

DISSERTATION

Relationship of pulse pressure variation and stroke volume variation
with cardiac output changes during mechanical ventilation in
ASA 2 & 3 patients, undergoing major spine surgeries in prone position.



This dissertation is in partial fulfilment of the requirement for the
M.D. Degree (branch X) Anaesthesiology examination of
The Tamil Nadu Dr. M.G.R. Medical University, Chennai, to be
conducted in April 2015.

CERTIFICATE

This is to certify that this dissertation titled

“Relationship of pulse pressure variation and stroke volume variation with cardiac output changes during mechanical ventilation in ASA 2 & 3 patients, undergoing major spine surgeries in the prone position.” is an original research work done by **Dr.RAJASEKAR A** towards partial fulfillment of the requirements for the award of MD Anaesthesiology degree.

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January 14, 2014

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Sub: **Fluid Research grant project:**
Relationship of pulse pressure variation and stroke volume variation with
cardiac output changes during mechanical ventilation in ASA 2 & 3 patients,
undergoing major prone spine surgeries.
Dr. Rajasekar A, PG Registrar, Anaesthesiology, Dr. Georgene Singh,
Dr. Sajan Philip George, Anaesthesiology

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Dear Dr. Rajasekar. A,

I enclose the following documents:

1. Institutional Review Board approval
2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
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Dear Dr. Rajasekar. A,

The Institutional Review Board (IRB, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "Relationship of pulse pressure variation and stroke volume variation with cardiac output changes during mechanical ventilation in ASA 2 & 3 patients, undergoing major prone spine surgeries." on November 12th 2013.

The Committees reviewed the following documents:

1. IRB application format
2. Curriculum Vitae' of Dr. Rajasekar. A, Dr. Georgene Singh, , Sajan Philip George
3. Proforma
4. Consent form (English, Hindi, Tamil & Telugu)
5. Information sheet (English, Hindi, Tamil & Telugu)
6. Inter Department Consent letters
7. No of documents 1-6



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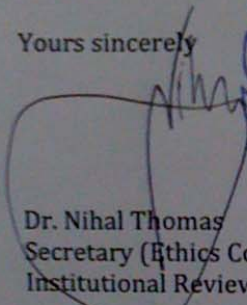
We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Policies.html in the CMC Intranet and in the CMC website link address: <http://www.cmch-vellore.edu/static/research/Index.html>.

Fluid Grant Allocation:

A sum of 77,500 INR (Rupees Seventy Seven Thousand Five Hundred only) will be granted for 2 years.

Yours sincerely


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ACKNOWLEDGEMENT

I express my sincere and heartfelt gratitude to Dr. Georgene Singh, for her encouragement, meticulous support and tremendous guidance during the study.

I express my sincere and heartfelt gratitude to Dr. Sajan Philip George, for his tremendous support and excellent assistance throughout the study.

I am thankful to Dr. Mary Korula, Professor and Head, Department of Anaesthesiology, Christian Medical College, Vellore for her support in conducting the study.

I am extremely grateful to My Colleagues and Anaesthesia Technicians for their help during the study.

I acknowledge the valuable help from Dr. Jeyaseelan, and Mrs. Kavitha, Department of Biostatistics for designing the study and for analysing the study results.

I am extremely grateful to all my patients who agreed to participate in this study.

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Abstract

TITLE OF THE ABSTRACT:

Relationship of Pulse Pressure Variation and Stroke Volume Variation with cardiac output changes during mechanical ventilation in ASA 2 & 3 patients, undergoing major spine surgeries in prone position.

DEPARTEMENT : ANAESTHESIOLOGY
NAME OF THE CANDIDATE : RAJASEKAR A
DEGREE AND SUBJECT : M.D., ANAESTHESIA
NAME OF THE GUIDE : DR.GEORGENE SINGH.

OBJECTIVES OF THE STUDY:

To determine the correlation between *Pulse Pressure Variation* and *Stroke Volume Variation* with *Cardiac Index* in ASA 2& 3 patients, during mechanical ventilation in patients undergoing major spine prone surgeries.

METHODS OF THE STUDY:

We conducted an observational study in 30 patients who underwent major spine surgeries in prone position, in *ASA class 2 and 3 patients* with either long-term Diabetes or Hypertension with possible *altered Arterial elastance*.

All the patients were given 10ml/kg of crystalloid before proning.

Baseline values of Cardiac Index (CI), Pulse Pressure Variation (PPV) and Stroke Volume Variation (SVV) were noted.

