aortic VTI) across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		Mean	SE		
Group I	Baseline vs 1 minute PLR	1.093	0.49	5.0	0.034
	Baseline vs 10 minute PLR	0.622	0.594	2.9	0.303
	1 minute PLR vs 10 minute PLR	-0.471	0.39	-2.1	0.237
Group II	Baseline vs 1 minute PLR	1.787	0.536	10.2	0.003
	Baseline vs 10 minute PLR	1.076	0.592	6.1	0.082
	1 minute PLR vs 10 minute PLR	-0.711	0.467	-3.7	0.141

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

We noticed that in group 2 cases there was a significant increase in average aortic VTI by 10.2% (p=0.003) at paired comparison interval of baseline to 1 minute after PLR **(Table 11)**. There was a significant increase in average aortic VTI at paired comparison interval of baseline versus 1 minute after PLR. The responses at other paired comparison intervals were not significant hemodynamically or statistically in group 2 cases.The changes of average aortic VTI in group 1 cases were at the rates of 5%, 2.9% and -2.1% respectively at paired comparison intervals of baseline versus 1 minute PLR, baseline versus 10 minute PLR and 1 minute PLR versus 10 minute PLR. These changes were not significant.

Table 12A – Aortic velocity time integral (aortic VTI) variability at various intervals in group 1 and 2

VTI variability	Group I		Group II		p value
	mean	SD	mean	SD	
Baseline	17.6	9.6	14.9	10.6	0.329
1 minute PLR	19.5	11.9	14.8	9.7	0.117
10 minute PLR	18.8	14.5	14.4	12.3	0.233

Table 12 B – Paired comparison for aortic velocity time integral (aortic VTI) variability across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		Mean	SE		
Group I	Baseline vs 1 minute PLR	1.947	2.304	11.1	0.405
	Baseline vs 10 minute PLR	1.248	3.318	7.1	0.71
	1 minute PLR vs 10 minute PLR	-0.699	3.127	-3.6	0.825
Group II	Baseline vs 1 minute PLR	-0.101	1.564	-0.7	0.949
	Baseline vs 10 minute PLR	-0.508	2.481	-3.4	0.84
	1 minute PLR vs 10 minute PLR	-0.407	2.354	-2.8	0.864

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

We observed that average aortic VTI variability did not vary significantly in either of the groups at any of the paired comparison intervals **(Table 12)**. In group 1 cases there was a 11.1% increase in aortic VTI variability which was not significant (p=0.405). The VTI variability in group 2 cases decreased at rates of 0.7%, 3.4% and 2.8% at paired comparison intervals of baseline versus 1 minute PLR, baseline versus 10 minute PLR and 1 minute PLR versus 10 minute PLR. These changes were not significant.

Table 13A – Stroke volume variability (SVV) at various intervals in group 1 and 2

SVV	Group I		Group II		p value
	mean	SD	Mean	SD	
Baseline	17.5	9.1	14.9	10.4	0.320
1 minute PLR	18.6	12.0	15.1	10.2	0.253
10 minute PLR	18.9	10.8	12.8	9.5	0.033

Table 13 B – Paired comparison for Stroke volume variability (SVV) across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		Mean	SE		
Group I	Baseline vs 1 minute PLR	1.109	2.146	6.3	0.609
	Baseline vs 10 minute PLR	1.323	2.571	7.6	0.611
	1 minute PLR vs 10 minute PLR	0.213	2.365	1.1	0.929
Group II	Baseline vs 1 minute PLR	0.222	1.695	1.5	0.897
	Baseline vs 10 minute PLR	-2.114	2.291	-14.2	0.365
	1 minute PLR vs 10 minute PLR	-2.336	2.058	-15.5	0.268

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

We observed that in group 2 cases, stroke volume variability decreased at baseline versus 10 minutes after PLR and 1 minute versus 10 minutes after PLR at 14.2% and 15.5% respectively, however this was not significant (p=0.365 and 0.268) **[Table 13]**. None of the other responses in stroke volume variability was significant hemodynamically or statistically in either of the groups at any of the paired comparison intervals.The stroke volume variability in group 1 cases increased at rates of 6.3%, 7.6% and 1.1% at paired comparison intervals of baseline versus 1 minute PLR, baseline versus 10 minute PLR and 1 minute PLR versus 10 minute PLR. These changes were not significant statictically or hemodynamically.

Table 14A – Systolic pressure variability (SPV) at various intervals in group 1 and 2

SPV	Group I		Group II		p value
	mean	SD	Mean	SD	
Baseline	4.74	3.05	4.53	2.51	0.782
1 minute PLR	4.08	2.10	3.84	2.28	0.701
10 minute PLR	5.06	3.27	2.63	1.34	0.001

Table 14B – Paired comparison for Systolic pressure variability (SPV) across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		mean	SE		
Group I	Baseline vs 1 minute PLR	-0.666	0.541	-14.1	0.229
	Baseline vs 10 minute PLR	0.317	0.747	6.7	0.674
	1 minute PLR vs 10 minute PLR	0.983	0.519	24.1	0.068
Group II	Baseline vs 1 minute PLR	-0.684	0.623	-15.1	0.284
	Baseline vs 10 minute PLR	-1.9	0.558	-41.9	0.002
	1 minute PLR vs 10 minute PLR	-1.216	0.383	-31.7	0.004

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

We noticed that systolic pressure variability decreased significantly in group 2 cases at intervals of baseline versus 10 minutes after PLR and 1 minute versus 10 minute after PLR at rates of 41.9% and 31.7% respectively (p=0.002 and 0.004) **[Table 14]**. A 15.1% decrease in SPV at paired comparison interval of baseline versus 1 minute after PLR in group 2 cases was not significant.In patients undergoing neurosurgical procedures (group 1 cases), changes in SPV occurred at baseline versus 1 minute after PLR and 1 minute versus 10 minutes after PLR at -14.1% and 24.1% rates respectively, however these changes were not significant (p=0.229 and 0.068). There was a 6.7% increase in systolic pressure variability at baseline versus 10 minutes after PLR in group 1 cases. This response was not significant.

Table 15A – Pulse pressure variability (PPV) at various intervals in group 1 and 2

PPV	Group I		Group II		p value
	mean	SD	mean	SD	
Baseline	4.97	4.90	5.07	3.98	0.934
1 minute PLR	4.01	3.89	4.84	3.16	0.401
10 minute PLR	5.77	7.02	2.81	1.63	0.045

Table 15B – Paired comparison for Pulse pressure variability (PPV) across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		mean	SE		
Group I	Baseline vs 1 minute PLR	-0.962	1.087	-19.4	0.384
	Baseline vs 10 minute PLR	0.793	1.373	16.0	0.568
	1 minute PLR vs 10 minute PLR	1.755	1.153	43.8	0.139
Group II	Baseline vs 1 minute PLR	-0.239	0.918	-4.7	0.797
	Baseline vs 10 minute PLR	-2.269	0.883	-44.8	0.017
	1 minute PLR vs 10 minute PLR	-2.029	0.625	-41.9	0.003

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

We noticed that pulse pressure variability decreased significantly in group 2 cases at intervals of baseline versus 10 minutes after PLR and 1 minute versus 10 minute after PLR at rates of 44.8% and 41.9% respectively (p=0.017 and 0.003) **[Table 15]**. At paired comparison interval of baseline versus 1 minute after PLR pulse pressure variability decreased by 4.7% in this group. This change was not significant. In patients undergoing neurosurgical procedures (group 1 cases), changes in PPV occurred at baseline versus 1 minute after PLR, baseline versus 10 minutes after PLR and 1 minute versus 10 minutes after PLR at rates of -19.4%, 16% and 43% respectively, however these changes were not significant (p=0.384, 0.568 and 0.139).

Table 16 A – Superior venacava collapsibility index (SVCCI) at various intervals in group 1 and 2

SVCCI	Group I		Group II		p value
	Mean	SD	mean	SD	
Baseline	9.54	3.60	10.54	6.02	0.454
1 minute PLR	9.10	4.65	10.80	8.72	0.367
10 minute PLR	8.06	4.70	8.31	5.74	0.860

Table 16 B – Paired comparison for Superior venacava collapsibility index (SVCCI) across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		mean	SE		
Group I	Baseline vs 1 minute PLR	-0.44	1.036	-4.6	0.674
	Baseline vs 10 minute PLR	-1.486	0.834	-15.6	0.086
	1 minute PLR vs 10 minute PLR	-1.046	0.819	-11.5	0.212
Group II	Baseline vs 1 minute PLR	0.254	1.756	2.4	0.886
	Baseline vs 10 minute PLR	-2.237	1.485	-21.2	0.145
	1 minute PLR vs 10 minute PLR	-2.491	1.381	-23.1	0.084

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

A 35% decrease in superior venacaval collapsibility index is considered as hemodynamic response. We observed that in group 2 cases, the superior venacaval collapsibility index (SVCCI) decreased at rates of 21.2% and 23.1% respectively at baseline versus 10 minutes after PLR and 1 minute versus 10 minutes after PLR, however this was not statistically significant (p=0.145 and 0.084 respectively) **(Table 16)**. A 15.6% and 11.5% decrease in SVCCI in group 1 cases at intervals of baseline versus 10 minutes after PLR and 1 minute versus 10 minutes after PLR was also not significant (p=0.086 and 0.212 respectively).

Table 17 A – Cardiac output at various intervals in group 1 and 2

Cardiac Output	Group I		Group II		p value
	Mean	SD	mean	SD	
Baseline	4.37	1.70	3.28	0.97	0.007
1 minute PLR	4.47	1.51	3.58	0.97	0.015
10 minute PLR	4.35	1.57	3.43	1.19	0.020

Table 17B – Paired comparison forCardiac outputacross various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		Mean	SE		
Group I	Baseline vs 1 minute PLR	0.1	0.113	2.3	0.386
	Baseline vs 10 minute PLR	-0.019	0.142	-0.4	0.893
	1 minute PLR vs 10 minute PLR	-0.119	0.088	-2.7	0.186
Group II	Baseline vs 1 minute PLR	0.303	0.128	9.2	0.027
	Baseline vs 10 minute PLR	0.146	0.145	4.5	0.325
	1 minute PLR vs 10 minute PLR	-0.158	0.11	-4.4	0.163

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

There was a significant increase (9.2%) in cardiac output at baseline versus 1 minute after PLR in group 2 cases (p=0.027) **[Table 17]**. Cardiac output changed at rates of 4.5% and -4.4% at paired comparison intervals of baseline versus 10 minute PLR and1 minute PLR versus 10 minute PLR respectively. These changes were not significant. The cardiac output did not change significantly in group1 cases at any of the paired comparison intervals after PLR.

Table 18 A – Cardiac index at various intervals in group 1 and 2

Cardiac Index	Group I		Group II		p value
	Mean	SD	Mean	SD	
Baseline	2.62	1.00	1.87	0.50	0.001
1 minute PLR	2.69	0.93	2.04	0.48	0.003
10 minute PLR	2.61	0.94	1.95	0.62	0.004

Table 18 B – Paired comparison for Cardiac index across various intervals in group 1 and 2, and the % of change at each interval

	Paired comparison	Paired difference		Percentage of change	p value
		mean	SE		
Group I	Baseline vs 1 minute PLR	0.068	0.071	2.6	0.344
	Baseline vs 10 minute PLR	-0.009	0.087	-0.3	0.914
	1 minute PLR vs 10 minute PLR	-0.078	0.055	-2.9	0.171
Group II	Baseline vs 1 minute PLR	0.171	0.074	9.1	0.029
	Baseline vs 10 minute PLR	0.076	0.087	4.1	0.389
	1 minute PLR vs 10 minute PLR	0.095	0.064	4.7	0.155

(SD – Standard Deviation, SE – Standard Error, PLR – Passive Leg Raising)

There was a significant increase (9.1%) in cardiac index at baseline versus 1 minute after PLR in group 2 cases (p=0.029) **[Table 18]**. Cardiac index increased at rates of 4.1% and 4.7% at paired comparison intervals of baseline versus 10 minute PLR and1 minute PLR versus 10 minute PLR respectively. These changes were not significant. The cardiac index did not change significantly in group1 cases at any of the paired comparison intervals after PLR.

In summary, there was significant change in hemodynamic parameters in patients undergoing CABG after PLR. There was significant increase in SBP, DBP and mean pulse pressure at paired comparison intervals of baseline versus hemodynamic response at 1 minute after PLR and baseline versus 10 minutes after PLR. SPV and PPV decreased significantly in this group at intervals of baseline versus 10 minutes after PLR and 1 minute versus 10 minute after PLR **(Table 5-7, 14, 15)**. For echocardiographic parameters in CABG patients there was significant increase in SV, aortic VTI, CO and CI at interval of baseline versus 1 minute after PLR. LVEDV increased significantly at both baseline versus 1 minute after PLR and baseline versus 10 minutes after PLR with a 8.4% and 5.6% change respectively. SVV decreased at baseline versus 10 minutes after PLR and 1 minute versus 10 minutes after PLR at 14.2% and 15.5% respectively, however this was not significant (p=0.365 and 0.268). The SVCCI decreased at rates of 21.2% and 23.1% respectively at baseline versus 10 minutes after PLR and 1 minute versus 10 minutes after PLR, however this was not statistically significant (p=0.145 and 0.084 respectively).**(Table 8-13, 17-18)**

In patients undergoing neurosurgical procedures (group 1 cases), changes in SPV occurred at baseline versus 1 minute after PLR and 1 minute versus 10 minutes after PLR at -14.1% and 24.1% rates respectively (p=0.229 and 0.068).**(Table 14)**

PPV changed during all paired comparison intervals at -19.4%, 16% and 43.8% respectively (p=0.384, 0.568 and 0.139).**(Table 15)** Echocardiographic variables of aortic VTI variability and SVCCI changed at paired intervals of baseline versus 1 minute after PLR; and both baseline versus 10 minutes after PLR and 1 minute versus 10 minutes after PLR respectively at rates of 11.1% (p=0.405), -15.6% (p=0.086) and -11.5% (p=0.212) **(Table 12, 16).** None of the clinical and echocardiographic responses in non-cardiac disease cases were statistically significant. Average VTI and LVEDV changed significantly in this group at baseline versus 1 minute after PLR, however this could not be designated as significant hemodynamic response to PLR as these variables changed at only 5% and 3.7% respectively.**(Table 9, 11)**

Table 19 - Correlation coefficient between clinical and echocardiography derived parameters at significant paired comparison intervals for coronary artery disease cases (Group 2)

Pearson Correlation GROUP II	LVEDV (Baseline vs 1 minute PLR)	Aortic VTI (Baseline vs 1 minute PLR)	SV (Baseline vs 1 minute PLR)	CO (Baseline vs 1 minute PLR)	CI (Baseline vs 1 minute PLR)
SBP (Baseline vs 1 minute PLR)	0.641**	0.521**	0.398*	0.340	0.340
DBP (Baseline vs 1 minute PLR)	0.596**	0.347	0.242	0.341	0.341
PP (Baseline vs 1 minute PLR)	0.408*	0.415*	0.323	0.200	0.200
SPV (Baseline vs 10 minute PLR)	-0.193	-0.001	0.167	0.077	0.077
PPV (Baseline vs 10 minute PLR)	-0.117	-0.126	-0.270	-0.330	-0.330

(** $p < 0.01$, * $p < 0.05$) [SBP- Systolic Blood Pressure, DBP – Diastolic Blood Pressure, PP- Pulse Pressure, SPV - Systolic Pressure Variability, PPV - Pulse Pressure Variability, LVEDV- Left Ventricular End Diastolic Volume, VTI- Velocity Time Integral, SV- Stroke Volume, CO – Cardiac Output, CI – Cardiac Index]

Karl-Pearson correlation coefficient was calculated across significant clinical and echocardiographic variables in group 2 cases to forecast the best combination of either in predicting the response to PLR **(Table 19)**. A paired combination of SBP baseline versus 1 minute after PLR to LVEDV baseline versus 1 minute after PLR or average aortic VTI at baseline versus 1 minute after PLR represented strong linear correlation to predict response to PLR (Pearson coefficient of 0.641 and 0.521 respectively at $p<0.01$). A paired combination of mean pulse pressure at baseline versus 1 minute after PLR to LVEDV baseline versus 1 minute after PLR or average aortic VTI at baseline versus 1 minute after PLR represented moderate linear correlation to predict response to PLR (Pearson coefficient of 0.408 and 0.415 respectively at $p<0.05$).

Table 20 – Comparison of Area Under Receiver Operating Characteristic (AUROC) curves at significant paired comparison intervals of clinical variables, for coronary artery disease (Group 2) cases

	AUC	SE[a]	95% CI[b]
SBP_Baseline_to_1_minute_PLR	0.810	0.0745	0.663 to 0.912
DBPMax_Baseline_to_1_minute_PLR	0.839	0.0689	0.697 to 0.932
PP_Baseline_to_1_minute_PLR	0.704	0.0849	0.547 to 0.832
SPV_Baseline_to_10_minute_PLR	0.636	0.0854	0.478 to 0.776
PPV_Baseline_to_10_minute_PLR	0.524	0.0925	0.368 to 0.676

Receiver operating characteristic (ROC) curves were generated for significant clinical and echocardiographic variables in group 2 cases varying the discriminating threshold for each parameter and area under curves were calculated. The areas under ROC curves data for clinical and echocardiographic variables are as in **Table 20 & 21 and Figure 1 & 2**. Paired comparison of DBP at baseline versus 1 minute after PLR had the highest AUC to predict response to PLR followed by SBP at baseline versus 1 minute after PLR (AUC 0.839, 95% CI 0.697-0.932 and AUC 0.810, 95% CI 0.663-0.912 respectively). Among TEE derived parameters, LVEDV at baseline versus 1 minute after PLR followed by aortic VTI at baseline versus 1 minute after PLR had the highest AUC to predict response to PLR (AUC 0.635, 95% CI 0.491-0.763 and AUC 0.608, 95% CI 0.464-0.739 respectively).