The changes in PPV and SVV *during (>20%) change in CI* was noted. Similar measurements were taken *after* correcting CI.

Data was analysed using the *Spearman's Rank Correlation Coefficient* between PPV and SVV and between PPV and Cardiac Index.

RESULTS AND CONCLUSION:

Out of 29 patients, 26 patients were ASA class 2 and three were ASA 3 patients.

We obtained a consistent statistically significant strong correlation between PPV and SVV (*correlation coefficient of $(r=0.87)$ and $(P<0.001)$*).

We found a consistent weakly negative correlation between PPV and CI with [*$r= (-0.21)$ and $[P (>0.3)]$*].

Though there was a *strong Clinical correlation* between CI and PPV, there was only a *weak statistical correlation*.

We conclude that PPV and SVV correlate with each other even in patients with *altered Arterial elastance* in the *prone position*.

Introduction

Anaesthetising patients requiring prone positioning demands incessant vigilance.

Numerous factors such as,

Physiological compensations as a consequence of positioning in prone,

Accompanying co-morbid pathological state and

The hemodynamic changes encountered throughout the surgery, warrants meticulous attention.

Addressing these issues altogether complicates patient management during the course of major prone surgeries.

Appropriate hemodynamic monitoring and evidencebased intravascular fluid replacement is of foremost importance for reducing morbidity and mortality associated with such major procedures.

Conventional Static measures such as Central Venous Pressure (CVP), Pulmonary Capillary Wedge Pressure (PCWP) are imprecise.

Recent evidences emphasize that inaccurate assessment of the fluid status is associated with undesirable consequence.

The Dynamic indicators depending on cardiorespiratory interaction such as Pulse Pressure Variation (PPV), Stroke Volume Variation (SVV),

Systolic Pressure Variation (SPV), Pleth Variability Index (PVI), Inferior and Superior Venacaval diameter and Aortic blood flow have consistently demonstrated their ability to accurately estimate the intravascular fluid status.

The objective of our study is to compare the reliability of alterations in pulse pressure variation with regard to the variation in stroke volume and cardiac index.

Even though, the capability of PPV and SVV to judge preload status during major spine procedures has previously been demonstrated, most of the studies have been done in the normal population and have assessed the response to volume loading by exposing the patient to a fixed dose of volume expanders.

Our concern is about patients with altered vascular compliance arising secondary to common diseases such as Diabetes, Hypertension, where either the disease process or the treatment of this disease is associated with impaired functioning of the autonomic system.

None of these studies address the acute significant hemodynamic fluctuations frequently encountered during the procedure in this subgroup of population.

Patients with longstanding Diabetes or Hypertension, the systemic vascular resistance are reduced and hence there is a theoretical probability that measures affected by arterial compliance (Pulse Pressure Variation [PPV]) are unreliable.

The aim is to discern whether PPV is reflective of the cardiac output even in patients with possible autonomic dysfunction as a consequence of either long-term Diabetes, Hypertension or their treatment.

Our emphasis is principally during occasions of sudden significant intraoperative hypotension.

Aims and Objectives

Aim: The aim of the study is to observe the trends in the Pulse pressure variation (PPV) and stroke volume variation (SVV) in relation to cardiac output changes in ASA 2 & 3 patients undergoing major spine surgeries in the prone position and to see if PPV correlates with SVV.

Objective : To determine the correlation between PPV (pulse pressure variation) & SVV (stroke volume variation) with cardiac output changes and to investigate whether PPV correlates with stroke volume variation in ASA 2& 3 patients for guiding intraoperative fluid and hemodynamic management , during mechanical ventilation in patients undergoing major spine surgeries in the prone position.

Review of literature

- Physiology of prone and its anaesthetic implications.
- Relative hypovolemia and Compensatory intravascular volume expansion.
- Quest for an ideal predictor
- Normal cardiopulmonary interaction
- Cardiopulmonary interactions during spontaneous ventilation.
- Cardiopulmonary Interaction during positive pressureventilation.
- Factors influencing the respiratory variations.
- Influence of hypovolemia.
- Pulse pressure changes during respiration.
- Systolic pressure variation.
- Stroke volume changes during respiration.
- Pleth variability index.
- Monitors to assess adequacy of tissue perfusion.
- Bedside assessment.
- Non dynamic measures /static measures.
- Invasive techniques.
- Non-invasive monitors.
- PICCO.
- LIDCO plus.
- FloTrac.
- PRAM (pressure recording analytical method).
- Descending Aortic Doppler.