Figure 1 – Comparison of Area Under Receiver Operating Characteristic (AUROC) curves at significant paired comparison intervals of clinical variables, for coronary artery disease (Group 2) cases

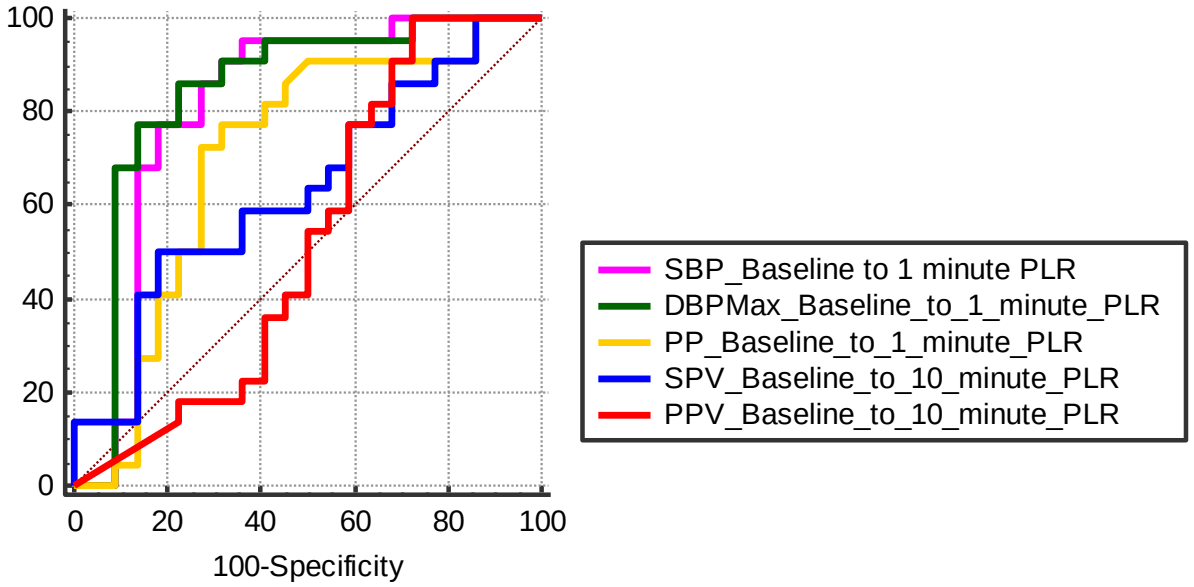

Table 21 – Comparison of Area Under Receiver Operating Characteristic (AUROC) curves at significant paired comparison intervals of echocardiographic variables, for coronary artery disease (Group 2) cases

	AUC	SE[a]	95% CI[b]
CI_Baseline_to_1_minute_PLR	0.583	0.0814	0.439 to 0.717
CO_Baseline_to_1_minute_PLR	0.583	0.0814	0.439 to 0.717
SV_Baseline_to_1_minute_PLR	0.581	0.0814	0.437 to 0.715
SVV_Baseline_to_1_minute_PLR	0.530	0.0827	0.388 to 0.669
VTI_Baseline_to_1_minute_PLR	0.608	0.0793	0.464 to 0.739
LVEDV_Baseline_to_1_minute_PLR	0.635	0.0794	0.491 to 0.763
SVCmax_Baseline_to_1_minute_PLR	0.553	0.0828	0.410 to 0.690

Figure 2 – Comparison of Area Under Receiver Operating Characteristic (AUROC) curves at significant paired comparison intervals of echocardiographic variables, for coronary artery disease (Group 2) cases

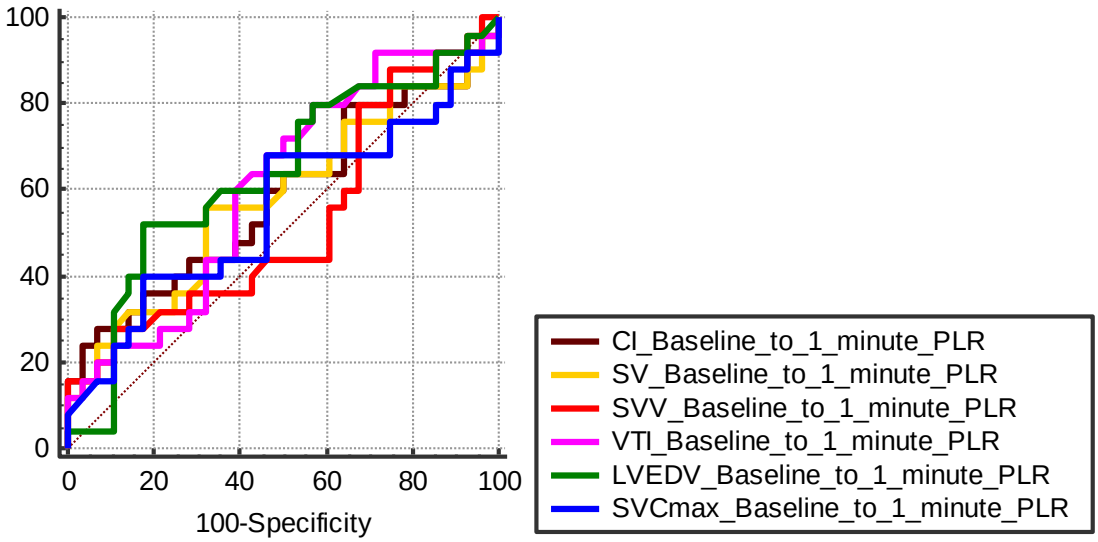

Table 22:- Accuracy of clinical parameter changes after PLR to predict fluid responsiveness in Group 2 cases

Group 2 cases	Criterion	Sens	95% CI	Spec	95% CI	+LR	95% CI	-LR	95% CI	+PV	95% CI	-PV	95% CI
SBP Baseline to 1 minute PLR	>7.22	96	79.6 - 99.9	72.41	52.8 - 87.3	3.48	1.9 - 6.3	0.055	0.008 - 0.4	75	56.6 - 88.5	95.5	77.2 - 99.9
	>9.84	88	68.8 - 97.5	79.31	60.3 - 92.0	4.25	2.1 - 8.8	0.15	0.05 - 0.4	78.6	59.0 - 91.7	88.5	69.8 - 97.6
	>14.29	68	46.5 - 85.1	89.66	72.6 - 97.8	6.57	2.2 - 19.8	0.36	0.2 - 0.6	85	62.1 - 96.8	76.5	58.8 - 89.3
Optimal cut-point	>7.22	96	79.6 - 99.9	72.41	52.8 - 87.3	3.48	1.9 - 6.3	0.055	0.008 - 0.4	75	56.6 - 88.5	95.5	77.2 - 99.9
DBP Baseline to 1 minute PLR	>5.48	92	74.0 - 99.0	75.86	56.5 - 89.7	3.81	2.0 - 7.3	0.11	0.03 - 0.4	76.7	57.7 - 90.1	91.7	73.0 - 99.0
	>8.7	88	68.8 - 97.5	75.86	56.5 - 89.7	3.65	1.9 - 7.1	0.16	0.05 - 0.5	75.9	56.5 - 89.7	88	68.8 - 97.5
	>15.38	80	59.3 - 93.2	89.66	72.6 - 97.8	7.73	2.6 - 23.0	0.22	0.1 - 0.5	87	66.4 - 97.2	83.9	66.3 - 94.5
Optimal cut-point	>12.99	88	68.8 - 97.5	82.76	64.2 - 94.2	5.1	2.3 - 11.5	0.15	0.05 - 0.4	81.5	61.9 - 93.7	88.9	70.8 - 97.6
PP Baseline to 1 minute PLR	>4.55	72	50.6 - 87.9	68.97	49.2 - 84.7	2.32	1.3 - 4.2	0.41	0.2 - 0.8	66.7	46.0 - 83.5	74.1	53.7 - 88.9
	>8.55	68	46.5 - 85.1	79.31	60.3 - 92.0	3.29	1.5 - 7.0	0.4	0.2 - 0.7	73.9	51.6 - 89.8	74.2	55.4 - 88.1
	>14.14	40	21.1 - 61.3	82.76	64.2 - 94.2	2.32	0.9 - 5.9	0.73	0.5 - 1.0	66.7	38.4 - 88.2	61.5	44.6 - 76.6
Optimal cut-point	>7.25	72	50.6 - 87.9	75.86	56.5 - 89.7	2.98	1.5 - 5.9	0.37	0.2 - 0.7	72	50.6 - 87.9	75.9	56.5 - 89.7

[SBP- Systolic Blood Pressure, DBP – Diastolic Blood Pressure, PP- Pulse Pressure, LR – Likelihood ratio, PV – Predictive value]

Table 23:- Accuracy of TEE parameter changes after PLR to predict fluid responsiveness in Group 2 cases

Group 2 cases	Criterion	Sens	95% CI	Spec	95% CI	+LR	95% CI	-LR	95% CI	+PV	95% CI	-PV	95% CI
LVEDV Baseline to 1 minute PLR	>4.17	60	38.7 - 78.9	55.17	35.7 - 73.6	1.34	0.8 - 2.2	0.73	0.4 - 1.3	53.6	33.9 - 72.5	61.5	40.6 - 79.8
	>11.76	52	31.3 - 72.2	82.76	64.2 - 94.2	3.02	1.2 - 7.3	0.58	0.4 - 0.9	72.2	46.5 - 90.3	66.7	49.0 - 81.4
	>15.12	32	14.9 - 53.5	89.66	72.6 - 97.8	3.09	0.9 - 10.4	0.76	0.6 - 1.0	72.7	39.0 - 94.0	60.5	44.4 - 75.0
Optimal cut-point	>11.76	52	31.3 - 72.2	82.76	64.2 - 94.2	3.02	1.2 - 7.3	0.58	0.4 - 0.9	72.2	46.5 - 90.3	66.7	49.0 - 81.4
SV Baseline to 1 minute PLR	>3.16	56	34.9 - 75.6	55.17	35.7 - 73.6	1.25	0.7 - 2.1	0.8	0.5 - 1.4	51.9	31.9 - 71.3	59.3	38.8 - 77.6
	>7.24	56	34.9 - 75.6	68.97	49.2 - 84.7	1.8	0.9 - 3.4	0.64	0.4 - 1.1	60.9	38.5 - 80.3	64.5	45.4 - 80.8
	>15.05	40	21.1 - 61.3	68.97	49.2 - 84.7	1.29	0.6 - 2.7	0.87	0.6 - 1.3	52.6	28.9 - 75.6	57.1	39.4 - 73.7
Optimal cut-point	>7.24	56	34.9 - 75.6	68.97	49.2 - 84.7	1.8	0.9 - 3.4	0.64	0.4 - 1.1	60.9	38.5 - 80.3	64.5	45.4 - 80.8
CO Baseline to 1 minute PLR	>5.52	48	27.8 - 68.7	58.62	38.9 - 76.5	1.16	0.6 - 2.1	0.89	0.5 - 1.4	50	29.1 - 70.9	56.7	37.4 - 74.5
	>10.43	44	24.4 - 65.1	72.41	52.8 - 87.3	1.59	0.8 - 3.3	0.77	0.5 - 1.2	57.9	33.5 - 79.7	60	42.1 - 76.1
	>15.06	40	21.1 - 61.3	75.86	56.5 - 89.7	1.66	0.7 - 3.7	0.79	0.5 - 1.2	58.8	32.9 - 81.6	59.5	42.1 - 75.2
Optimal cut-point	>26.52	28	12.1 - 49.4	93.1	77.2 - 99.2	4.06	0.9 - 17.8	0.77	0.6 - 1.0	77.8	40.0 - 97.2	60	44.3 - 74.3
CI Baseline to 1 minute PLR	>5.52	48	27.8 - 68.7	58.62	38.9 - 76.5	1.16	0.6 - 2.1	0.89	0.5 - 1.4	50	29.1 - 70.9	56.7	37.4 - 74.5
	>9.84	44	24.4 - 65.1	62.07	42.3 - 79.3	1.16	0.6 - 2.2	0.9	0.6 - 1.4	50	28.2 - 71.8	56.2	37.7 - 73.6
	>15.06	40	21.1 - 61.3	75.86	56.5 - 89.7	1.66	0.7 - 3.7	0.79	0.5 - 1.2	58.8	32.9 - 81.6	59.5	42.1 - 75.2
Optimal cut-point	>26.52	28	12.1 - 49.4	93.1	77.2 - 99.2	4.06	0.9 - 17.8	0.77	0.6 - 1.0	77.8	40.0 - 97.2	60	44.3 - 74.3

[LVEDV- Left Ventricular End Diastolic Volume, SV- Stroke Volume, CO – Cardiac Output, CI – Cardiac Index, LR – Likelihood ratio, PV – Predictive value]

Further to this the best threshold of clinical and TEE derived parameters to predict fluid responsiveness was assessed in group 2 cases. This was done at significant intervals of comparison after PLR maneuver. For clinical parameters the analysed intervals were SBP-baseline versus 1 minute after PLR, DBP baseline versus 1 minute after PLR; andpulse pressure -baseline versus 1 minute after PLR **(Table 22)**. For TEE derived parameters the analysed intervals for threshold accuracy data were LVEDV - baseline versus 1 minute after PLR, SV - baseline versus 1 minute after PLR,CO - baseline versus 1 minute after PLR andCI -baseline versus 1 minute after PLR **(Table 23)**. These variables were depicted as delta PLR clinical and delta PLR TEE for the ease description. The best threshold for systolic blood pressure (delta PLR Clinical SBP) was at a criterion of 7.22% increment after PLR, with sensitivity 96% (CI 95 = 79.6 - 99.9) and specificity 72.41% (CI 95 = 52.8 - 87.3). The best threshold for diastolic blood pressure (delta PLR Clinical DBP) was at a criterion of 12.99% increment after PLR, with sensitivity 88% (CI 95 = 68.8 - 97.5) and specificity 82.76% (CI 95 =64.2 - 94.2). The best threshold for pulse pressure (delta PLR Clinical PP) was at a criterion of 7.25% increment after PLR, with sensitivity 72% (CI 95 = 50.6 - 87.9) and specificity 75.86% (CI 95 = 56.5 - 89.7).

Among the TEE assessed parameters, the best threshold for LVEDV (delta PLR TEE LVEDV) was at a criterion of 11.76% increment after PLR, with sensitivity 52% (CI 95 = 31.3 - 72.2) and specificity 82.76% (CI 95 = 64.2 - 94.2).A 7.24% increment of stroke volume after PLR (delta PLR TEE SV) predicted fluid responsiveness with a sensitivity of 56% (CI 95 = 34.9 - 75.6) and specificity of 68.07% (CI 95 = 49.2 - 84.7). A 10.43% increment of cardiac output after PLR (delta PLR TEE CO) predicted fluid responsiveness with a sensitivity of 44% (CI 95 =24.4 - 65.1) and specificity of 72.41% (CI 95 = 52.8 - 87.3). A 9.84% increment of cardiac index after PLR (delta PLR TEE CI) predicted fluid responsiveness with a sensitivity of 44% (CI 95 = 24.4 - 65.1) and specificity of 62.07% (CI 95 = 42.3 - 79.3).

DISCUSSION

In this study we examined the clinical and echocardiographic response to a physiologic fluid load induced by PLR in patients without and with coronary artery disease undergoing elective neurosurgery or CABG respectively. Till date few adequately powered studies have evaluated fluid responsiveness using TEE in two such different groups of cases in the intraoperative scenario. To our knowledge very few studies have analysed fluid responsiveness to PLR in patients with coronary artery disease undergoing CABG. [77]

It is important to assess fluid responsiveness in patients undergoing high risk surgery. Dynamic indices are better than static indices to grade fluid responsiveness. The dynamic evaluation of fluid responsiveness in our study was done using TEE. TEE is routinely used in all CABG procedures in our centre and for high risk neurosurgery cases where venous air embolism risk is high or if hemodynamic instability due to blood loss is anticipated. Previous studies show TEE monitoring can improve perioperative outcome in non-cardiac surgery. [79, 80, 81]

Studies assessing the dynamic indices of fluid responsiveness have used different methods varying from less invasive techniques like FloTrac/Vigileo monitor (FloTrac, Edwards Life sciences, Irvine, CA) to noninvasive methods like LiDCO in intensive care unit scenario.[82, 83, 84] However, the use of TEE though considered more invasive than FloTrac monitor, provides more data on structure and function of heart as well as more accurate estimates of static and dynamic hemodynamic variables especially in CAD patients. Hence we used TEE for our study.

The methodological strengths of our study are as follows:-

We had chosen PLR instead of intravenous fluid infusions to assess fluid responsiveness. PLR is a highly physiologic maneuver as not even a single drop of extraneous fluid is infused. Administration of intravenous fluids either colloids or crystalloids can lead to adverse events many of which might be postoperatively, and thus outside the study duration. Hence such adverse events can be hidden and grossly under reported. Moreover, the auto-transfusion occurring after PLR is with patients own whole blood from the lower limbs and splanchnic compartment. The physiologic advantage of such a shift of body fluid cannot be compared with any of the extraneous fluids available. PLR can induce sympathetic activation in awake indviduals by increasing the intrathoracic blood volume. However, we did PLR maneuver in patients under general anesthesia, hence any such confounder could be eliminated.

Also we did not use the PLR maneuver as a treatment method in shock. None of our patients were hemodynamically unstable or hypovolemic preoperatively. Hence none of our patients did loose the advantage of intravenous fluid therapy. This further helped us in standardizing the patient population by avoiding a confounding factor of highest degree i.e. hypovolemia.

In group 2, we chose cases with coronary artery disease subject to CABG. Choosing such a group helped in eliminating bias and error in the definition of coronary artery disease as only patients with definite criteria satisfying coronary vessel occlusion undergo CABG. The treatment decision to undergo CABG was not influenced in any way by the study protocol. Further choosing only patients with good LV function assists in standardization within this group.

Our study results showed that non-coronary artery disease patients undergoing neurosurgical procedures did not have hemodynamic response to fluid load induced

either immediately after or 10 minutes of PLR, whereas patients with CAD had significant hemodynamic response to PLR at 1 minute after PLR which was not sustained at 10 minutes **[Table 4 – 18].** Patients without CAD undergoing neurosurgical procedures failed to significantly respond to the fluid load induced by PLR neither clinically nor in the TEE derived dynamic variables. A 2.5% decrease in heart rate in this group after PLR though statistically significant (p=0.027) was not of hemodynamic relevance [**Table 4].** The decrease in SPV (14.1%) and PPV (19.4%) immediately after PLR was not significant (p=0.229 and 0.384 respectively) in this group **[Table 14, 15].** A significant increase in LVEDV and aortic VTI in non-coronary artery disease cases fails to attain hemodynamic relevance as the increase was suboptimal (3.7% and 5% respectively) **[Table 9, 11].**

Lan H et al[85] studied the ability of left ventricular end-diastolic volume variations (LVEDVV) measured by TEE compared with stroke volume variation (SVV) obtained by the FloTrac/Vigileo monitor to predict fluid responsiveness, in patients undergoing craniotomy with goal directed therapy. A total of 26 adult patients of ASA physical status 3 and 4, with LV EF > 35%, scheduled to undergo craniotomy were enrolled to their study. A total of 53.8% patients did the surgery for the reason of brain tumor and 46.2% patients for intracranial aneurysm. About 70% of patients had co-morbidities of hypertension. Volume expansion was undertaken with colloid infusion in their study. Volume expansion induced a significant increase in CO (from 3.5 ± 0.5 to 4.0 ± 0.6 L/min/m^2, p =0.006) and CI (from 2.2±0.2 to 2.6±0.4 L/min/m^2, p =0.008). At the same time, the authors observed significant decreases SVV (from 17.8±2.8 to 11.0±2.8%, p<0.001) and TEE derived LVEDVV (from 22.1±7.3 to 13.6± 3.8%, p<0.001). No significant changes were found in Vigileo derived SV (from 54.4±10.0 to 59.3± 8.5, p = 0.084), VTI (from 18.7±2.7 to 19.5± 3.4%, p =0.503) and TEE-SV (from 53.3±8.0 to

58.2± 10.7, p =0.156). The authors found a significant correlation between SVV and LVEDVV obtained by TEE (R2 =0.4182, p <0.001). Bland-Altman analysis of pooled data showed mean bias and precisions of LVEDVV and SVV at 3.4% and 4.85%, respectively. The area under the ROC curve were as follows: 0.971 (95% CI: 0.945–0.997) for SVV (p<0.001), 0.890 (95% CI: 0.783–0.998) for LVEDVV (p<0.001). The authors found sensitivity of SVV (15%) as 0.990 and the specificity as 0.975. The authors further stated that a threshold value of LVEDVV greater than 15.3% helped to discriminate hypovolemia with a sensitivity of 0.912 and a specificity of 0.815. The authors concluded that for fluid responsiveness of patients during craniotomy in ASA III-IV physical status, LVEDVV measured by left ventricular short diameter of axle using M type echocardiographic measurement seems an acceptable monitoring indicator. However, this study had multiple limitations. Only patients with hypovolemia, defined by authors as systemic hypotension (mean BP < 65 mmHg) with cardiac index <2.5 L/min/m2 and a SVV > 15%, were subject to colloid infusion. Hence final data analysis was limited to only 10 patients of the total 26, as only 10 patients received colloid infusion. Thus the study was underpowered and the results cannot be extrapolated to all ASA III-IV physical status neurosurgical cases. Moreover, 46.2% of the cases in study population had intracranial aneurysm, a condition which can predispose the patients multiple systemic illnesses which could have confounded the results though. Also, hypovolemia per se must have confounded the results of this study.

Byon HJ[86] et al evaluated the clinical usefulness of static and dynamic variables for the prediction of fluid responsiveness in children, 6 months to 9 yr of age, undergoing elective neurosurgery under general anaesthesia. Dynamic parameters were assessed using trans-thoracic echocardiography in their study. Thirty-three mechanically ventilated children received 10 ml/ kg of colloid for 10 min while hemodynamically

stable intraoperatively. Arterial pressure, heart rate, central venous pressure (CVP), and pleth variability index (PVI) were the static parameters assessed. Dynamic parameters of fluid responsiveness assessed included variation in systolic pressure, pulse pressure (including delta down and delta up), respiratory aortic blood flow velocity (DVpeak), and inferior vena cava diameter. Each parameter was measured before and after volume expansion. Patients were classified as responders to fluid loading if their stroke volume index (SVI) increased by at least 10%. There were 15 volume responders and 18 non-responders in this study population. Of the variables examined, DVpeak ($r = 0.516$, $p = 0.004$) and PVI ($r = 0.49$, $p = 0.004$) before volume expansion were significantly correlated with changes in SVI. The receiver-operating characteristic (ROC) curve analysis showed that PVI and DVpeak predicted fluid responsiveness better. Areas under the ROC curves of PVI and DVpeak were statistically larger than that of CVP ($p = 0.006$ and 0.014, respectively). However, those of other variables were similar to that of CVP. The authors concluded that DVpeak and PVI can be used to predict fluid responsiveness in mechanically ventilated children under general anesthesia, undergoing neurosurgical procedures. The other static and dynamic variables assessed in this study were not found to predict fluid responsiveness significantly in children. The authors further state that of the dynamic variables, PPV has been consistently shown to be the best predictor of fluid responsiveness in adults. However, in their study, PPV was not found to be useful for predicting fluid responsiveness during general anesthesia in children. The findings of this study were similar to other studies in paediatrc population which concurs with the findings of previous paediatric studies. [87, 88, 89] PPV is a variable which is affected by arterial elastance also compared to SVV. Arterial elastance in children is low, and therefore, pressures transmitted by an increase in stroke volume may be partially absorbed, and pressure variations caused by an increase in stroke volume may be absent

from the arterial pressure waveform, which could have contributed to the low predictive ability of PPV in either of these studies.

In our study, patients with CAD had significant increase in SBP, DBP and pulse pressure immediately after PLR. This increase was sustained until 10 minutes of maintaining PLR. SBP increased by 17.4% and 13.3%; and DBP increased by 21.2% and 17.2% and at 1 and 10 minutes ($p<0.001$) respectively after PLR compared to baseline **[Table 5 – 7].** SBP, DBP and pulse pressure decreased at rates of 3.5%, 3.4% and 2.2% respectively at 10 minutes after PLR compared to baseline. Significant changes in SPV and PPV were not immediate as both decreased only at 10 minutes after PLR **[Table 14, 15].** We attribute this to the fact that SPV and PPV are affected by vessel wall plasticity. Vessel wall plasticity in CAD patients can be reduced due to atheromatous changes in blood vessels, hence causing delayed reduction in SPV and PPV. The variations in the above clinical hemodynamic parameters in patients with CAD suggest that there was significant fluid responsiveness in this group and this response remained sustained up to 10 minutes.

TEE derived dynamic LV volumetric data on LVEDV and SV in CAD cases of our study showed an increase of 8.4% ($p<0.001$) and 11.2% ($p<0.003$) respectively for each **[Table 9, 10].** Correspondingly the aortic VTI, CO and CI increased by 10.2% ($p=0.003$), 9.2% ($p=0.027$) and 9.1% ($p=0.029$) respectively in this group **[Table 11, 17, 18].** However, the decrease in SVV in this group of cases at 10 minutes after PLR was not significant (14.2%, $p=0.365$) **[Table 13].** Also the decrease in SVCCI (21.2%, $p=0.145$) at 10 minutes after PLR does not attain hemodynamic significance as previous studies denote only a 35% or more change in SVCCI as hemodynamic response **[Table 16]**. It is demonstrated here that the variations in TEE derived hemodynamic data in patients with coronary artery disease were not sustained up to 10 minutes unlike clinical

variables. We assume this to the reason that the increase in systemic vascular resistance (SVR) after PLR must have sustained the increase in SBP, DBP and pulse pressure, whereas the effect on LV filling must have waned off at 10 minutes after leg raising. However, central venous pressure monitoring and subsequent analysis of SVR was not part of our study protocol. The much suboptimal increase in SVC diameter after leg raising in CAD cases can be attributed to the method of conducting PLR in our study. Among the multitude methods of inducing PLR we chose the method in which the patient was made semi-recumbent first followed by leg raising, all with automated adjustments of the electronic operated operating theatre table. This methodology must have induced a partial SVC emptying, hence contributing to the suboptimal increase in SVC diameter after PLR. We attribute same etiology to the suboptimal change in SVCCI.

In our study we found a combination of SBP with LVEDV, DBP with LVEDV; and SBP with aortic VTI represented strong linear correlation in detecting a response to PLR in patients with CAD (Pearson coefficient 0.641, 0.596 and 0.521 respectively at $p<0.01$). Combinations of SBP with SV, pulse pressure with LVEDV; and PP with aortic VTI represented moderate linear correlation to predict response to PLR (Pearson coefficient 0.398, 0.408 and 0.415 respectively at $p<0.05$) **[Table 19]**.

Among the clinical parameters; DBP after 1 minute of PLR (AUC 0.839, 95% CI 0.697-0.932) followed by SBP after 1 minute of PLR (AUC 0.810, 95% CI 0.663-0.912), pulse pressure after1 minute of PLR (AUC 0.704, 95% CI 0.547-0.832), SPV after 10 minutes of PLR (AUC 0.636, 95% CI 0.478-0.776) and PPV after 10 minutes of PLR (AUC 0.524, 95% CI 0.368-0.676); were found to be predictive of clinical response to leg raising in that order **[Table 20 and Figure 1]**.

Among the TEE variables we studied; LVEDV after 1 minute of PLR (AUC 0.635, 95% CI 0.491-0.763) followed by aortic VTI after 1 minute of PLR (AUC 0.608, 95% CI 0.464-0.739), CO after 1 minute of PLR (AUC 0.583, 95% CI 0.439-0.717) and SV after 1 minute of PLR (AUC 0.581, 95% CI 0.437-0.715); were found to be predictive of clinical response to leg raising in that order.CO and CI predicted response in PLR in CAD cases with similar accuracy **[Table 21 and Figure 2]**.

Chaves RCF et al[90] systematically reviewed the response to fluid load in spontaneously breathing patients. In total, 649 spontaneously breathing patients were assessed for fluid responsiveness from 15 studies. Of those, 340 (52%) were deemed fluid responsive. Assessed methods to predict fluid responsiveness in this meta-analysis were pulse pressure variation (ΔPP); systolic pressure variation (ΔSP); ΔPP during forced inspiratory effort; ΔSP during forced inspiratory effort (ΔSPf); ΔPP during the Valsalva maneuver (ΔPPV); ΔSP during the Valsalva maneuver (ΔVSP); lowest pulse pressure (PPmin); stroke volume variation (ΔSV); passive leg raising (PLR)-induced change in stroke volume (ΔSV-PLR); PLR induced change in radial pulse pressure (ΔPP-PLR); PLR-induced change in the velocity peak of femoral artery flow (ΔVF-PLR); deep inspiration maneuver induced change in pulse pressure (ΔPPdim); respiratory change in velocity peak of femoral artery flow (ΔVF); deep inspiration maneuver-induced change in velocity peak of femoral artery flow (ΔVFdim); ΔPP during forced inspiratory breathing (ΔPPFB); PLR induced change in stroke volume index (SVi-PLR); change in cardiac output (ΔCO); inferior vena cava collapsibility index (cIVC); E wave velocity; aortic velocity time index (VTI) variations during PLR (ΔVTI-PLR); VTI $\leq$ 21 cm; aortic velocity variation (AoVV); inferior vena cava maximum diameter (IVCmax); and ΔCO between baseline and after PLR (ΔCO-PLR). Fluid challenge was performed in seven (46.6%) studies through an I.V. infusion of 500 ml of saline; five studies (33.3%)

with 500 ml of hydroxyethyl starch (HES); one (6.7%) study with 6 ml/kg of HES; one (6.7%) study applied 10 mL/kg of crystalloid; and one (6.7%) study used 5 ml/kg saline. Adopted definitions of fluid responsiveness were an increase in SV > 10% or > 15%; an increase in stroke volume index (SVi) ≥ 15%; an increase in CI ≥ 10% or ≥ 15%; an increase in CO ≥ 10% or 12% or an VTI ≥ 15%. Out of 34 reported maneuvers for predicting fluid responsiveness in spontaneously breathing patients, 13 (38%) maneuvers had excellent accuracy (AUC from 0.9 to 1), 9 (26%) had adequate accuracy (AUC from 0.8 to 0.89), 6 (18%) had fair accuracy (AUC from 0.7 to 0.79), 5 (15%) had poor accuracy (AUC from 0.6 to 0.69) and 1 maneuver (3%) was classified as failure (AUC from 0.5 to 0.59). Pulse pressure variation during the Valsalva maneuver (ΔPPV) of 52% (AUC ± SD: 0.98 ± 0.03) and passive leg raising-induced change in stroke volume (ΔSV-PLR) > 13% (AUC ± SD: 0.96 ± 0.03) showed the highest accuracy to predict fluid responsiveness in spontaneously breathing patients as per this meta-analysis. The main finding of this systematic review is that, regardless of intrinsic limitations of each reported maneuver, fluid responsiveness can be assessed in spontaneously breathing patients with acceptable accuracy. Approximately two-thirds (19/29) of reported maneuvers were deemed adequate or excellent to predict fluid responsiveness in spontaneous breathing patients without ventilatory support and 60% (3/5) were deemed excellent in mechanically ventilated patients in a spontaneous mode.

Wiesenack C et al [91] studied volume responsiveness in 20 patients undergoing elective coronary artery bypass grafting, after induction of anaesthesia, using volume replacement by infusion of 6% hydroxyethyl starch 200/0.5 at dose of 7mL/kg. On an average 542 mL of hydroxyethyl starch was infused at a rate of 1mL/kg/min. The authors evaluated the accuracy of simultaneously assessed stroke volume variation and pulse pressure variation using an improved algorithm for pulse contour analysis (PiCCO

plus®, V 5.2.2), compared to the respiratory changes in TEE derived aortic blood velocity (ΔVpeak) and intrathoracic blood volume index. Baseline stroke volume variation correlated significantly with changes in stroke volume index (ΔSVI) ($r2 = 0.66$; $p = 0.05$) as did baseline pulse pressure variation ($r2 = 0.65$; $p = 0.05$), whereas baseline values of ΔVpeak, intrathoracic blood volume index, CVP and PCWP showed no correlation to ΔSVI. Pulse contour analysis underestimated the volume-induced increase in cardiac index measured by transpulmonar thermodilution $p = 0.05$). The authors suggested that stroke volume variation and its surrogate pulse pressure variation derived from pulse contour analysis using an improve algorithm can serve as indicators of fluid responsiveness in normoventilated cardiac surgical.

Belloni L et al [92] studied dynamic parameters of fluid responsiveness by LiDCO and TEE in 19 patients during off-pump coronary artery bypass surgery. Fluid challenge was performed with 7 mL/kg of hydroxyethyl starch over 5 minutes, 20 minutes after induction of anesthesia, before skin incision and sternotomy, and without inotrope infusion. The study results confirmed the ability of PPV and SVV to predict fluid responsiveness in mechanically ventilated patients during general anesthesia and authors suggested the choice of LiDCO as a reliable, minimally invasive, and simple method to obtain these markers in the operating room.

Song Y et al [77] studied the respirophasic variation in carotid artery blood flow peak velocity (DVpeak-CA) measured by pulsed wave Doppler ultrasound as a predictor of fluid responsiveness in mechanically ventilated patients with coronary artery disease. Forty patients undergoing elective CABG were enrolled to the study. Subjects were classified as responders if stroke volume index (SVI) increased ≥15% after volume expansion (6 ml/kg). The DVpeak-CA was calculated as the difference between the

maximum and minimum values of peak velocity over a single respiratory cycle, divided by the average. CVP, PCOP, PPV, and DVpeak-CA were recorded before and after volume expansion. PPV and DVpeak-CA correlated significantly with an increase in SVI after volume expansion. Area under the ROC curve of PPV and DVpeak-CA were 0.75 [95% CI 0.59–0.90] and 0.85 (95% CI 0.72– 0.97). The optimal cut-off values for fluid responsiveness of PPV and DVpeak-CA in their study were 13% (sensitivity and specificity of 0.74 and 0.71) and 11% (sensitivity and specificity of 0.85 and 0.82), respectively. The authors did a subgroup analysis in 17 subjects having pulse pressure hypertension (≥ 60 mm Hg). The PPV failed to predict fluid responsiveness (AUROC 0.70, P=0.163)in this sub-group, whereas the predictability of DVpeak-CA remained unchanged (AUROC 0.90, P=0.006). The authors concluded that Doppler assessment of respirophasic DVpeak-CA seems to be a highly feasible and reliable method to predict fluid responsiveness in mechanically ventilated patients undergoing coronary revascularization.

It is inferred here that majority of the studies assessing fluid responsiveness in perioperative scenario in CAD patients used intravenous fluids. Though adverse events to this intraoperatively were not reported in any of these studies postoperative complications to colloid infusions in the study population cannot be excluded. Our study was more physiological in that we used a highly physiologic maneuver of fluid loading i.e. PLR.

As clearly mentioned earlier we re-emphasize the need for dynamic indices for predicting volume responsiveness. It is now proved beyond doubt that, static indices like CVP, PAOP and variables obtained from echocardiographic evaluation such as RVEDV and LVEDA cannot accurately sense the changes in ventricular preload and are therefore not good predictors of fluid responsiveness. It has been shown that both RAP and PAOP

tend to erroneously estimate the transmural pressures in subjects with PEEP (extrinsic or intrinsic). It should also be understood that the post fluid therapy increase in end diastolic volume depends mainly on how the partitioning of the fluid happens into the different zones of cardiovascular compliances organized in series [Right Atrium-Right Ventricle-Pulmonary circulation-Left Atrium-Left Ventricle]. It should also be noted that rise in stroke volume as a result of increase in LVEDV mainly depends on the ventricular function because a decrease in contractility of the ventricles will decrease the relationship of slope between LVEDV and SV.

The assessed parameters were classified as clinical and TEE based for the clarity of description in our study. Both static and dynamic parameters were included in the clinical and TEE derived parameters of our study. Such a classification is unique to our study. Use of TEE for fluid responsiveness evaluation had the unique benefit in our study as TEE monitoring is a standard of care for complex neurosurgical cases and all CABG procedures in our institution. Cardiac output measured by TEE have been shown to correlate well with measurements of CO obtained using thermo dilution technique with Pulmonary Artery Catheter (PAC) which is considered as the gold standard, but is far more invasive and when compared to TEE had greater degree of complications. It is proven that SV and CO calculated with TEE is more definitive when compared to bio-impedance plethysmogram. TEE is now considered to be relatively safe and non-invasive. However the insertion and manipulation of the TEE probe may cause oropharyngeal, esophageal and gastric trauma. The occurrences of TEE associated complications are in the range of 0%-0.5%, which is minimal when compared to the benefits offered by it in terms of cardiac status evaluation. In our study there was no adverse events reported due to insertion and placement of TEE probe.

LIMITATIONS

Patient safety is a key consideration in applying evidence to practice. PLR is a safe and simple maneuver. Several researchers have noted that the effects of PLR in the critically ill are reversed when the legs are returned to the horizontal position [44, 45, 50] and it does not result in acute fluid overload in patients who are not responsive to preload. In the studies presented on PLR, there were no reports of patients leaving the study because of the maneuver. However, Bertolissi M et al [93] in their study inferred that in patients with depressed RV function, PLR caused a decrease in the RV end-diastolic volume index (from 171 ± 50 to 142 ± 32 mL/m2; $p<0.05$) and the RV end-systolic volume index (from 124 ± 45 to 91 ± 22 mL/m2; $p > 0.05$). In contrast, patients with preserved RV function had a PLR-induced increase in the RV end-diastolic volume index (mean [SD], from 105 ± 17 to 133 ± 29 mL/m2; $p< .05$), and the RV end-systolic volume index (from 61 ± 13 to 77 ± 24 mL/m2; $p< .05$). Implication of this finding is to use caution when performing PLR in patients with depressed RV function (ie, ejection fraction < 40%). This study in coronary artery disease cases was underpowered hence the results cannot be extrapolated to other cases with coronary artery disease. However, in our study we included only cases with good LV function.

Changes in arterial compliance, in comparison with normal vascular tone, may cause the change in pulse pressure to inaccurately reflect the change in SV. If the arterial compliance decreases (eg, vasoconstriction due to pain or vasopressor medications), the pulse pressure may increase. Conversely, if the arterial compliance increases (eg:- vasodilatation due to sepsis), the pulse pressure may be decreased. Contraindications to the use of the PLR include patients with traumatic brain injury, because the PLR may increase intracranial pressure. Other limitations include patients with fractures of the

lower extremities and leg amputations, because these conditions may cause a difference in the volume of unstressed blood recruited by the maneuver.[94]

Echocardiographic measurements though only semi-invasive, are operator dependent and with high inter-rater variability. In our study we standardized this by the same investigator performing the measurements across both the groups.

CONCLUSIONS

- We found that TEE is an efficient tool which provides dynamic parameters to evaluate fluid responsiveness. This can be consolidated with static and dynamic parameters evaluated clinically.
- The clinical and TEE derived variables to be studied for the best evaluation of fluid responsiveness after PLR are as follows – Clinical parameters:- Systolic blood pressure, Diastolic blood pressure, Pulse pressure, Systolic pressure variability and Pulse pressure variability; and for TEE derived parameters:- Cardiac output, Cardiac index, Left ventricular end diastolic volume, Stroke volume, Stroke volume variability, Aortic velocity time integral and Superior venaecava diameter.
- Patients without coronary artery disease did not significantly respond to fluid load induced by PLR in our study. Patients with CAD had significant hemodynamic improvement in both clinical and echocardiographic parameters at 1 minute after PLR, the effects were only partially sustained at 10 minutes.
- A paired combination of blood pressure to LVEDV or VTIAo represents strong linear correlation to predict such response in CAD patients.
- An increment in diastolic blood pressure proved to be the best clinical parameter to assess fluid responsiveness to PLR; whereas, pulse pressure variability was least sensitive clinical parameter to assess such a response.
- An increment in cardiac output or cardiac index proved to be the best TEE derived parameter to assess fluid responsiveness to PLR; whereas, a change in superior vanaecava diameter was the least sensitive TEE derived parameter to assess such a response.