- Echocardiography.
- Thoracic Bio-impedance.
- Bio-reactance.
- Pulse dye densitometry.
- The magnitude of the issue.
- Pathophysiology of HTN.
- Anaesthetic implications in hypertensive patients.
- Perioperative risks with Anti- hypertensives.
- Hypertension associated change in pulse pressure.
- Pathophysiology of DiabetesMellitus.
- Autonomic dysfunction.
- How our study is different from pre-existing similar studies.

Physiology of prone and its anaesthetic implications

Cardiovascular alterations:

Adopting prone position has multitude of effects in the cardiovascular physiology.

Reduction in the Systemic Vascular Resistance leads to a drop in CARDIAC INDEX.

The principal aetiology for fall in Cardiac Index on implementing prone posture is acute decline in STROKE VOLUME,

However alteration in the HEART RATE is unimportant.

The reduced stroke volume causes hypotension immediately on prone positioning the patient.

The reason postulated for this reduction is because of decreased preload, especially when the knees are below the level of thorax i.e. the knee chest position (when Relton Hall frame is applied).

Collective effect of Elevated Intrathoracic pressure (reduces effective arterial fill up), diminished preload and decline in LV compliance was also postulated.

Reduction in stroke volume evokes accelerated reflex sympathetic system hyperfunction.

Usage of modified Relton–Hall position is associated with a 17% decline in the cardiac index.

Reduction in the cardiac index occurs partly secondary to Inferior cava compression.

Modifications in the Respiratory system

Prone position has got a favourable impact on FRC when compared to supine position,

It is probably because of the improved contraction of the diaphragm and recruitment of collapsed alveoli.

The arterial oxygen tension is also improved in prone position.

The resistance offered by the compression of the chest wall has minimal influence on the airflow, since the airway resistance is unaltered.

Even though the chest wall compliance is reduced, the Static compliance an element which is a measure of combined chest wall and lung compliance is not altered significantly

In contrast to the common understanding, recent research suggested that the dorsal region of the lung receives enhanced pulmonary perfusion.

The ventilation is improved as the inter-pleural pressure difference is lower than in supine posture.

The favourable modification in the ventilation and perfusion provides improved oxygenation.

Compression injuries

Compression of peripheral nerves increases the incidence of peripheral nerve injuries.

The trachea can also get compressed.

Inappropriate positioning can lead to compression of the eye and development of grave complication of postoperative vision loss.

Unusual extension or rotation of the neck may compromise cerebral circulation

Prone position increases the possibility of air accumulation within the cranium.

Extreme flexion can cause undue stretch on the spinal cord.(1)

Since inadequate perfusion pressure has been implicated as a contributor to the most common (peripheral nerve injury) as well as infrequent devastating (POVL) injuries, accurate assessment of the adequacy of perfusion is obligatory.

In the recent years, development of improved measures in positioning precludes undesirable effects of abdominal compression.

Relative hypovolemia and Compensatory intravascular volume expansion (CIVE).

Use of anaesthetic agents induce vasodilation and thereby causes redistribution of the blood to the peripheral compartment, which leads to diminished venous return and reduced cardiac output. The reduction in cardiac output is also attributable to minimal myocardial depression by anaesthetic medications.

When the patient is positioned in prone, this relative hypovolemia is exaggerated.

So it is essential to preserve perfusion pressure by correcting the decreased preload, by administration of 5-7 ml/kg of balanced salt solution, before exposing the patient to prone position.

The infusion of fluids helps to maintain preload and hence the myocardium can operate at the optimal position in the Frank-Starling relationship.

Before subjecting the patient to fluid administration the cardiac and renal functional reserve of the patient to be ascertained to prevent hypervolemia.

Quest for an ideal predictor

To guarantee adequacy of oxygen delivery, precise estimation of cardiac output is imperative.

Prediction on volume status determined by static measures are imprecise half the time, Even when judged by the experts.(2)

Static measures - Central Venous Pressure (CVP), Pulmonary Capillary Wedge Pressure (PCWP) demonstrated imperfect correlation with response to volume loading.

Hence these measures were out-dated by variables, which determines preload state depending on the cardiopulmonary interactions termed as Dynamic indices(2), such as Pulse Pressure Variation (PPV), Stroke Volume Variation (SVV), Systolic Pressure Variation (SPV), Pleth Variability Index (PVI), Inferior and Superior venacaval diameter and Aortic blood flow.

Overzealous fluid administration, predisposes to perioperative complications and delay discharge.(3)

The challenges due to the surgical and patient related factors are worsened further by adopting unusual positions.