BIBLIOGRAPHY

1. Lerch C, Yonekawa Y, Muroi C, Bjeljac M, Keller E. Specialized neurocritical care, severity grade, and outcome of patients with aneurysmal subarachnoid hemorrhage. Neurocrit Care 2006; 5: 85-92.

2. Espiner EA, Leikis R, Ferch RD, MacFarlane MR, Bonkowski JA, Frampton CM et al. The neuro-cardio-endocrine response to acute subarachnoid haemorrhage. Clin Endocrinol (Oxf) 2002; 56: 629-35.

3. Manea MM, Comsa M, Minca A, Dragos D, Popa. C. Brain-heart axis. J Med Life, 2015. 8: 266-71.

4. Salem R, Vallée F, Dépret F, Callebert J, Maurice JP, Marty P et al. Subarachnoid hemorrhage induces an early and reversible cardiac injury associated with catecholamine release: one week follow-up study. Crit Care, 2014. 18: 558.

5. McLaughlin N, Bojanowski MW, Girard F, Denault A. Pulmonary edema and cardiac dysfunction following subarachnoid hemorrhage. Can J Neurol Sci, 2005. 32: 178-85.

6. Lennihan L, Mayer SA, Fink ME, Beckford A, Paik MC, Zhang H et al. Effect of hypervolemic therapy on cerebral blood flow after subarachnoid hemorrhage : a randomized controlled trial. Stroke 2000; 31: 383-91.

7. Mutoh T, Kazumata K, Ajiki M, Ushikoshi S, Terasaka S. Goal-directed fluid management by bedside transpulmonary hemodynamic monitoring after subarachnoid hemorrhage. Stroke 2007; 38: 3218-24.

8 Mori K, Arai H, Nakajima K, Tajima A, Maeda M. Hemorheological and hemodynamic analysis of hypervolemic hemodilution therapy for cerebral vasospasm after aneurysmal subarachnoid hemorrhage. Stroke 1995; 26: 1620-6.

9. Sen J, Belli A, Albon H, Morgan L, Petzold A, Kitchen N. Triple-H therapy in the management of aneurismal subarachnoid haemorrhage. Lancet Neurol 2003; 2: 614-21.

10. Reynolds MR, Buckley RT, Indrakanti SS, Turkmani AH, Oh G, Crobeddu E et al. The safety of vasopressor-induced hypertension in subarachnoid hemorrhage patients

with coexisting unruptured, unprotected intracranial aneurysms. J Neurosurg, 2015; 123: 862-71.

11. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001; 345: 1368- 77.

12. Bundgaard-Nielsen M, Secher NH, Kehlet H. 'Liberal' vs. 'restrictive' perioperative fluid therapy-a critical assessment of the evidence. Acta Anaesthesiol Scand 2009; 53: 843-51.

13. Doherty M, Buggy DJ. Intraoperative fluids: how much is too much? Br J Anaesth. 2012;109:69-79

14. Lenkin AI, Kirov MY, Kuzkov VV, Paromov KV, Smetkin AA, Lie M et al. Comparison of goal-directed hemodynamic optimization using pulmonary artery catheter and transpulmonary thermodilution in combined valve repair: a randomized clinical trial. Crit Care Res Pract. 2012;2012:821218.

15. Lichtwarck-Aschoff M, Beale R, Pfeiffer UJ. Central venous pressure, pulmonary artery occlusion pressure, intrathoracic blood volume, and right ventricular end-diastolic volume as indicators of cardiac preload. J Crit Care. 1996;11: 180-8.

16. Levin A, Klassen J, Halperin ML. Challenging consults: application of principles of physiology and biochemistry to the bedside. Osmotic diuresis: the importance of counting the number of osmoles excreted. Clin Invest Med. 1995; 18: 401-5.

17. Preisman S, Pfeiffer U, Lieberman N, Perel A. New monitors of intravascular volume: a comparison of arterial pressure waveform analysis and the intrathoracic blood volume. Intensive Care Med. 1997; 23: 651- 7.

18. Singh S, Kuschner WG, Lighthall G. Perioperative intravascular fluid assessment and monitoring: a narrative review of established and emerging techniques. Anesthesiol Res Pract. 2011; 2011: 231493.

19. Della Rocca G, Costa MG. Preload index and fluid responsiveness: different aspects of the new concept of functional hemodynamic monitoring. Minerva Anestesiol. 2008; 74:349-51.

20. Hofer CK, Cannesson M. Monitoring fluid responsiveness. Acta Anaesthesiol Taiwan, 2011; 49: 59-65.

21. Kastrup M, Markewitz A, Spies C, Carl M, Erb J, Grosse J et al. Current practice of hemodynamic monitoring and vasopressor and inotropic therapy in post-operative cardiac surgery patients in Germany: results from a postal survey. Acta Anaesthesiol Scand 2007; 51:347-358.

22. McIntyre LA, Hebert PC, Fergusson D, Cook DJ, Aziz A: A survey of Canadian intensivists' resuscitation practices in early septic shock. Crit Care 2007; 11:R74.

23. Marik PE, Baram M, Vahid B: Does the central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. Chest 2008, 134:172-178.

24. Wagner JG, Leatherman JW. Right ventricular end-diastolic volume as a predictor of the hemodynamic response to a fluid challenge. Chest 1998; 113:1048-54.

25. Charron C, Caille V, Jardin F, Vieillard-Baron A. Echocardiographic measurement of fluid responsiveness. Curr Opin Crit Care. 2006;12:249-54.

26. Diebel LN, Wilson RF, Tagett MG, Kline RA. End-diastolic volume. A better indicator of preload in the critically ill. Arch Surg, 1992;127: 817-21.

27. Tousignant CP, Walsh F, Mazer CD. The use of transesophageal echocardiography for preload assessment in critically ill patients. Anesth Analg, 2000; 90: 351-5.

28. Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients. A systematic review of the literature. Crit Care Med 2009; 37:2642-2647.

29. Michard F, Teboul JL: Using heart-lung interactions to assess fluid responsiveness during mechanical ventilation. Crit Care 2000; 4:282-289.

30. Theres H, Binkau J, Laule M, Heinze R, Hundertmark J, Blobner M et al. Phase-related changes in right ventricular cardiac output under volume-controlled mechanical ventilation with positive end-expiratory pressure. Crit Care Med 1999; 27:953-958.

31. Natalini G, Rosano A, Taranto M, Faggian B, Vittorielli E, Bernaardini A. Arterial versus plethysmographic dynamic indices to test responsiveness for testing fluid administration in hypotensive patients: a clinical trial. Anesth Analg 2006; 103:1478-1484.

32. Cannesson M, Besnard C, Durand PG, Bohe J, Jacques D. Relation between respiratory variations in pulse oximetry plethysmographic waveform amplitude and arterial pulse pressure in ventilated patients. Crit Care 2005; 9:R562-R568.

33 Feissel M, Teboul JL, Merlani P, Badie J, Faller JP, Bendjelid K. Plethysmographic dynamic indices predict fluid responsiveness in septic ventilated patients. Intensive Care Med 2007; 33:993-999.

34. Cannesson M, Desebbe O, Rosamel P, Delannoy B, Robin J, Bastien O et al. Pleth variability index to monitor the respiratory variations in the pulse oximeter plethysmographic waveform amplitude and predict fluid responsiveness in the operating theatre. Br J Anaesth 2008; 101:200-206.

35. Cannesson M, Delannoy B, Morand A, Rosamel P, Attof Y, Bastien O et al. Does the Pleth variability index indicate the respiratory induced variation in the plethysmogram and arterial pressure waveforms? Anesth Analg 2008; 106:1189-1194.

36. Jardin F, Vieillard-Baron A. Ultrasonographic examination of the venae cavae. Intensive Care Med. 2006; 32: 203-06

37. Jue J, Chung W, Schiller NB. Does inferior vena cava size predict right atrial pressures in patients receiving mechanical ventilation? J Am Soc Echocardiogr. 1992; 5:613-9.

38 Barbier C, Loubières Y, Schmit C, Hayon J, Ricôme J-L, Jardin F et al. Respiratory changes in inferior vena cava diameter are helpful in predicting fluid responsiveness in ventilated septic patients. Intensive Care Med. 2004; 30:1740–1746.

39. Airapetian N, Maizel J, Alyamani O, Mahjoub Y, Lorne E, Levrard M et al. Does inferior vena cava respiratory variability predict fluid responsiveness in spontaneously breathing patients? Crit Care. 2015;13:400.

40. Vieillard-Baron A, Chergui K, Rabiller A, Peyrouset O, Page B, Beauchet A et al. Superior vena caval collapsibility as a gauge of volume status in ventilated septic patients. Intensive Care Med. 2004;30:1734-9.

41 Rutlen DL, Wackers FJT, Zaret BL. Radionuclide assessment of peripheral intravascular capacity: a technique to measure intravascular volumes changes in the capacitance circulation in man. Circulation 1981; 64:146–152

42. Thomas M, Shillingford J. The circulatory response to a standard postural change in ischaemic heart disease. Br Heart J 1965; 27:17–27

43. Wong DH, O'Connor D, Tremper KK, Zaccari J, Thomson P, Hill D. Changes in cardiac output after acute blood loss and position change in man. Crit Care Med 1989; 17:979–983.

44. Boulain T, Achard JM, Teboul JL, Richard C, Perrotin D, Ginies G. Changes in BP induced by passive leg raising predict response to fluid loading in critically ill patients. Chest 2002; 121:1245-1252.

45. Monnet X, Rienzo M, Osman D, Anguel N, Richard C, Pinsky MR et al. Passive leg raising predicts fluid responsiveness in the critically ill. Crit Care Med. 2006; 34:1402-1407.

46. Lafanechere A, Pene F, Goulenok C, Delahaye A, Mallet V, Choukroun G et al. Changes in aortic blood flow induced by passive leg raising predict fluid responsiveness in critically ill patients. Crit Care 2006, 10:R132

47. Lamia B, Ochagavia A, Monnet X, Chemla D, Richard C, Teboul JL. Echocardiographic prediction of volume responsiveness in critically ill patients with spontaneously breathing activity. Intensive Care Med 2007; 33:1125-1132.

48. Maizel J, Airapetian N, Lorne E, Tribouilloy C, Massy Z, Slama M. Diagnosis of central hypovolemia by using passive leg raising. Intensive Care Med 2007, 33:1133-1138.

49. Biais M, Vidil L, Sarrabay P, Cottenceau V, Revel P, Sztark F. Changes in stroke volume induced by passive leg raising in spontaneously breathing patients: comparison between echocardiography and Vigileo/FloTrac device. Crit Care 2009; 13:R195.

50. Thiel SW, Kollef MH, Isakow W: Non-invasive stroke volume measurement and passive leg raising predict volume responsiveness in medical ICU patients: an observational cohort study. Crit Care 2009; 13:R111.

51. Preau S, Saulnier F, Dewavrin F, Durocher A, Chagnon JL: Passive leg raising is predictive of fluid responsiveness in spontaneously breathing patients with severe sepsis or acute pancreatitis. Crit Care Med 2010; 38:819-825.

52. Monnet X, Teboul J-L Passive leg raising: five rules, not a drop of fluid! Crit Care 2015; 19:18

53. Monnet X, Bataille A, Magalhaes E, Barrois J, Le Corre M, Gosset C et al. End-tidal carbon dioxide is better than arterial pressure for predicting volume responsiveness by the passive leg raising test. Intensive Care Med 2013; 39:93–100.

54 Bubenek-Turconi SI, Craciun M, Miclea I, Perel A: Noninvasive continuous cardiac output by the Nexfin before and after preload-modifying maneuvers: a comparison with intermittent thermodilution cardiac output. Anesth Analg 2013; 117:366–372.

55. Marik PE, Levitov A, Young A, Andrews L. The use of bioreactance and carotid Doppler to determine volume responsiveness and blood flow redistribution following passive leg raising in hemodynamically unstable patients. Chest. 2013; 143:364–370.

56. Kupersztych-Hagege E, Teboul JL, Artigas A, Talbot A, Sabatier C, Richard C et al. Bioreactance is not reliable for estimating cardiac output and the effects of passive leg raising in critically ill patients. Br J Anaesth 2013; 111:961–966.

57. Mahjoub Y, Touzeau J, Airapetian N, Lorne E, Hijazi M, Zogheib E et al. The passive leg-raising maneuver cannot accurately predict fluid responsiveness in patients with intra-abdominal hypertension. Crit Care Med 2010; 38:1824–1829.

58. Vincent JL, Weil MH. Fluid challenge revisited. Crit Care Med 2006;34:1333–1337.

59. Keren H, Burkhoff D, Squara P. Evaluation of a noninvasive continuous cardiac output monitoring system based on thoracic bioreactance. Am J Physiol. 2007; 293:H583-H589.

60. Raval NY, Squara P, Cleman M, Yalamanchili K, Winklmaier M, Burkhoff D. Multicenter evaluation of noninvasive cardiac output measurement by bioreactance technique. J Clin Monitor Comput. 2008; 22:113-119.

61 Squara P, Rotcajg D, Denjean D, Estagnasie P, Brusset A. Comparison of monitoring performance of Bioreactance vs. pulse contour during lung recruitment maneuvers. Crit Care. 2009; 13:R125.

62. Cavallaro F, Sandroni C, Marano C, La TG, Mannocci A, De WC et al. Diagnostic accuracy of passive leg raising for prediction of fluid responsiveness in adults: systematic review and meta-analysis of clinical studies. Intensive Care Med 2010; 36:1475-1483.

63 Monnet X, Marik P, Teboul J-L. Passive leg raising for predicting fluid responsiveness: a systematic review and meta-analysis. Intensive Care Med 2016;42:1935-1947.

64. Eltzschig HK, Rosenberger P, Loffler M, Fox JA, Aranki SF, Shernan SK. Impact of intraoperative transesophageal echocardiography on surgical decisions in 12,566 patients undergoing cardiac surgery. Ann Thorac Surg 2008; 85:845–852.

65 American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography: practice guidelines for perioperative transesophageal, echocardiography. An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Anesthesiology 2010; 112:1084–1096.

66. Denault AY, Couture P, McKenty S, Boudreault D, Plante F, Perron R et al. Perioperative use of transesophageal echocardiography by anesthesiologists: impact in noncardiac surgery and in the intensive care unit. Can J Anaesth 2002; 49:287–293.

67. Rebel A, Klimkina O, Hassan Z-U. Transesophageal echocardiography for the noncardiac surgical patient. Int Surg 2012; 97:43–55.

68. Gracia I, Fabregas N. Craniotomy in sitting position: anesthesiology management. Curr Opin Anaesthesiol 2014; 27:474–483.

69 Mittal C, Qureshi W, Singla S, Ahmad U, Huang MA. Pretransplant left ventricular diastolic dysfunction is associated with post transplant acute graft rejection and graft failure. Dig Dis Sci 2014; 59:674–680.

70. Spier BJ, Larue SJ, Teelin TC, Leff JA, Swize LR, Borkan SH et al Review of complications in a series of patients with known gastro-esophageal varices undergoing transesophageal echocardiography. J Am Soc Echocardiogr 2009; 22:396–400.

71 . Pantham G, Waghray N, Einstadter D, Finkelhor RS, Mullen KD. Bleeding risk in patients with esophageal varices undergoing transesophageal echocardiography. Echocardiography. 2013 ;30:1152-5.

72. Morin J-F, Mistry B, Langlois Y, Ma F, Chamoun P, Holcroft C. Fluid overload after coronary artery bypass grafting surgery increases the incidence of post-operative complications. World J Cardiovasc Surg. 2011;1:18–23.

73. Bellomo R, Raman J, Ronco C. Intensive care unit management of the critically ill patient with fluid overload after open-heart surgery. Cardiology. 2011;96:169–76.

74. Andre AS, DelRossi AL. Hemodynamic management of patients in the first 24 hours after cardiac surgery. Crit Care Med. 2005;33:2082–93.

75. Snygg J, Bech-Hanssen O, Lönn L, Andersson B, Aneman A. Fluid therapy in acute myocardial infarction: evaluation of predictors of volume responsiveness. Acta Anaesthesiol Scand. 2009;53:26-33.

76 Sobczyk D, Nycz K, Andruszkiewicz P, Wierzbicki K, Stapor M. Ultrasonographic caval indices donotsignificantly contribute to predicting fluid responsiveness immediately after coronary artery bypass grafting when compared to passive leg raising. Cardiovasc Ultrasound. 2016;14:23.

77. Song Y, Kwak YL, Song JW, Kim YJ, Shim JK. Respirophasic carotid artery peak velocity variation as a predictor of fluid responsiveness in mechanically ventilated patients with coronary artery disease. Br J Anaesth. 2014;113:61-6

78. Wetterslev M, Haase N, Johansen RR, Perner A. Predicting fluid responsiveness with transthoracic echocardiography is not yet evidence based. Acta Anaesthesiol Scand 2013; 57: 692–697.

79. Funk DJ, Moretti EW, Gan TJ. Minimally invasive cardiac output monitoring in the perioperative setting. Anesth Analg. 2009;108:887–97.

80. Gula LJ, Massel D, Redfearn DP, Krahn AD, Yee R, Klein GJ et al. Impact of routine transoesophageal echocardiography on safety, outcomes, and cost of pulmonary vein ablation: inferences drawn from a decision analysis model. Europace. 2010;12:1550–7.

81. Heiberg J, El-Ansary D, Royse CF, Royse AG, Alsaddique AA, Canty DJ. Transthoracic and transoesophageal echocardiography: a systematic review of feasibility and impact on diagnosis, management and outcome after cardiac surgery. Anaesthesia. 2016;71:1210–21.

82. Tsai YF, Liu FC, Yu FP. FloTrac/Vigileo system monitoring in acute-care surgery: current and future trends. Expert Rev Med Devices. 2013;10:717–28.

83. Senn A, Button D, Zollinger A, Hofer CK. Assessment of cardiac output changes using a modified FloTrac/Vigileo algorithm in cardiac surgery patients. Crit Care. 2009;13:R32.

84. Biancofiore G, Critchley LA, Lee A, Yang XX, Bindi LM, Esposito M et al. Evaluation of a new software version of the FloTrac/Vigileo (version 3.02) and a comparison with previous data in cirrhotic patients undergoing liver transplant surgery. Anesth Analg 2011; 113:515–22.

85. Lan H, Zhou X, Xue J, Liu B, Chen G The ability of left ventricular end-diastolic volume variations measured by TEE to monitor fluid responsiveness in high-risk surgical patients during craniotomy: a prospective cohort study. BMC Anesthesiol. 2017;17:165.

86. Byon HJ, Lim CW, Lee JH, Park YH, Kim HS, Kim CS et al. Prediction of fluid responsiveness in mechanically ventilated children undergoing neurosurgery. Br J Anaesth. 2013 ;110:586-91.

87. Durand P, Chevret L, Essouri S, Haas V, Devictor D. Respiratory variations in aortic blood flow predict fluid responsiveness in ventilated children. Intensive Care Med 2008; 34: 888–94

88. Pereira de Souza Neto E, Grousson S, Duflo F, Ducreux C, Joly H, Convert J et al Predicting fluid responsiveness in mechanically ventilated children under general anaesthesia using dynamic parameters and transthoracic echocardiography. Br J Anaesth 2011; 106: 856–64

89. Tran H, Froese N, Dumont G, Lim J, Ansermino JM. Variation in blood pressure as a guide to volume loading in children following cardiopulmonary bypass. J Clin Monit Comput 2007; 21: 1–6

90 Chaves RCF, Corrêa TD, Neto AS, Bravim BA, Cordioli RL, Moreira FT et al. Assessment of fluid responsiveness in spontaneously breathing patients: a systematic review of literature. Ann Intensive Care. 2018;8:21

91 Wiesenack C, Fiegl C, Keyser A, Prasser C, Keyl C. Assessment of fluid responsiveness in mechanically ventilated cardiac surgical patients. Eur J Anaesthesiol. 2005;22:658-65.

92 Belloni L, Pisano A, Natale A, Piccirillo MR, Piazza L, Ismeno G et al. Assessment of Fluid-Responsiveness Parameters for Off-Pump Coronary Artery Bypass Surgery: A Comparison Among LiDCO, Transesophageal Echochardiography, and Pulmonary Artery Catheter. J Cardiothorac Vasc Anesth 2008; 22 : 243-248

93. Bertolissi M, Broi U, Soldano F, Bassi F. Influence of passive leg elevation on the right ventricular function in anaesthetized coronary patients. Crit Care. 2003;7:164-170.

94. Cherpanath T, Aarts L, Groeneveld J, Geerts B. Defining fluid responsiveness: a guide to patient-tailored volume titration. J Cardiothorac Vasc Anesth. 2014;28:745-754.

Technical Advisory Committee (Clinical Studies)

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY
THIRUVANANTHAPURAM – 695011, INDIA

TAC Registration No: SCT-/S/2016/524 **Date:22.09.2016**

Project title: Comparison of fluid responsiveness between patients with and without coronary artery disease by passive leg raising using Transesophageal echocardiography

Principal Investigator:
Name: Dr Varun S Degree: MBBS, MD Address: Senior Resident, Department of Anaesthesiology, SCTIMST, Trivandrum
Co-Principal Investigator(s)
(1) Name: Dr S Manikandan Degree: MBBS, MD, PDCC Address: Additional Professor, Department of Anaesthesiology, SCTIMST, Trivandrum
(2) Dr Thomas Koshy Degree: MBBS, MD, PDCC Professor, Department of Anaesthesiology, SCTIMST, Trivandrum
(3) Dr. K Jayakumar Degree: MBBS, MS, MCh Professor and HOD, Department of CVTS, SCTIMST, Trivandrum

Members who participated in the TAC meeting on 06/09/2016

Dr. Rupa Sreedhar (Chairperson)
Dr. Prasantakumar Dash
Dr. Sylaja P.N
Dr. Ashalatha R
Dr. Krishna Kumar K
Dr. Syam. K
Dr. Bijulal S
Dr. Jayadevan E.R.
Dr. Varghese T. Panicker
Dr. K. Shivakumar (Member Secretary)

Dr. Rupa Sreedhar, Dr. Sylaja P.N, Dr. Jayadevan E.R, Dr. Bijulal S, and Dr. Ashalatha R, stayed away from the proceedings when the projects in which they are involved (# 517,519,520,521,523,528,531) as investigators were discussed

Risk Classification of the project (Minimum/ Moderate/ High): Minimum
Requirement of DSMB: Yes
Recommended members of DSMB:

1. Dr. Easwer, Additional Professor, Department of Neurosurgery, SCTIMST
2. Dr Smita V, Assistant Professor, Department of Anaesthesiology, SCTIMST
3. Dr. Ajay Prasad Hrishi P, Assistant Professor, Department of Anaesthesiology, SCTIMST
4. Dr. Jayanand Sudhir B, Assistant professor, Department of Neurosurgery, SCTIMST
5. Dr. Unnikrishnan P, Assistant Professor, Department of Anaesthesiology, SCTIMST

Recommendations of TAC:
Recommended for consideration of IEC in the light of the responses received from the investigator

The PI may note that there can be no additions / alterations in the documents approved by TAC when they are submitted to the IEC.

Signature of the Member Secretary, TAC (Clinical Studies)

Note for IEC
Copy of the investigator's responses to questions/suggestions from TAC is attached (Appendix-1).

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
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Institutional Ethics Committee
(IEC Regn No. ECR/189/Inst/KL/2013)

SCT/IEC/980/DECEMBER-2016 06.01.2017

Dr. Varun. S
Senior Resident
Department of Anaesthesiology
SCTIMST, Thiruvananthapuram

Dear Dr. Varun,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "COMPARISON OF FLUID RESPONSIVENESS USING TRANSESOPHAGEAL ECHOCARDIOGRAPHY IN PATIENTS WITHOUT CORONARY ARTERY DISEASE UNDERGOING NEUROSURGICAL PROCEDURES VERSUS PATIENTS WITH CORONARY ARTERY DISEASE UNDERGOING CORONARY ARTERY BYPASS GRAFT SURGERY" (IEC/980) on 17th December, 2016.

The following documents were reviewed:

1. *Covering letter addressed to the Chairman, IEC, SCTIMST, dated 23.11.2016 with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Patient Information Sheet and Informed Consent Form in English and Malayalam*
7. *CV of Principal Investigator and Co-Principal Investigators*

The following members of the Ethics Committee were present at the meeting held on 17th December, 2016 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Justice Gopinathan. P.S	BSc. LLB	Male	Legal Expert (Chairperson)	No
2.	Dr. Harikrishna Varma PR	PhD	Male	Biomedical Scientist	Yes
3.	Dr. Meenu Hariharan	DM	Female	Clinician (Gastro-Enterologist)	No
4.	Dr. Rema M. N	MD	Female	Pharmacologist	No
5.	Dr. R V G Menon	PhD	Male	Lay Person	No
6.	Smt. Sathi Nair	MA	Female	Lay Person	No
7.	Dr. K R S Krishnan	ME, PhD	Male	Biomedical Scientist/Engineer	No
8.	Dr. Kala Kesavan. P	MD	Female	Pharmacologist	No
9.	Dr. Christina George	MD	Female	Psychiatrist	No
10.	Dr. P. Manickam	PhD	Male	Scientist - Epidemiologist	No
11.	Dr. Mala Ramanathan	MSc, PhD, MA	Female	Ethicist/Social Scientist (Member Secretary)	Yes

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC

Consent form

Participant's name: **Date of Birth / Age (in years)**:

I_____, son/daughter/husband/wife/relative(specify relation) of _____(name of patient) hereby declare that (Please tick boxes)

- I have read the above information provided to me regarding the study - **"Comparison of fluid responsiveness using Transesophageal echocardiography in patients without coronary artery disease undergoing neurosurgical procedures versus patients with coronary artery disease undergoing coronary artery bypass graft surgery"** [ ]
- I have clarified any doubts that I had. [ ]
- I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights [ ]
- I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access [ ]
- I understand that my identity will not be revealed in any information released to third parties or published [ ]
- I voluntarily agree to take part in this study [ ]
- I have been provided with the contact numbers of the principal investigator, in case I want to know more about the study and participants rights [ ].
- I received a copy of this signed consent form [ ]

Name Signature/thumb impression of patient/legally acceptable representative:
Date:

Name and signature of witness:
Relation to participant: Date:

<u>Person Obtaining Consent</u>

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in non-technical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

Name and signature with date:

രോഗിയുടെ സമ്മത പത്രം

പങ്കെടുക്കുന്ന ആളുടെ പേര് : ജനന തീയതി/വയസ്സ് :

.....മകനായ/മകളായ ഞാൻ.....അടിയിൽ വിവരിച്ചിരിക്കുന്ന കാര്യങ്ങൾ അറിഞ്ഞ് ബോധ്യപ്പെട്ടിരിക്കുന്നു.

(ബോക്സിനുള്ളിൽ (√) അടയാളപ്പെടുത്തുക).

പഠന ശീർഷകം:

സിരാസംബന്ധമായ ശസ്ത്രക്രിയക്ക് വിധേയരാവുന്ന, കൊറോണറി ശുദ്ധരക്തക്കുഴൽ അസുഖമില്ലാത്ത രോഗികളിലും കൊറോണറി ശുദ്ധരക്തക്കുഴൽ അസുഖം ഉള്ള കൊറോണറി ശുദ്ധരക്തക്കുഴൽ ബൈപ്പാസ് ഗ്രാഫ്റ്റ് ശസ്ത്രക്രിയക്കു വിധേയരാവുന്ന രോഗികളിലുമുള്ള ദ്രാവക പ്രതികരണത്തിന്റെ താരതമ്യം ട്രാൻസിസോഫാജിയൽ എക്കോകാർഡിയോഗ്രഫി (ടി. ഇ. ഇ) ഉപയോഗിച്ചു നടത്തുന്ന പഠനം.

മുകളിൽ പറഞ്ഞിരിക്കുന്ന പഠനത്തെ കുറിച്ചുള്ള വിവരങ്ങൾ ഞാൻ വായിച്ചു മനസ്സിലാക്കി. . [ ]

എനിക്ക് ഉണ്ടായിരുന്ന സംശയങ്ങൾ ഞാൻ ചോദിച്ച് മനസ്സിലാക്കിയിട്ടുണ്ട്. [ ]

ഈ പഠനത്തിൽ പങ്കെടുക്കുന്നത് എന്റെ മാത്രം തീരുമാനമാണെന്നും എനിക്ക് എപ്പോൾ വേണമെങ്കിലും ഇതിൽ നിന്നും പിൻമാറാം എന്നും ഞാൻ മനസ്സിലാക്കുന്നു. അത് എന്റെ ചികിത്സയെയോ എന്റെ അവകാശങ്ങളേയോ ബാധിക്കുകയില്ലയെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]

ഞാൻ പഠനത്തിൽ നിന്നും പിൻമാറിയാലും എന്റെ മെഡിക്കൽ റിപ്പോർട്ട് ഈ പഠനത്തിൽ ഏർപ്പെട്ട ഡോക്ടർമാർക്കും സ്ഥാപനത്തിലെ എത്തിക്സ് കമ്മറ്റിയിലെ അംഗങ്ങൾക്കും പരിശോധിക്കാൻ അവകാശമുണ്ട്. ഇതിനായി എന്റെ സമ്മതം ഞാൻ കൊടുക്കുന്നു. [ ]

എന്റെ വ്യക്തിവിവരങ്ങൾ എവിടെയും വെളിപ്പെടുത്തുകയില്ല എന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]

ഞാൻ പൂർണ്ണമനസ്സാലെ ഈ പഠനത്തിൽ പങ്കെടുക്കുവാൻ സമ്മതിക്കുന്നു. [ ]

സംശയനിവാരണത്തിനായി പ്രധാന ഗവേഷകന്റെ ഫോൺ നമ്പർ എനിക്ക് നൽകിയിട്ടുണ്ട്. . [ ]

സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു കോപ്പി എനിക്ക് കിട്ടി. [ ]

പേര് :

ഒപ്പ് :

തീയതി :

സാക്ഷിയുടെ പേര് :

രോഗിയുമായുള്ള ബന്ധം :

ഒപ്പ് :

സമ്മതപത്രം ഒപ്പിടുവിച്ച വ്യക്തി

ഈ സമ്മതപത്രത്തിൽ ഗവേഷണത്തെപ്പറ്റിയുള്ള വിവരങ്ങൾ ആവശ്യാനുസരണം ഉണ്ടെന്ന് ഞാൻ സ്ഥിരീകരിക്കുന്നു. രോഗിയോട് ഈ പഠനത്തെ കുറിച്ച് ലഘുവായ ഭാഷയിൽ വിവരിച്ച് കൊടുക്കുകയും അവരുടെ സംശയങ്ങൾ ദൂരീകരിക്കുകയും ചെയ്തിട്ടുണ്ട്. പഠനത്തിനിടയിൽ ഉണ്ടായേക്കാവുന്ന അപകടങ്ങളെപ്പറ്റിയും ദൂഷ്യഫലങ്ങളെപ്പറ്റിയും രോഗിയോട് വിവരിച്ചിട്ടുണ്ട്. സംശയങ്ങൾ ചോദിക്കുവാൻ പ്രോത്സാഹിപ്പിക്കുകയും അവ ദൂരീകരിക്കുകയും ചെയ്തിട്ടുണ്ട്.

പേര് :

ഒപ്പ് : തീയതി :

Title of the study:

Comparison of fluid responsiveness using Transesophageal echocardiography in patients without coronary artery disease undergoing neurosurgical procedures versus patients with coronary artery disease undergoing coronary artery bypass graft surgery

Name of the Investigators:

Dr. Varun S, Dr. Manikandan. S, Dr. Thomas Koshy, Dr. K Jayakumar

You are scheduled to undergo a major surgical procedure which can lead to some hemodynamic changes during the procedure. Different patients respond to these changes differently. Hence, these changes need intense monitoring and transesophageal echocardiography is a modality which helps in identifying the cause as well as response to treatment during the periods of hemodynamic instability.

You are being requested to participate in this study which compares different parameters which detects the hemodynamic changes in response to passive leg raising under general anaesthesia between patients with and without coronary artery disease. This study will require observation of parameters derived from transesophageal echocardiography used for monitoring during your surgery. This tool is used as part of monitoring during anaesthesia in this institute and worldwide. We have planned to include about 50 patients from this hospital in this study.

What is esophagus?

Esophagus is the part of digestive tract extending from mouth to the stomach. The lower part of esophagus lies behind the heart. Hence, a device can be used which can scan the heart better from behind by lying in the middle or lower part of the esophagus.

What is echocardiography?

Echocardiography is a simple non-invasive method to scan the heart like the ultrasound scan. Echocardiography can be done by placing a specific type of ultrasound emitting device over the chest or in the esophagus.

What is Transesophageal echocardiography(TEE)?

TEE is an ultrasound scan of your heart. During TEE an ultrasound probe is inserted through your mouth into the esophagus.The ultrasound shows the structure and functions of the heart muscles and valves from different angles. This tool has been used all over the world in neurosurgical patients undergoing major surgeries and found to be safe. This tool is used routinely in cardiothoracic surgeries – especially coronary artery bypass graft surgery. This tool is semi-invasive in nature.

What is passive leg raising?

Passive leg raising is a method used to shunt more blood to heart and brain. The lower limb blood vessels of every human being have a reserve of nearly half a litre of blood in it. By raising the legs simultaneously this blood partly moves to the blood volume of other parts of body especially – heart and brain. This method is traditionally used for symptomatic relief of sudden unconsciousness. Blood from lower limb reserve moves to heart and thereby to systemic circulation. This method avoids the need of artificial intravenous fluids and also has the advantage of reversibility of systemic changes once the legs are returned to neutral position. This method is some what similar to a "natural, reversible and physiological blood transfusion."

Who will be included in this study?

We are planning to include 50 patients from our hospital as two groups (25 patients in each group). Patients undergoing major neurologic surgery whom require a transesophageal echocardiography device for their monitoring during surgery due to one of the many factors as decided by the anaesthesiologist caring them will be included in one group. Patients who are planned for cardiac coronary artery bypass graft surgery for ischemic heart disease will be included in other group. Patients undergoing coronary artery bypass graft surgery are routinely monitored by transesophageal echocardiography in our hospital. We are planning to include patients within age group of 18 to 65 years. We are not including patients with uncontrolled hypertension; patients for emergency surgery; presence of esophageal pathologies and past history of gastrointenstinal surgery; abnormal bleeding tendencies; and patients with osteoarthritis limiting limb movement. We are not including pregnant and breast feeding patients. We are also not including patients who participated in another study in this institution in the preceeding one month.

If you take part what will you have to do?

On the day of surgery you will be taken inside the operation theatre. Monitors to check your heart beat, blood pressure and oxygen saturation level will be attached. A small venous cannula will be inserted under local anesthesia in the hand for fluid and drug administration. Arterial cannula also will be inserted under local anesthesia for monitoring the blood pressure as a routine practice. General Anaesthesia will be induced as per the routine anesthesia protocol in the hospital. After the patient is fully sedated and paralyzed; and connected to the ventilator, a transesophageal echocardiography probe will be inserted through the mouth into the esophagus. After this the parameters to be studied are recorded. Following this a passive leg raising will be done using electronic adjustments of the operating table, thereby raising both your legs simultaneously. Cardiac parameters are recorded using transesophageal echocardiography during this time. After recording the parameters you will be returned to neutral position using electronic adjustments of the operating table and once again echocardiographic parameters will be recorded. After this, surgery is started as planned by the surgical team. Transesophageal echocardiography tool will be used to monitor the hemodynamic changes throughout your surgery. At the end of surgery transesophageal echocardiography probe will be removed.

No additional intravenous fluids or drugs, apart from what you receive as per routine anaesthesia protocol of this hospital irrespective of your participation in this study, will be used for the purpose of the study. We will be taking recordings from thetransesophageal echocardiography device which will be otherwise used in your surgery; irrespective of your participation in this study. Under no circumstance transesophageal echocardiography device shall be placed on you just for the sake of conducting this study.

Does transesophageal echocardiography use have any side effects?

Majority of people do not have any side effects. This procedure will be done under complete general anaesthesia. Hence you will not be aware of the procedure and also you will remain pain free. The reported side effects are sore throat and numbness of throat when used in awake patients but the incidence of these complications in our study will be remote as the patient is in general anesthesia. Other reported complications are very rare and include - injuries to teeth, oral cavity or esophagus. These complications are very rare in patients under general anesthesia

Futhermore, the patients with risk of getting injured are excluded by the detailed and comprehensive exclusion criteria of our study, which will be strictly adhered to.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way. In addition, if you experience any side effects, the study will be stopped and you will be given additional treatment.

What will happen if you develop any study related injury?

We do not expect any injury to happen to you on account of your participation in this study as the anaesthesia technique and monitoring tools would be same even if you were not part of the study. But if you do develop any side effects or problems due to the study, these will be treated at no cost to you. We are unable to provide any monetary compensation, however.

Will you have to pay for the cost of using the devices?

Transesophageal echocardiography will be used as a part of routine anaesthesia protocol for your surgery as your disease condition requires complex procedures which require advanced monitoring for your safety. You will not be required to pay any extra charges for participation in this study.

What happens after the study is over?

After the recordings for the study are taken with transesophageal echocardiography the same tool will be used to monitor patient hemodynamics throughout the length of the surgery. After surgery is over the transesophageal echocardiography probe will be removed before shifting the patient to intensive care unit.

Will your personal details be kept confidential?