All these factors predispose them to untoward perioperative complications.

Normal cardiopulmonary interaction

Frank-Starling relation and the dynamic predictors :

Frank -Starling curve illustrates variations in Stroke Volume in relation to Left Ventricular preload.

The preload, contraction and afterload are inter-reliant as represented by the Frank-Starling curve.

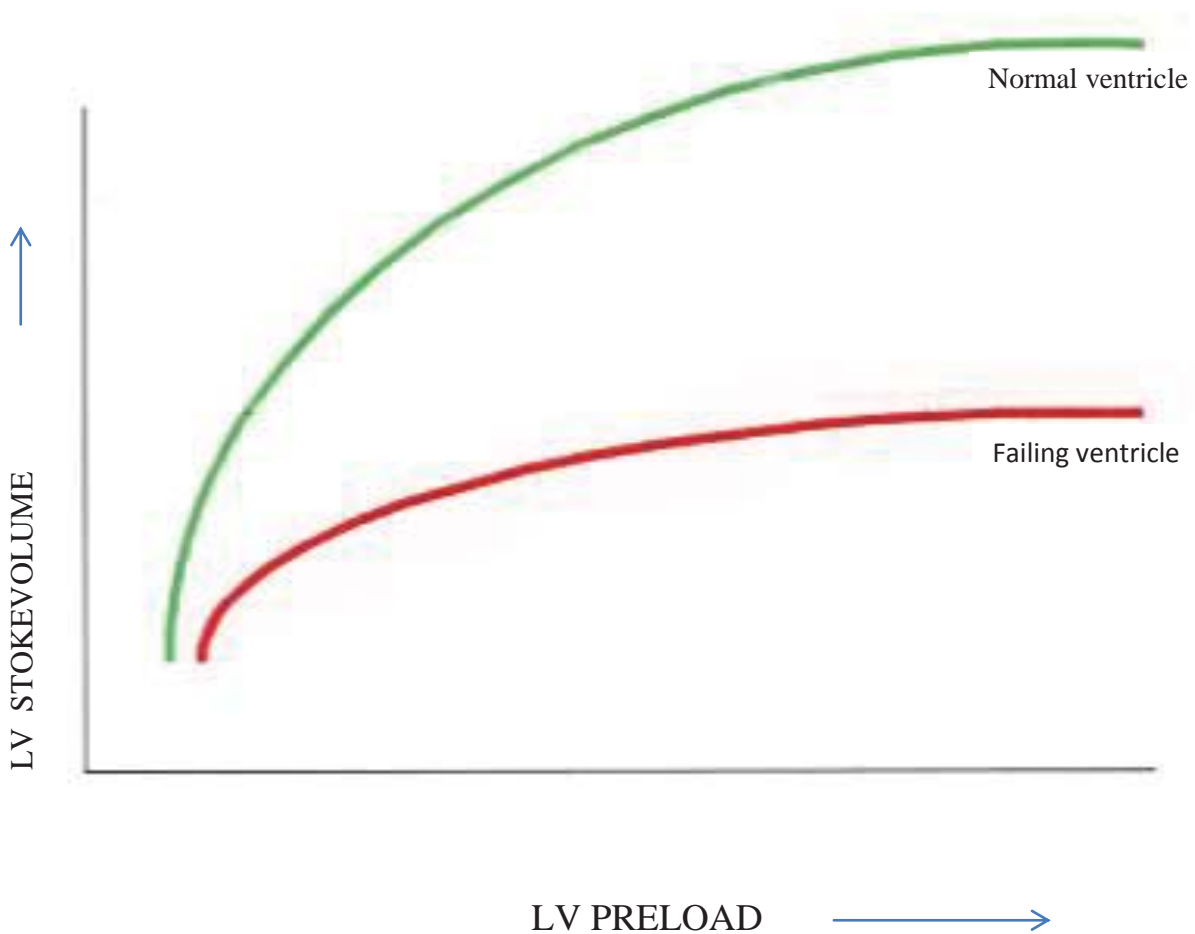


Fig.1.The frank starling left ventricular preload and stroke volume relationship curve.

The upper curve represents the normally contracting ventricle.

The lower curve signifies ventricle with impaired contraction.

Preload

The LVEDP (Left ventricular end diastolic pressure) specifies the volume of blood available in the left ventricle at end diastolic period.

Identifying the physiological state of preload, contraction and afterload during periods of hypotension, facilitate execution of suitable measures for the correction of the involved parameter.