The results of this study will be used for thesis submission as a part of academic research and will be submitted to a medical journal for publication, but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr. Varun S, (Principal investigator) Mobile number: 9041426743. email: varunsureshtmc@gmail.com

Dr S Manikandan, Additional Professor, Anaesthesiology, SCTIMST, Trivandrum – 11; 9446334711, kanmanis@sctimst.ac.in

For any further clarifications and concerns regarding the study's ethics clearance, please contact: The Member Secretary, Institutional Ethics Committee, SCTIMST, Trivandrum – 11. Phone: 0471-2524234, email: iec.mem.sec@sctimst.ac.in

പഠന ശീർഷകം:

സിരാസംബന്ധമായ ശസ്ത്രക്രിയക്ക് വിധേയരാവുന്ന, കൊറോണറി ശുദ്ധരക്തക്കുഴൽ അസുഖമില്ലാത്ത രോഗികളിലും കൊറോണറി ശുദ്ധരക്തക്കുഴൽ അസുഖം ഉള്ള കൊറോണറി ശുദ്ധരക്തക്കുഴൽ ബൈപ്പാസ് ഗ്രാഫ്റ്റ് ശസ്ത്രക്രിയക്കു വിധേയരാവുന്ന രോഗികളിലുമുള്ള ദ്രാവക പ്രതികരണത്തിന്റെ താരതമ്യം ട്രാൻസിസോഫാജിയൽ എക്കോകാർഡിയോഗ്രഫി (റ്റി. ഇ. ഇ) ഉപയോഗിച്ചു നടത്തുന്ന പഠനം.

ഗവേഷകന്റെ പേര്

ഡോ. വരുൺ എസ്, ഡോ. മണികണ്ഠൻ എസ്, ഡോ. തോമസ് കോശി. ഡോ. കെ ജയകുമാർ

ശസ്ത്രക്രിയാവേളയിൽ, ചില മാറ്റങ്ങൾ രക്തചംക്രമണവ്യവസ്ഥയിലുണ്ടാകാനിടയുള്ള ഒരു ഗൗരവതരമായ ശസ്ത്രക്രിയക്ക് താങ്കൾ വിധേയനാകാൻപോവുകയാണ്. ഈ മാറ്റങ്ങളോട് വ്യത്യസ്ത രോഗികൾ വിഭിന്നമായാണ് പ്രതികരിക്കുന്നത്. ആകയാൽ ഈ മാറ്റങ്ങൾ സജീവമായ നിരീക്ഷണത്തിന് വിധയമാക്കേണ്ടതുണ്ട്. രക്തചംക്രമണവ്യവസ്ഥയിലെ അസ്ഥിരതയുടെ ഘട്ടത്തിൽ കാരണങ്ങളും, ചികിത്സയോടുള്ള പ്രതികരണങ്ങളും കണ്ടെത്താൻ സഹായകമായ ഒരു പ്രക്രിയയാണ് ട്രാൻസിസോഫാജിയൽ എക്കോകാർഡിയോഗ്രഫി.

പൊതുവായ മയക്കലിന് വിധേയമാക്കി കൊറോണറി ശുദ്ധരക്തക്കുഴൽ അസുഖമുള്ളവരും ഇല്ലാത്തവരുമായ രോഗികളിൽ ഭാഗികമായി കാലുയർത്തിക്കൊടുക്കുന്നതിലൂടെ ഉണ്ടാകുന്ന പ്രതികരണങ്ങളിലൂടെ രക്തചംക്രമണ വ്യവസ്ഥയിലെ മാറ്റങ്ങൾ തിരിച്ചറിയുന്ന വ്യത്യസ്ത ഘടകങ്ങളെ താരതമ്യം ചെയ്യുന്ന ഈ പഠനത്തിൽ പങ്കാളിയാകാൻ താങ്കളോട് അഭ്യർത്ഥിക്കുന്നു. താങ്കളുടെ ശസ്ത്രക്രിയാസമയത്ത് നിരീക്ഷണത്തിനായുപയോഗിക്കുന്ന ട്രാൻസിസോഫാജിയൽ എക്കോകാർഡിയോഗ്രഫിയിലൂടെ ആർജിക്കുന്ന വ്യത്യസ്ഥ ഘടകങ്ങളുടെ നിരീക്ഷണം ഈ പഠനത്തിനാവശ്യമാണ്. ഈ സ്ഥാപനത്തിലും ലോകമെമ്പാടും ഈ ഉപകരണം മയക്കലിന്റെ ഭാഗമായി ഉപയോഗിക്കുന്നു. ഈ ആശുപത്രിയിലെ 50 രോഗികളിൽ ഈ പഠനം നടത്താൻ ഞങ്ങളുദ്ദേശിക്കുന്നു.

എന്താണ് ഈസോഫാഗസ് ?

വായമുതൽ ആമാശയം വരെയുള്ള അന്നനാളത്തിന്റെ ഭാഗമാണ് ഈസോഫാഗസ്. ഈസോഫാഗസിന്റെ താഴെയുള്ള ഭാഗം ഹൃദയത്തിന് പിൻവശത്ത് സ്ഥിതിചെയ്യുന്നു. ആകയാൽ ഒരു ഉപകരണം കൊണ്ട് ഈസോഫാഗസിന്റെ താഴെയോ മദ്ധ്യഭാഗത്തോ പുറകിൽനിന്നു മെച്ചപ്പെട്ടവിധം ഹൃദയത്തിന്റെ ചിത്രീകരണം നടത്താനാവും.

എന്താണ് എക്കോകാർഡിയോഗ്രഫി ?

എക്കോകാർഡിയോഗ്രഫി എന്നത് ലളിതവും ഹൃദയത്തിന്റെ ഉള്ളിൽ കടക്കാതെയുള്ള ചിത്രീകരണം നടത്തുന്ന- അൾട്രാസൗണ്ട് ചിത്രീകരണം പോലുള്ള- ഒരു രീതിയാണ്. ഒരു പ്രത്യേകതരം ഉയർന്ന ആവൃതിയുള്ള ശബ്ദം പുറപ്പെടുവിക്കുന്ന ഉപകരണം നെഞ്ചിനുമുകളിലോ, ഈസോഫാഗസിനുള്ളിലോ വച്ച് എക്കോകാർഡിയോഗ്രഫി ചെയ്യാം.

എന്താണ് ട്രാൻസിസോഫാജിയൽ എക്കോകാർഡിയോഗ്രഫി (റ്റി.ഇ.ഇ) ?

ട്രാൻസിസോഫാജിയൽ എക്കോകാർഡിയോഗ്രഫി എന്നാൽ താങ്കളുടെ ഹൃദയത്തിന്റെ ചീത്രീകരണം ഉയർന്ന ആവൃതിയുള്ള ശബ്ദം ഉപയോഗിച്ച് ചെയ്യാൻ ഉപയോഗിക്കുന്ന ഉപകരണമാണ്. ഇതിനായി വായിലൂടെ ഈസോഫാഗസിലേക്ക് (അന്നനാളം) ഉയർന്ന ആവൃതിയുള്ള ശബ്ദം ഉപയോഗിച്ച് ചിത്രീകരണം നടത്താനുള്ള കുഴൽ ഇടേണ്ടതുണ്ട്. ഉയർന്ന ആവൃതിയുള്ള ശബ്ദം വ്യത്യസ്ത കോണുകളിൽ നിന്നും ഹൃദയ പേശികളുടെയും വാൽവുകളുടെയും ഘടനയും പ്രവർത്തനവും കാണിച്ചുതരും. ഈ ഉപകരണം പ്രധാനപ്പെട്ട ശസ്ത്രക്രിയക്ക് വിധേയരാകുന്ന

ന്യൂറോ ശസ്ത്രക്രിയാ രോഗികളിൽ ലോകമെമ്പാടും ഉപയോഗിക്കുന്നതും സുരക്ഷിതമെന്ന് കണ്ടെത്തപ്പെട്ടിട്ടുള്ളതുമാണ്. കാർഡിയോതൊറാസിക് ശസ്ത്രക്രിയകളിൽ സാധാരണയായി ഈ ഉപകരണം ഉപയോഗിക്കുന്നു- പ്രത്യേകിച്ചും കൊറോണറി ശുദ്ധരക്തക്കുഴൽ ബൈപാസ് ശസ്ത്ര ക്രിയകളിൽ. ശരീരത്തിനുള്ളിൽ ഭാഗികമായി കടക്കുന്നസ്വഭാവമാണ് ഈ ഉപകരണത്തിന്.

എന്താണ് കാലുയർത്തിക്കൊടുക്കൽ ?

ഹൃദയത്തിലേക്കും തലച്ചോറിലേക്കും കൂടുതൽ രക്തമെത്തിക്കാനുതകുന്ന രീതിയാണ് കാലു യർത്തിക്കൊടുക്കൽ. മനുഷ്യരുടെ കാലിന്റെ താഴ്ഭാഗത്തുള്ള രക്തക്കുഴലുകളലിൽ ഏകദേശം അര ലിറ്ററോളും രക്തം സംഭരിച്ചിട്ടുണ്ടാകും. കാലുകൾ ഒരേസമയം ഉയർത്തുന്നതിലൂടെ ഈ രക്തം ഭാഗികമായി ശരീരത്തിന്റെ മറ്റുഭാഗങ്ങളിലേക്ക് പ്രത്യേകിച്ചും ഹൃദയത്തിലേക്കും തലച്ചോറിലേക്കും നീങ്ങും. പെട്ടെന്നുണ്ടാകുന്ന ബോധക്കേടിന് ലാക്ഷണീകമായ ആശ്വാസം ലഭിക്കാൻ പാരമ്പര്യ മായി ഈ രീതി ഉപയോഗിച്ചുവരുന്നു. കാലിലെ സംഭരിച്ചട്ടുള്ള രക്തം ഹൃദയത്തിലേക്കും അതു വഴി ചംക്രമണവ്യവസ്ഥയിലേക്കും നീങ്ങുന്നു. ഈ രീതി കൃത്രിമമായി ഞരമ്പിലൂടെ ദ്രാവകം നൽകുന്നത് ഒഴിവാക്കാനും കാലുകൾ സാധാരണ നിലയിലാക്കുന്നതിലൂടെ ചംക്രമണവ്യവസ്ഥ യിലെ മാറ്റങ്ങൾ പൂർവ്വസ്ഥിതിയിലാക്കുന്നതിനും കഴിയും. സ്വാഭാവികമായ, തിരിച്ചുകൊണ്ടുവരാ വുന്ന ശാരീരികമായ രക്തം നൽകലിനോട് ഏകദേശം സാമ്യമുള്ളതാണ് ഈ രീതി.

ആരെയൊക്കെ ഈ പഠനത്തിൽ ഉൾപ്പെടുത്തും ?

ഞങ്ങൾ നമ്മുടെ ആശുപത്രിയിലെ 50 ഗോഗികളെ രണ്ട് ഗ്രൂപ്പുകളിലായി (25 രോഗികൾ ഒരു ഗ്രൂപ്പിൽ) ഉൾപ്പെടുത്താൻ ഉദ്ദേശിക്കുന്നു. ഗൗരവതരമായ ന്യൂറോളജിക് ശസ്ത്രക്രിയക്ക് വിധേയമാ കുന്ന, പലതിലൊരു ഘടകമായി ട്രാൻസിസോഫാജിയൽ എക്കോകാർഡിയോഗ്രഫി ഉപകരണം നിരീക്ഷണത്തിനാവശ്യമുള്ളതായി രോഗിയെ പരിചരിക്കുന്ന അനസ്തീഷ്യോളജിസ്റ്റ് നിശ്ചയിക്കുന്ന, രോഗികളെ ഒരുഗ്രൂപ്പിലുൾപ്പെടുത്തും. ഹൃദയ കൊറോണറി ശുദ്ധരക്തക്കുഴൽ ബൈപാസ് ഗ്രാഫ്റ്റ് ശസ്ത്രക്രിയക്ക് വിധേയരാകാൻപോകുന്ന ഇസ്ക്കീമിക് ഹൃദയരോഗമുള്ള രോഗികളെ മറ്റൊരു ഗ്രൂപ്പിലും ഉൾപ്പെടുത്തും. കൊറോണറി ആർട്ടറി ബൈപാസ് ഗ്രാഫ്റ്റ് ശസ്ത്രക്രിയക്ക് വിധേയ രാകുന്ന രോഗികളെ നമ്മുടെ ആശുപത്രിയിൽ സാധാരണയായി ട്രാൻസിസോഫാജിയൽ എക്കോകാർഡിയോഗ്രഫി നിരീക്ഷണത്തിന് വിധേയരാക്കുന്നുണ്ട്. 18 വയസ്സിനും 65 വയസ്സിനുമിട യിലുള്ള രോഗികളെയാണ് ഉൾപ്പെടുത്താനുദ്ദേശിക്കുന്നത്. അനിയന്ത്രിതമായ രക്തസമ്മർദ്ദം, അടി യന്തിരമായ ശസ്ത്രക്രിയ, ഈസോഫാഗസിലുള്ള അസുഖങ്ങളുടെ സാന്നിദ്ധ്യം, ഗാസ്ട്രോ ഇന്റ സ്റ്റയിനൽ ശസ്ത്രക്രിയയുടെ ചരിത്രം, അസാധാരണമായ രക്തസ്രാവ സാദ്ധ്യതകൾ, കാലുകളുടെ ചലനത്തെ പരിമിതപ്പെടുത്തുന്ന ഓസ്റ്റിയോ ആർത്രൈറ്റിസ് എന്നിവയുള്ള രോഗികളെ പഠനത്തി ലുൾപ്പെടുത്തില്ല. മുലയൂട്ടുന്നവരെയോ ഗർഭിണികളെയോ ഉൾപ്പെടുത്തില്ല. കഴിഞ്ഞ ഒരുമാസത്തി നുള്ളിൽ ഈ ആശുപത്രിയിൽ മറ്റൊരുപഠനത്തിൽ പങ്കെടുത്ത രോഗികളെയും ഉൾപ്പടുത്തില്ല.

പങ്കെടുക്കുകയാണെങ്കിൽ താങ്കളെന്ത് ചെയ്യണം ?

ഈ പഠനത്തിൽ പങ്കെടുക്കുവാൻ താങ്കൾ സമ്മതിക്കുകയാണെങ്കിൽ ശസ്ത്രക്രിയയുടെ ദിവസം നിങ്ങളെ ഓപ്പറേഷൻ തിയേറ്ററിൽ കൊണ്ടുപോയി ഹൃദയമിടിപ്പ്, രക്തസമ്മർദ്ദം, ശരീരത്തിലെ ഓക്സിജന്റെ അളവ് എന്നിവ പരിശോധിക്കാനുള്ള ഉപകരണങ്ങൾ നിങ്ങളുടെ ശരീരത്തിൽ ഘടി പ്പിക്കും. ലോക്കൽ അനസ്തേഷ്യ തന്നതിനുശേഷം നിങ്ങളുടെ കൈയിൽ ദ്രാവകങ്ങൾ, മരുന്ന് എന്നിവ നൽകുവാൻ ഒരു കുഴൽ കടത്തിവിടുന്നതായിരിക്കും. രക്തസമ്മർദ്ദം അളക്കാനായി സാധാരണപോലെ ആർട്ടീരിയൽ കാനുല കടത്തും. അതിനുശേഷം നിങ്ങൾക്ക് ആശുപത്രിയിലെ അനസ്തേഷ്യ നടപടിക്രമങ്ങൾക്ക് അനുസരിച്ചുള്ള അനസ്തേഷ്യ നൽകുന്നതായിരിക്കും. നിങ്ങളെ പൂർണ്ണമായി മയക്കിയശേഷം സാധാരണ ചെയ്യുന്നരീതിയിൽ വെന്റിലേറ്റർ യന്ത്രവുമായി ബന്ധിപ്പി ക്കുന്നു. ഇതിനുശേഷം റ്റി.ഇ.ഇയുടെ സ്കാൻ കുഴൽ നിങ്ങളുടെ വായിലൂടെ അന്നനാളത്തിലേക്ക് ഇടുന്നതാണ്. അതിനുശേഷം വേണ്ടുന്ന സൂചികകൾ രേഖപ്പെടുത്തും. അതിനു തുടർച്ചയായി കാലുകൾ ഉയർത്തുന്നതിനായി ഓപ്പറേഷൻ ടേബിൾ ഇലക്ട്രോണിക്കലായി ക്രമപ്പെടുത്തും അതു

വഴി താങ്കളുടെ രണ്ടുകാലുകളും ഒരേസമയത്ത് ഉയർത്തപ്പെടും. ഈ സമയം ഹൃദയസൂചികകൾ ട്രാൻസിസോഫാജിയൽ എക്കോ കാർഡിയോഗ്രഫി ഉപയോഗിച്ച് രേഖപ്പെടുത്തും. അതിനുശേഷം ഓപ്പറേഷൻ ടേബിൾ ഇലക്ട്രോണിക്കലായി ക്രമപ്പെടുത്തി താങ്കളെ സാധാരണ സ്ഥിതിയിലാക്കുകയും എക്കോകാർഡിയോഗ്രഫി സൂചികകൾ രേഖപ്പെടുത്തുകയും ചെയ്യും. അതിനുശേഷം ശസ്ത്രക്രിയാസംഘം ശസ്ത്രക്രിയ ആരംഭിക്കും.

താങ്കൾ ഈ പഠനത്തിൽ പങ്കെടുത്താലുമില്ലെങ്കിലും സാധാരണയായി മയക്കൽ പ്രക്രിയയ്ക്കായി ഉപയോഗിക്കുന്നതിലുപരി ദ്രവങ്ങളോ മരുന്നോ ഈ പഠനത്തിനായി ഉപയോഗിക്കുകയില്ല. താങ്കൾ ഈ പഠനത്തിൽ പങ്കെടുത്താലുമില്ലെങ്കിലും ശസ്ത്രക്രിയയ്ക്കായുപയോഗിക്കുന്ന ട്രാൻസിസോഫാജിയൽ എക്കോകാർഡിയോഗ്രഫി ഫലങ്ങൾ രേഖപ്പെടുത്തും. ഈ പഠനത്തിനായിമാത്രം ഒരു സാഹചര്യത്തിലും ട്രാൻസിസോഫാജിയൽ എക്കോകാർഡിയോഗ്രഫി ഉപകരണം താങ്കളിൽ ഘടിപ്പിക്കുകയില്ല.

റ്റി.ഇ.ഇ ഉപകരണം ഇപയോഗിക്കുന്നതുകൊണ്ടുള്ള പാർശ്വഫലങ്ങൾ?

ഭൂരിപക്ഷം ആളുകൾക്കും പാർശ്വ ഫലങ്ങളുണ്ടാകില്ല. പൂർണ്ണമായ മയക്കലിനുശേഷമാണ് ഇതുപയോഗിക്കുന്നത്, ആകയാൽ താങ്കൾ ഈ നടപടിയെപ്പറ്റി അറിയുകയില്ല, വേദനയില്ലാതിരിക്കുകയും ചെയ്യും. ചിലർക്ക് തൊണ്ടയിൽ തരിപ്പും, മന്ദതയും ഉണർന്നിരിക്കുന്ന അവസ്ഥയിലുപയോഗിച്ചാൽ അനുഭവപ്പെടാറുണ്ട് പക്ഷേ രോഗി പൊതുവായ മയക്കലിന് വിധേയമാണെന്നതിനാൽ, ഞങ്ങളുടെ പഠനത്തിൽ ഈ സങ്കീർണ്ണതകൾ ഉണ്ടാവാനുള്ള സാധ്യത വിദൂരമാണ്. പല്ലുകൾക്ക് പരിക്ക്, വായ്ക്കും ഈസോഫാഗസിനുമുള്ള പരിക്ക് എന്നിവയാണ് രേഖപ്പെടുത്തപ്പെട്ടിട്ടുള്ള മറ്റ് സങ്കീർണ്ണതകൾ. തന്നെയുമല്ല ഒഴിവാക്കുന്ന വിഭാഗത്തിലാകയാൽ പരുക്ക് പറ്റാൻ സാധ്യതയുള്ള രോഗികളെ കർശനമായി ഒഴിവാക്കുകയും ചെയ്യും.

ആരംഭിച്ച ശേഷം ഈ പഠനത്തിൽ നിന്ന് പിന്മാറുവാൻ സാധിക്കുമോ?

ഈ പഠനത്തിൽ പങ്കെടുക്കുക എന്നത് നിങ്ങളുടെ മാത്രം തീരുമാനം അനുസരിച്ചാണ്. ഇതിൽ പങ്കെടുക്കാതിരിക്കാൻ നിങ്ങൾക്ക് പൂർണ്ണ സ്വാതന്ത്ര്യമുണ്ട്. ആ തീരുമാനം നിങ്ങളുടെ ചികിത്സയെ ഒരു തരത്തിലും ബാധിക്കില്ല. പഠനം തുടങ്ങിയതിനുശേഷവും നിങ്ങൾക്ക് എന്തെങ്കിലും പാർശ്വഫലങ്ങളുണ്ടായാൽ പഠനം നിർത്തുന്നതും അധികമായി ചികിത്സിക്കുന്നതുമായിരിക്കും.

ഈ പഠനവുമായി ബന്ധപ്പെട്ട് താങ്കൾക്ക് എന്തെങ്കിലും പരുക്കുണ്ടായാൽ എന്തു സംഭവിക്കും?

അനസ്തേഷ്യ സങ്കേതവും നിരീക്ഷണ ഉപകരണങ്ങളും താങ്കൾ പഠനത്തിൽ പങ്കെടുക്കുന്നില്ലെങ്കിലും ഒന്നു തന്നെയാകൽ പഠന ഫലമായി താങ്കൾക്ക് അപകടം സംഭവിക്കാനുള്ള സാധ്യതയില്ല. എന്നാൽ തന്നെയും എന്തെങ്കിലും പാർശ്വഫലങ്ങളോ പ്രശ്നങ്ങളോ ഉണ്ടായാൽ യാതൊരുവിധ അധിക ചെലവുമില്ലാതെ അതിനുവേണ്ട ചികിത്സ നിങ്ങൾക്ക് ചെയ്തു തരുന്നതാണ്. പക്ഷെ അതിനു പകരമായി പണം തരുന്നതായിരിക്കില്ല.

പഠനത്തിന് ഉപകരണം ഉപയോഗിക്കുന്നതിന്റെ ചിലവ് രോഗി കൊടുക്കേണ്ടതുണ്ടോ?

താങ്കളുടെ രോഗാവസ്ഥയും ശസ്ത്രക്രിയയുടെ സങ്കീർണ്ണതയുംമൂലം മയക്കലിന്റെ സാധാരണ നടപടികളുടെ ഭാഗമായി ട്രാൻസിസോഫാജിയൽ എക്കോകാർഡിയോഗ്രഫി പോലുള്ള ആധുനീക മായ നിരീക്ഷണസംവിധാനം താങ്കളുടെ സുരക്ഷക്കായി ഉപയോഗിക്കേണ്ടതുണ്ട്. ഈ പഠനത്തിൽ പങ്കെടുക്കുന്നതിന് താങ്കൾ കൂടുതൽ പണം മുടക്കേണ്ടതില്ല

പഠനം കഴിയുമ്പോൾ എന്തുണ്ടാകും?

പഠനാവശ്യത്തിനായുള്ള രേഖപ്പടുത്തലുകൾക്കുശേഷം ട്രാൻസിസോഫാജിയൽ എക്കോകാർഡിയോഗ്രഫി ശസ്ത്ക്രിയയിലുടനീളം രക്തചംക്രമണവ്യവസ്ഥയെ നിരീക്ഷിക്കാൻ ഉപയോഗിക്കും. ശസ്ത്രക്രിയ പൂർത്തിയാക്കിയ ശേഷം ഐ.സി.യുവിലേക്ക് മാറ്റുന്നതിനുമുൻപ് റ്റി. ഇ. ഇ മാറ്റുന്നതാണ്.

നിങ്ങളുടെ വ്യക്തിപരമായ വിവരങ്ങൾ രഹസ്യമായി സൂക്ഷിക്കുമോ?

ഈ പഠനത്തിന്റെ ഫലങ്ങൾ പഠന ഗവേഷണത്തിന്റെ ഭാഗമായി തീസിസിനുപയോഗിക്കുന്നതും ഏതെങ്കിലും മെഡിക്കൽ പ്രസിദ്ധീകരണത്തിൽ കൊടുക്കുന്നതുമായിരിക്കും. പക്ഷെ ഒന്നിലും നിങ്ങളുടെ പേരോ അഡ്രസ്സോ പ്രസിദ്ധീകരിക്കില്ല. നിങ്ങളുടെ മെഡിക്കൽ വിവരങ്ങൾ ഈ പഠനത്തോട് ബന്ധപ്പെട്ട ആളുകൾ പരിശോധിക്കുന്നതായിരിക്കും.

നിങ്ങൾക്ക് ഇതിനെപ്പറ്റി കൂടുതൽ എന്തെങ്കിലും അറിയുവാനുണ്ടെങ്കിൽ, ദയവു ചെയത് ബന്ധപ്പെടുക - ഡോ. വരുൺ എസ് (പ്രധാന ഗവേഷകൻ) മൊബൈൽ ഫോൺ നമ്പർ : 9041426743. ഇ-മെയിൽ varunsureshtmc@gmail.com.,

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PROFORMA FOR DATA COLLECTION

Comparison of fluid responsiveness using Transesophageal echocardiography in patients without coronary artery disease undergoing neurosurgical procedures versus patients with coronary artery disease undergoing coronary artery bypass graft surgery

Patient age: Diagnosis :
Weight: Height: Proposed surgery :
Sex: BSA: Date of surgery :

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Group 1 / 2

Factors	Include	Exclude	Factors	Include	Exclude
Patient consent	Yes	No	Abnormal coagulation profile.	No	Yes
Nature of procedure	Elective	Emergency			
Age	18-65	< 18, >65	Presence of esophageal pathologies (esophageal mass , stricture , tracheo-esophageal fistula , esophageal varices, peptic ulcer, scleroderma)	No	Yes
Sinus Rhythm	Yes	No			
Preoperative routine transthoracic echocardiography	Yes	No			
Cardiac Pathologies (valvular heart disease, intracardiac shunts, peripheral vascular disease) or	No	Yes	History of active upper GI bleed/recent upper GI bleed.	No	Yes
Pre op Heart rate	> 50	< 50	History of previous esophageal/upper GI surgery	No	Yes
Lung Pathologies (like asthma, COPD and tuberculosis) pathologies	No	Yes			
Systemic HT stage III & above	No	Yes			
Heart block	No	Yes			
Pregnancy , Nursing	No	Yes			
			Supine position intraoperatively	Yes	No

Parameters [three recordings and average(avg)]	Baseline				After PLR (immediate)				After PLR (10 minutes)			
	1	2	3	avg	1	2	3	Avg	1	2	3	avg
HR												
Systolic BP (maximum)												
Systolic BP (minimum)												
Diastolic BP(maximum)												
Diastolic BP(minimum)												
SVC diameter(maximum)												
SVC diameter(minimim)												
LVEDV (maximum)												
LVEDV (minimum)												
SV (maximum)												
SV(minimum)												
SVV												
PPV												
LVOT Diameter												
PIP												
TV												
EtCO2												
CVP												
LVOT VTI												

Adverse events (if any)	Treatment	Further Intervention
Sore throat		
Arrthymias		
Esophageal injury		
Others		

Name & Signature of Investigator :

Abbreviations:

PLR – passive leg raising; BSA – body surface area; Temp(*C) – temperature in degree centigrade; EtCO2 - end tidal carbondioxide; HR(bpm) – heart rate (beats per minute); PIP – peak inspiratory pressure; SBP – systolic blood pressure; SVC – superior venacava; LVOT – left ventricular outflow tract; LVOT VTI – left ventricular outflow tract velocity time integral; SV – stroke volume; CO – cardiac output; CI – cardiac index; LVEDV – left ventricular end diastolic volume; CVP – central venous pressure; SVV – stroke volume variation, TV – tidal volume; SVV – stroke volume variation

slno	group	mrd	diagnosis	surgery	do.surgery	age	sex	wt	ht	bsa	t0.hr.max	t0.hr.min	t0.sbp.max	t0.sbp.min	t0.dbp.max	t0.dbp.min
1	1	339623	r frontal glioma	cranotiomy	16.12.2016	36	m	75	170	1.88	65	64	109	107	80	76
2	1	423239	r frontal glioma	cranotiomy	22.12.2016	37	f	63	160	1.67	52	51	122	120	77	74
3	1	380588	l frontal glioma	cranotiomy	07.12.2017	30	m	72	175	1.87	56	55	89	85	54	51
4	1	426655	planum sphenoidale menngioma	cranotiomy	13.02.2017	43	m	72	170	1.84	53	52	128	121	77	73
5	1	422887	l frontal lesion	cranotiomy	15.02.2017	51	f	68	151	1.69	94	92	120	111	59	55
6	1	426444	r mid 3rd parasagittal meningioma	cranotiomy	02.03.2017	47	f	41	152	1.32	62	61	105	100	59	56
7	1	421127	l frontal parafalcine meningioma	cranotiomy	13.03.2017	64	f	66	157	1.7	78	77	119	116	64	61
8	1	417576	l frontal glioma	cranotiomy	20.03.2017	30	f	82	180	2.02	66	65	95	90	55	53
9	1	429491	r parasagittal meningioma	cranotiomy	24.03.2017	42	f	64	157	1.67	56	55	100	92	53	48
10	1	431944	l parietocooipital meningioma	cranotiomy	04.07.2017	45	f	54	153	1.51	54	53	96	92	60	57
11	1	436564	l parietal glioma	cranotiomy	10.08.2017	44	m	85	177	2.04	57	56	97	92	58	52
12	1	429397	l parasagittal frontal meningioma	cranotiomy	14.08.2017	35	m	81	170	1.96	76	75	99	96	66	63
13	1	425729	l frontal glioma	cranotiomy	18.08.2017	42	m	60	152	1.59	74	73	96	94	54	53
14	1	439066	l parasagittal meningioma	cranotiomy	11.10.2017	65	m	65	182	1.81	68	67	127	123	78	74
15	1	439667	l frontotemporal metastasis	cranotiomy	10.10.2017	42	m	56	157	1.56	79	78	105	94	65	60
16	1	439278	choroid plexus papilloma	cranotiomy	24.10.2017	38	f	38	157	1.7	89	82	113	102	64	55
17	1	440140	r frontal meningioma	cranotiomy	26.10.2017	64	f	62	150	1.61	61	60	89	84	43	42
18	1	404404	frontal midline epidermoid	cranotiomy	30.10.2017	34	f	65.2	154	1.67	74	70	118	110	69	63
19	1	440628	r sphenoid wing meningioma	cranotiomy	01.11.2017	63	f	48.7	144	1.4	110	105	171	167	90	87
20	1	434404	r trigeminal neuralgia	mvd	06.11.2017	36	f	71.7	158	1.77	89	88	123	121	63	56
21	1	437834	r temperoparietal glioma	cranotiomy	08.11.2017	63	m	72	164	1.81	67	65	113	113	67	66
22	1	431956	r mca aneurysm	clipping	10.11.2017	63	m	55	165	1.59	53	51	114	103	64	58
23	1	430371	r insular glioma	cranotiomy	14.11.2017	38	m	61	160	1.65	69	68	98	93	58	47
24	1	441196	l sphenoid wing meningioma	cranotiomy	20.11.2017	23	m	45.4	129.5	1.28	86	85	113	110	73	71
25	1	230775	l frontal ependymoma	cranotiomy	22.11.2017	21	f	49.6	158.5	1.48	64	62	113	108	59	54
26	1	442729	colloid cyst third ventricle	cranotiomy	01.12.2017	42	m	75	160	1.48	95	94	94	85	57	54
27	1	442708	l temporal hgg	cranotiomy	04.12.2017	53	m	64	157	1.57	56	55	108	107	68	67
28	1	412560	l temperoparietal recurrent meningioma	cranotiomy	05.12.2017	46	m	73.8	170	1.87	47	45	146	141	80	76
29	1	443056	l frontal hgg	cranotiomy	15.12.2017	29	m	65.1	170.5	1.76	64	61	116	114	71	69

Group 1: t0-baseline; t1-1 minute after PLR; t2 - 10 minutes after PLR ; max- maximum; min - minimum

t0.svc.max	t0.svc.min	t0.lvedv.max	t0.lvedv.min	t0.sv.max	t0.sv.min	t0.vti.max	t0.vti.min	t0.lvot	t0.pip	t0.tv	t0.etco2	t1.hr.max	t1.hr.min	t1.sbp.max	t1.sbp.min	t1.dbp.max	t1.dbp.min	t1.svc.max	t1.svc.min	t1.lvedv.max	t1.lvedv.min	t1.sv.max	t1.sv.min
1.3	1.1	77	66	56	38	17.8	12	2	16	488	38	57	56	141	136	74	72	1.4	1.1	113	77	61	57
1.6	1.5	92	85	67	56	21.6	17.9	2	23	451	28	57	56	134	128	87	86	1.7	1.5	95	80	72	57
1.6	1.4	98	90	82	62	21	15.9	2.2	19	465	28	55	54	89	83	50	48	1.5	1.4	95	89	78	74
1.1	1	101	84	46	46	15.8	15.8	1.9	17	501	31	54	53	126	122	79	74	1.2	1.1	101	72	44	37
1.2	1.1	99	83	50	39	18.1	14.1	1.9	29	469	28	94	93	127	120	62	58	1.5	1.3	86	71	67	45
1.4	1.2	90	82	55	40	23.6	16.8	1.7	14	373	38	66	65	117	110	68	64	1.8	1.6	103	95	59	39
1.2	1.1	67	58	27	22	17.5	14	1.7	26	405	34	79	78	103	97	53	49	1.3	1.2	71	60	38	29
1.5	1.4	90	79	49	37	17.4	14.6	1.8	20	534	33	59	57	90	86	54	51	1.3	1.2	85	82	54	36
1	0.8	92	83	74	63	34.1	29	1.8	22	487	27	57	56	142	136	77	74	1.2	1.1	112	105	73	61
1.4	1.3	82	77	53	44	23.4	19.7	1.7	19	475	30	55	54	104	101	70	66	1.6	1.5	90	86	65	48
1.8	1.6	117	112	105	92	31.2	27.6	2.1	16	436	36	56	55	104	100	58	54	1.8	1.7	121	110	115	86
1.6	1.4	91	88	47	41	20.1	17.6	2	17	401	29	76	74	101	96	69	67	1.5	1.4	92	87	56	53
1	0.9	117	116	97.5	95.5	28.3	27.7	2.1	20	501	27	76	75	96	94	54	53	1	1	100	105	76.7	74.3
2.2	2	156	139	144.7	129.25	36	32.2	2.2	17	367	38	65	64	101	99	57	56	2.2	1.9	157	138	148	116
1.4	1.3	60	42	44.6	34.7	19.2	14.7	1.7	16	410	24	81	80	120	108	75	70	1.4	1.2	67	47	58.56	43.35
1.3	1.2	86	76	60.04	46.03	19.9	15.2	2	19	531	30	72	69	98	93	51	47	1.4	1.2	89	86	60.36	47.86
1.4	1.3	96	91	77	75	25.2	24	2.1	22	456	27	63	60	128	121	60	53	1.5	1.4	119	85	82	81
1.5	1.4	119	115	87.41	73.55	29.7	25	1.9	18	459	27	67	65	113	109	65	59	1.4	1.2	117	110	86.52	67.28
1.5	1.3	65	50	51.5	39.8	17	13.1	2	12	352	29	104	102	165	159	92	88	1.3	1.2	79	68	68.65	50.92
1.4	1.2	125	104	95.4	80.6	27.1	21.5	1.9	18	386	28	87	85	123	118	62	58	1.4	1.3	124	114	91.14	86.86
1.8	1.7	149	106	107	90	36.2	25.9	2.3	17	375	29	70	68	114	111	67	65	1.9	1.8	146	99	105	80
1.1	1	104	98	84.71	71.3	22.8	27.1	2	17	382	27	53	52	111	108	62	59	1	0.9	109	99	87.3	70.04
1.4	1.3	83	80	66.29	60.36	21.9	19.9	2	15	377	28	68	67	110	106	57	54	1.5	1.4	92	84	63.19	57.73
1.3	1.2	74	69	53.7	49.74	22.1	20.5	1.8	28	380	27	85	83	117	115	77	73	1.2	1	81	70	53.18	46.44
1.4	1.2	86	72	71.88	59.72	26.3	21.8	1.9	21	392	31	63	60	114	106	61	56	1.4	1.3	87	73	67.57	61.08
1.3	1.2	99	90	59.84	54.91	18.5	17	2	18	436	29	94	93	97	95	62	61	1.6	1.4	111	103	73.63	63.78
1.5	1.4	90	88	47.44	41.55	20.1	17.6	2	18	463	29	50	49	102	101	62	61	1.6	1.5	92	85	56.49	53.69
1.5	1.4	97	94	88.41	77.39	24.5	21.4	2.1	18	432	30	47	45	140	137	79	76	1.5	1.4	96	87	79.89	78.29
2	1.9	96	86	86	66	22	20.2	2	19	454	32	61	58	114	113	70	68	2	2	108	93	81	70