Accurate diagnosis and prompt management based on clinical evidence will helpin the optimisation of perfusion pressure and will avoid the harmful effects of either under-filling or overloading or inappropriate use of vasoactive agents.

Cardiopulmonary interactions during spontaneous respiration

In a spontaneously breathing patient during the inspiratory phase, the venous return to the right chambers increases, because of the negative intrathoracic pressure.

Unlike spontaneous respiration, mechanical ventilation increases pleural pressure with inspiration and the relationship is reversed.

Cardiopulmonary Interaction during positive pressure ventilation:

While considering the impact of intrathoracic pressure on cardiac output in a patient who is subjected to mechanical ventilation, the changes are appreciated depending on the phase of cardiac cycle and on the phase of respiration.

The relationship is better understood by relating the changes in reference with the frank starling curve.

Impact of respiration on major vessels such as Venacava, pulmonary artery and aorta are interrelated.(4)

During inspiration, initially the blood flow in the central venous structures (Venacaval flow) decreases, which is followed by diminished pulmonary blood flow, later by aortic blood flow.

Gravity and the intra-alveolar pressure cause an uneven distribution of the pulmonary arterial blood throughout the lung.

This results in physiological partition of the pulmonary blood flow in an upright lung into three zones.

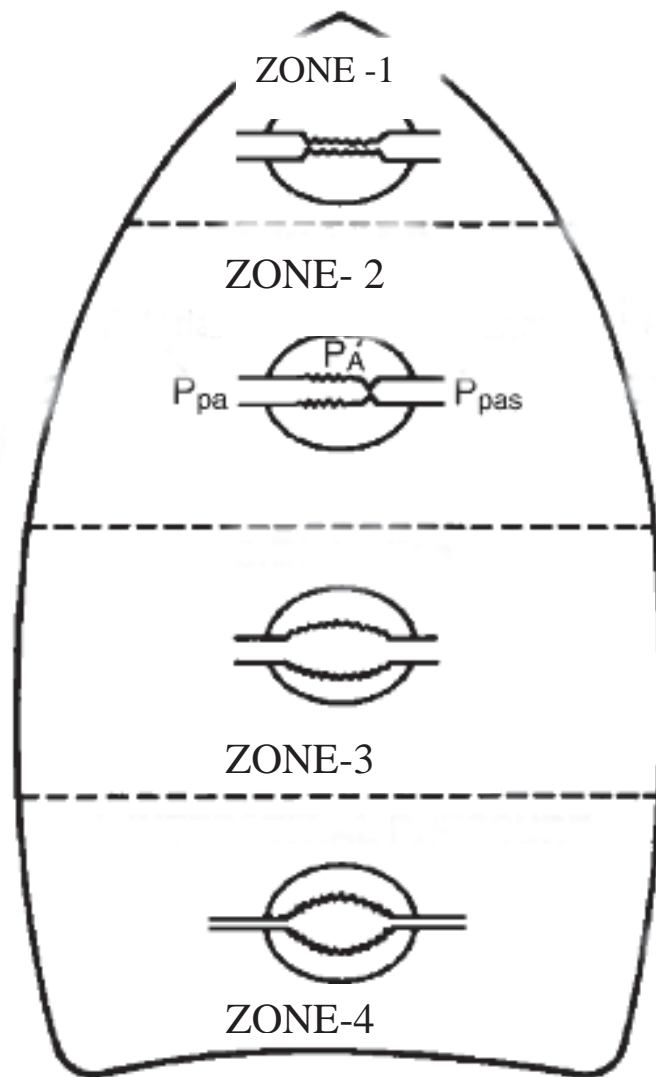


Fig.2. Schematic illustration of the zones of the lung.

Zone -1 is characterised by high alveolar pressure,

The pulmonary arterial pressure is higher than alveolar pressure in Zone -2,

In zone -3 both the pulmonary arterial and venous pressures are higher than alveolar pressure.

Inspiration causes increase in Zone 1 and 2 which arises as a result of elevated Right ventricular afterload, leading to reduced RV outflow, which in turn results in reduced Left ventricular filling.(4)

While on the other hand, due to the compression of the pulmonary vessels, the Left ventricular venous return increases subsequently the left ventricular stroke volume also increases.

But the Left ventricular afterload decreases on account of an increase in the pleural pressure.

Because of the influence of Zone 1 effect (alveolar pressure > pulmonary arterial), Left ventricular filling was augmented.

These normal changes will get exaggerated in hypovolemic state.(2)

The influence of reduced venous return to right heart will take a short while, to get revealed on Left ventricular stroke volume.