Group 1: t0-baseline; t1-1 minute after PLR; t2 - 10 minutes after PLR ; max- maximum; min - minimum

t1.vti.max	t1.vti.min	t1.pip	t1.tv	t1.etco2	t2.hr.max	t2.hr.min	t2.sbp.max	t2.sbp.min	t2.dbp.max	t2.dbp.min	t2.svc.max	t2.svc.min	t2.lvedv.max	t2.lvedv.min	t2.sv.max	t2.sv.min	t2.vti.max	t2.vti.min	t2.pip	t2.tv	t2.etco2	lvidd	lvids	ef
19.3	18	15	476	31	63	62	132	130	69	66	1.4	1.1	93	77	69	66	21.9	20.7	15	490	30	3.1	1.8	72
23.1	18.1	23	460	24	50	49	133	131	90	88	1.5	1.4	93	87	80	67	25.7	21.3	23	473	24	3.6	2.4	61
18.8	17.2	19	476	27	52	51	86	81	47	45	1.6	1.5	99	88	68	65	16.4	16.1	19	470	27	3.9	2.3	69
15	13.5	17	499	30	54	53	123	115	73	70	1.2	1.1	86	75	44	37	15	13.5	17	500	30	3.7	2.1	73
18.3	13.5	30	460	28	93	92	142	136	73	68	1.2	1.2	77	74	62	50	20.2	12.7	29	470	29	2.4	1.1	47
25.4	16.8	14	375	31	66	65	107	95	55	50	1.7	1.6	88	78	54	40	23.4	17.6	14	373	31	3.6	2.4	61
24	18.7	27	401	34	78	77	104	98	57	49	1.4	1.3	70	58	37	32	24.2	17.7	27	401	36	3.3	1.6	61
21.1	14.4	21	541	33	57	56	88	85	54	51	1.3	1.2	96	87	44	35	17.2	14	21	551	32	2.9	1.2	45
34	28.8	24	491	26	57	56	109	104	55	53	1.4	1.2	75	74	69	55	32	25.4	24	487	26	4.2	2.4	58
29	21.2	20	478	31	56	55	92	86	54	53	1.2	1.1	86	80	50.5	40.7	22.3	17.9	20	466	29	3.1	1.7	71
34.4	25.6	17	431	35	57	56	110	104	64	58	1.9	1.8	120	110	112	90	33.5	27	17	426	36	3.1	2.2	60
23.9	22.7	17	398	28	75	74	100	95	68	63	1.5	1.4	91	85	58	45	24.8	19.3	17	407	28	3.6	2.4	63
22.3	21.6	21	499	26	76	75	94	91	54	51	1	1	109	108	78.3	56.57	22.6	16.4	21	488	26	3.2	1.9	71
36.9	28.9	17	375	38	67	66	111	101	63	60	1.9	1.8	153	133	143.3	103.8	35.7	25.8	18	378	38	5.1	3	66
25.2	18.7	16	401	26	82	81	115	101	72	70	1.4	1.2	65	50	58.5	43	18.7	25	16	407	26	2.9	2	59
20	15.8	19	498	29	68	67	96	94	51	48	1.3	1.1	99	92	52.18	41.49	17.3	13.7	19	499	31	4.5	2.5	76
31.4	22.3	22	476	28	63	62	121	117	55	52	1.3	1.2	121	91	89	85	31.9	24.1	22	478	28	2.9	2	59
29.4	22.9	18	436	28	69	62	120	113	72	63	1.2	1.1	117	105	100.38	81.94	34.1	27.8	18	472	28	2.7	1.4	80
22.6	16.7	12	343	31	104	98	169	152	87	76	1.4	1.2	62	52	56.77	36.13	18.7	12.2	13	348	30	3.1	1.9	74
25.8	24.6	18	375	29	85	83	114	110	55	53	1.5	1.3	127	116	99.26	75.71	28.1	21.4	18	382	28	4.4	2.6	73
35.5	24	17	371	28	67	66	112	109	67	64	1.8	1.7	143	125	104	99	34.7	30.4	18	372	30	6.6	3.8	74
27.9	22.4	17	379	28	53	52	114	109	68	65	1	0.9	104	101	85.17	63.98	27.2	20.5	17	380	27	3.1	1.8	72
20.9	19.1	15	376	27	68	67	111	108	59	55	1.4	1.3	95	90	66.48	56.92	22	18.8	15	378	28	4.3	2.5	73
21.9	19.9	28	382	28	81	80	117	115	79	77	1.3	1.2	76	66	48.83	48.1	20.1	20	28	386	27	3	1.7	70
24.7	22.3	21	396	30	62	59	114	103	61	54	1.4	1.3	86	73	65.95	64.2	24.1	23.5	21	390	30	3.9	2.3	69
22.8	19.7	18	432	29	98	97	98	96	66	61	1.5	1.4	94	91	75.39	66.28	23.3	20.5	18	430	29	3.7	2.1	73
23.9	22.7	18	465	29	51	49	106	104	64	63	1.6	1.5	91	86	58.5	45.73	24.8	19.3	18	464	29	3.6	2.4	63
22.1	21.7	18	434	30	45	44	140	139	78	75	1.5	1.4	98	92	82.02	70.48	22.7	19.5	18	437	30	4.6	2.6	74
27	23.2	19	456	32	58	57	114	108	68	67	1.8	1.8	99	83	76	73	25.3	24.3	19	456	32	5.1	3.2	67

Group 1: t0-baseline; t1-1 minute after PLR; t2 - 10 minutes after PLR ; max- maximum; min - minimum

slno	group	mrd	diagnosis	surgery	do.surgery	age	sex	wt	ht	bsa	t0.hr.max	t0.hr.min	t0.sbp.max	t0b.sbp.min	t0.dbp.max	t0.dbp.min
1	2	318692	cad, tvd, gdlv	cabg	15.03.2017	64	m	51.6	151	1.47	60	59	106	102	58	56
2	2	426388	cad, tvd, dm, htn	cabg	22.03.2017	51	m	62.5	167	1.702	74	73	135	131	64	59
3	2	426194	cad, tvd, old iwmi, dm, htn	cabg	28.03.2017	55	m	64.2	164	1.71	72	71	134	131	74	70
4	2	429783	cad, tvd, gdlv, nstemi, smoker	cabg	24.04.2017	65	m	57	166	1.622	55	54	109	103	56	46
5	2	428677	cad, tvd, gdlv, dm, htn, dlp	cabg	18.05.2017	43	m	67.8	170	1.79	66	65	109	104	64	59
6	2	431913	cad, tvd, ckd, t2dm, htn	cabg	24.05.2017	65	m	65	161	1.7	52	51	102	97	54	50
7	2	429453	cad, tvd, dlp, gdlv.htn, t2dm, lmca, mild pah	cabg	05.06.2017	65	m	54	149	1.49	58	57	140	129	71	64
8	2	432311	cad, tvd, lmca, gdlv, htn,t2dm	cabg	07.06.2017	55	m	72	159	1.78	70	69	95	93	69	65
9	2	431039	cad, tvd, dm, gdlv	cabg	12.06.2017	65	m	68	165	1.77	53	51	106	95	58	54
10	2	431281	cad, tvd, t2dm, htn	cabg	19.06.2017	65	m	75	171	1.887	66	65	109	106	64	63
11	2	433768	cad, lmca, gdlv, t2dm, dlp	cabg	20.06.2017	60	m	65	160	1.7	69	68	95	90	63	60
12	2	431909	cad, tvd, gdlv, dm, htn, smooker	cabg	21.06.2017	57	m	68	162	1.78	58	57	89	85	51	49
13	2	433044	cad, tvd, lmca, gdlv	cabg	22.06.2017	49	m	59	169	1.669	73	72	108	105	70	68
14	2	431901	cad, tvd, gdlv, dm, htn	cabg	23.06.2017	61	m	52	158	1.52	57	56	115	111	59	56
15	2	433026	cad, tvd, gdlv, dm	cabg	05.07.2017	55	m	82	181	2.03	62	61	107	102	61	58
16	2	433286	cad, lmca, gdlv, t2dm, dlp, old cva	cabg	17.07.2017	65	m	69	169	1.79	55	54	114	108	59	58
17	2	434616	cad, tvd, gdlv, htn, dlp	cabg	18.07.2017	64	m	104	173	2.235	49	47	123	120	67	66
18	2	433919	cad, nstemi, tvd, gdlv, dm	cabg	19.07.2017	58	m	92	178	2.132	61	60	126	121	72	70
19	2	433428	cad, dm, dlp	cabg	20.07.2017	54	m	71	155	1.748	65	64	98	94	61	58
20	2	9604222	cad, tvd, gdlv, htn, dlp	cabg	21.07.2017	65	m	56	161	1.582	42	41	100	90	52	48
21	2	434172	cad, tvd	cabg	25.07.2017	65	m	65	165	1.71	54	49	74	72	44	42
22	2	431393	cad, tvd, gdlv, htn, dm	cabg	02.08.2017	55	m	71	155	1.748	72	71	112	110	88	87
23	2	434612	cad, tvd, awmi, gdlv, dm	cabg	25.09.2017	57	m	73	164	1.823	70	69	88	87	53	52
24	2	436708	cad, tvd, gdlv, nstemi, smoker, htn	cabg	28.09.2017	65	m	52	159	1.515	60	59	110	102	58	55
25	2	9404205	cad, tvd, gdlv, tia, htn, dm	cabg	12.10.2017	65	m	68	169	1.786	54	53	111	107	63	62

Group 2: t0-baseline; t1-1 minute after PLR; t2 - 10 minutes after PLR; max- maximum; min - minimum

t0.svc.max	t0.svc.min	t0.lvedv.max	t0.lvedv.min	t0.sv.max	t0.sv.min	t0.vti.max	t0.vti.min	t0.lvot	t0.pip	t0.tv	t0.etco2	t1.hr.max	t1.hr.min	t1.sbp.max	t1.sbp.min	t1.dbp.max	t1.dbp.min	t1.svc.max	t1.svc.min	t1.lvedv.max	t1.lvedv.min	t1.sv.max	t1.sv.min
1.64	1.44	86	76	60	46	19.9	15.2	2	18	348	38	57	56	126	120	66	62	1.7	1.62	89	86	60	47
1.4	1.15	90	82	55	40	23.6	16.8	1.7	16	400	28	69	69	155	151	80	78	1.8	1.5	103	95	59	39
1.2	0.9	99	83	50	39	18.1	14.1	1.9	14	398	29	86	85	147	143	90	85	1.5	1.3	86	71	67	45
1.09	0.98	56	49	50	45	17.6	15.7	1.9	12	386	32	48	47	117	106	55	49	1.45	0.92	59	48	53	42
1.13	0.9	87	80	82	74	29	27	1.93	11	389	30	62	60	125	120	80	76	1.36	1.25	102	96	76	70
1.13	0.98	61	60	28	27	10.9	10.6	1.81	18	391	32	52	51	119	117	70	68	1.18	1.03	80	57	27	25
1.25	1.15	65	64	46	45	22.8	22.3	1.6	15	387	25	57	56	166	150	87	80	1.11	0.948	67	65	47	46
1.55	1.49	74	67	25	24	9.93	9.43	1.9	16	393	25	65	64	108	102	75	71	1.43	1.35	79	62	41	36
1.29	1.15	99	93	75	60	21.6	17.4	2.1	13	378	23	52	51	123	120	70	69	1.38	1.27	95	91	69	62
1.57	1.45	57	52	50	43	13.2	11.3	2.2	15	389	27	59	58	142	138	81	78	1.89	1.45	65	58	57	50
1.54	1.44	62	56	51	43	16.3	13.8	2	20	387	28	64	63	124	118	80	78	1.41	1.35	72	68	57	50
1.69	1.56	85	65	69	57	22.1	18.2	2	21	375	27	59	58	99	98	59	57	1.57	1.49	73	72	53	43
1.29	1.25	85	81	66	64	23.3	22.5	1.9	11	398	30	70	69	124	117	81	76	1.41	1.38	86	82	61	53
1.03	0.927	77	67	67	60	19.4	17.2	2.1	16	352	24	60	59	131	129	73	65	1.37	1.27	79	71	68	56
1.37	1.25	68	67	61	52	19.4	16.6	2	19	435	28	63	62	136	132	81	79	1.53	1.4	95	91	77	75
2.26	2	87	85	78	75	27.5	26.3	1.9	16	369	26	53	52	132	127	73	71	1.71	1.61	103	100	93	83
2.21	1.97	117	112	98	90	23.5	21.8	2.4	20	531	23	48	47	136	131	77	75	1.87	1.84	120	115	111	108
1.76	1.69	120	105	90	84	21.7	20.3	2.3	21	486	24	60	59	125	123	75	74	2.07	1.99	109	103	91	82
1.45	1.43	76	72	46	32	14.5	10.1	2	19	396	26	63	62	118	113	75	74	1.39	1.23	86	85	65	51
1.34	1.22	78	72	53	38	16.8	12	2	13	396	22	46	45	129	125	71	70	1.37	1.36	88	82	63	54
1.59	1.31	70	61	49	45	14.1	13	2.1	12	319	33	52	51	98	97	60	59	1.5	1.13	81	74	65	64
1.48	1.36	67	58	49	37	14.1	10.7	2.1	18	384	31	71	70	146	140	112	108	1.5	1.26	75	66	58	46
1.43	1.17	70	67	46	38	14.7	12	2	25	379	38	68	67	100	97	65	64	1.45	1.29	80	68	52	43
1.25	1.23	70	60	54	51	19	18.1	1.9	14	372	27	61	60	127	123	69	68	1.29	1.27	85	70	70	65
1.23	1.03	93	80	71	67	18.6	17.6	2.3	12	312	32	53	51	134	128	76	72	1.34	1.04	109	93	93	84

Group 2: t0-baseline; t1-1 minute after PLR; t2 - 10 minutes after PLR; max- maximum; min - minimum

t1.vti.max	t1.vti.min	t1.pip	t1.tv	t1.etco2	t2.hr.max	t2.hr.min	t2.sbp.max	t2.sbp.min	t2.dbp.max	t2.dbp.min	t2.svc.max	t2.svc.min	t2.lvedv.max	t2.lvedv.min	t2.sv.max	t2.sv.min	t2.vti.max	t2.vti.min	t2.pip	t2.tv	t2.etco2	lvidd	lvids	ef
20	15.8	19	392	40	58	57	116	115	62	60	1.6	1.51	99	92	52	41	17.3	13.7	19	392	40	2.6	1.79	67
25.4	16.8	18	403	31	66	65	142	137	69	65	1.7	1.5	88	78	54	40	23.4	17.6	17	399	31	3.6	2.4	61
18.3	13.5	15	400	30	82	81	136	132	84	80	1.2	1.1	77	74	62	50	20.2	12.7	15	389	31	3.39	2.14	68
18.8	14.9	12	389	35	46	45	108	102	54	50	1.29	1.03	63	54	31	30	12.5	12.4	12	390	35	2.6	1.79	67
26.9	24.8	11	378	30	62	61	126	122	80	77	1.03	0.89	100	92	83	78	29	27.5	11	392	29	3.48	2.02	70
12	11	18	389	25	51	50	112	110	62	60	1.39	1.25	57	56	27	26	10.5	10.3	18	390	24	3.05	2.37	71
23.2	22.9	14	390	25	57	55	147	141	78	75	1.36	1.25	76	74	38	36	24.7	23.7	14	392	25	2.54	1.29	66
14.5	12.6	16	396	25	64	63	105	101	75	72	1.38	1.27	74	64	31	27	10.9	9.34	17	399	25	2.59	1.93	65
22	19.8	13	387	22	50	49	117	115	69	68	1.44	1.35	92	90	62	57	22.8	16.4	13	389	22	3.39	2.16	67
14.9	13.1	15	390	30	63	62	126	120	74	66	1.87	1.75	63	62	56	48	14.7	12.7	17	378	27	2.92	2.02	63
18.3	15.8	20	392	29	67	66	126	120	83	75	1.44	1.36	64	59	59	42	20.7	14.7	21	378	31	3.25	2.07	67
17	13.6	22	398	27	59	58	99	97	58	57	1.64	1.59	80	79	54	46	17.3	14.5	22	381	29	2.72	1.89	65
24.2	20.7	11	385	32	69	68	111	108	68	67	1.47	1.39	84	80	73	67	25.8	23.7	11	379	31	2.18	1.21	78
19.7	16.2	16	332	23	56	55	134	130	75	69	1.47	1.35	80	76	57	55	16.5	16	18	343	24	3.12	1.54	83
24.4	24	19	440	28	64	63	130	128	75	72	1.54	1.45	86	84	68	63	21.6	20	16	433	27	2.5	1.13	87
29.6	26.5	16	368	27	51	50	131	130	73	72	1.75	1.71	98	86	83	64	29.4	22.7	16	371	27	3.14	1.48	85
24.6	24	20	521	23	48	47	131	129	76	75	2.09	1.97	121	101	109	104	24.1	23.1	21	541	22	4.01	2.23	76
23.9	21.7	21	486	23	60	59	129	128	79	75	2.07	2.06	108	103	93	92	22.3	22.2	19	488	22	3.66	2.11	74
20.7	16.2	19	316	25	62	61	110	108	71	70	1.49	1.31	83	81	52	51	16.5	16.2	19	324	22	2.42	1.64	62
20.2	17.1	13	390	22	44	42	122	119	64	63	1.27	1.15	76	72	50	46	15.8	14.5	12	376	21	3.41	1.94	75
20.6	20.5	12	320	33	54	53	99	98	63	60	1.92	1.51	73	70	56	49	19.8	17.2	12	314	32	4.23	2.57	70
16.7	13.3	18	382	31	69	68	142	139	107	105	1.61	1.27	86	71	80	65	23	18.8	19	380	30	3.25	2.07	67
16.5	13.6	25	375	36	73	71	116	113	73	72	1.43	1.41	78	74	51	39	16.1	12.3	24	385	40	3.39	2.14	68
24.5	23	14	370	27	65	63	125	121	70	65	1.5	1.45	88	72	76	71	26.9	24.9	14	383	28	3.52	2.01	75
22.4	20.3	15	260	34	53	51	137	134	78	76	1.45	1.39	99	90	80	73	18.9	17.6	15	332	31	3.25	1.75	79

Group 2: t0-baseline; t1-1 minute after PLR; t2 - 10 minutes after PLR; max- maximum; min - minimum

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INTRODUCTION Hemodynamic stability is one of the key concept of perioperative management in patients undergoing major surgical procedures like neurosurgery. Among the many methods the anesthesiologist target optimising intravascular volume to achieve hemodynamic stability. The clinical determination of the intravascular volume can be extremely difficult in those undergoing major surgery. This becomes more difficult if the patient has underlying cardiac disease like coronary artery disease.

The concept of fluid responsiveness attains relevance in maintaining optimal homeostasis, in the context that fluid loading is the first step in the resuscitation of hemodynamically unstable patients. Hypovolemia is a common complication encountered perioperatively in patients who undergo major surgery. In neurosurgical practice hypovolemia is compounded by the use of aggressive measures to reduce the raised intracranial pressure, e.g:- osmotic therapy using drugs like mannitol which induce a phase of hypervolemia, followed by hypovolemia or as in the case of uncompensated diuresis.

This pharmacologic cerebral decompression leads to volume loss with resultant fall in blood pressure and loss of neuro-autoregulatory mechanism which increases the risk of the dreaded complication of cerebral ischemia. Prior studies have proven that a careful fluid management strategy in patients undergoing neurologic surgery resulted in better outcome. It has been proven that the mainstay of management of hypovolemic patients is nevertheless intravenous fluids.

Hence, calculation of dosage parameters of intravenous fluids is of paramount importance. Inadequate volume replenishment leads to hypoperfusion of tissues and thereby worsens organ dysfunction which may be further compounded by uncorrected hypovolemia, resulting in the use of inappropriate infusions of vasopressor agents, thus worsening the viscous cycle of ischemia. However, fluid overloading also impedes oxygen delivery and compromise patient outcome especially in patients with associated cardiac dysfunction.

Overzealous fluid resuscitation results in increased rate of complications the most common being pulmonary edema and cardiac failure thereby resulting in poor outcome represented as increased duration of hospitalisation in ICU setting; and increased morbidity and mortality. Recent studies have put forth the concept of timely and aggressive resuscitation of critically ill patients which may limit and/or revert tissue hypoxia and thereby improve the outcome.

The landmark study by Rivers et al concluded that early goal-directed therapy driven protocols, will prevent organ dysfunction and improve overall survival rate in patients with severe sepsis and prevent subsequent septic shock. Likewise protocols which optimize the preload and resultant cardiac output improvement in

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