Owing to the time taken for the Right ventricular output (pulmonary blood flow) to reach Left ventricular preload.

It is generally perceived after few cardiac cycles manifesting in the expiration phase.

Factors influencing the respiratory variations(2)

Tidal volume,

Chest wall compliance,

Positive End Expiratory Pressure.

Also governed by the existing physiological status of the patient i.e. (the location of patient's hemodynamics on the Frank Starling curve).

Fluctuations in Heart rate variability may affect the respiratory changes.

Influence of hypovolemia

During hypovolemia all these alterations are exaggerated,

On account of the increased predisposition to collapse during hypovolemia,

Right atrium is more vulnerable for compression by the raising pleural pressure and increased distribution of zone 1 and 2.

When preload is less (hypovolemic circumstances),even marginal changes in preload causes substantial change in stroke volume.(4)

Pulse pressure changes during respiration

The alterations in the left ventricular output is the primary contributing factor for the changes in pulse pressure.(4)

Pulse pressure is predominantly regulated by stroke volume and the arterial compliance.

Once the ventricular preload and stroke volume are modified by positive pressure ventilation, it will be reflected in the pulse pressure as pulse pressure variation.

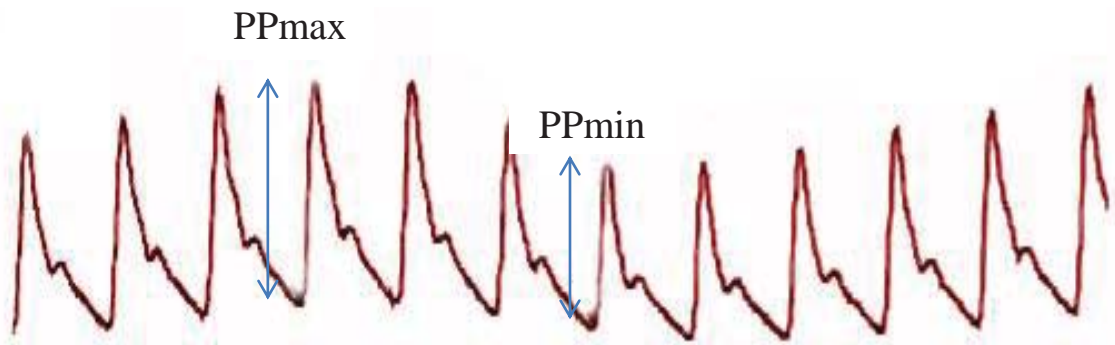
During mechanical ventilation, the inspiratory effects on right ventricular preload results in decrease of Pulse pressure during expiration, owing to the transit time taken by the Right ventricular stroke volume to reach Left ventricle.

The pulse pressure variation is calculated from the maximal pulse pressure (PPmax) during single respiratory cycle and the Minimal pulse pressure (PPmin) during the same respiratory cycle.

It is expressed as a percentage.

The pulse pressure variation is obtained from commonly obtainable arterial pressure transducer system.

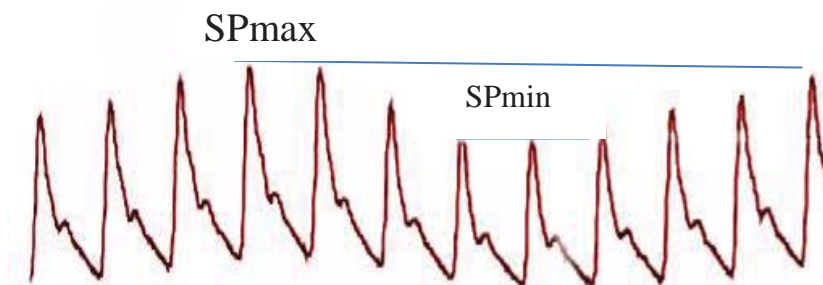
Calculation of PPV



$$PPV = \frac{(PPV \text{ max} - PPV \text{ min})}{\frac{1}{2} \times (PPV \text{ max} + PPV \text{ min})} \times 100$$

Systolic pressure variation

In mechanically ventilated patients, changes in the maximal and minimal systolic blood pressure can be used to compute the systolic pressure variation.



Stroke volume changes during respiration

Similar to the occurrence of Pulse Pressure Variation (PPV), fluctuations in stroke volume manifest as Stroke Volume Variation (SVV).

Stroke volume variation measures stroke volume of left ventricle by means of examination of the area under the arterial pressure curve over one respiratory cycle.

There is fundamental difference between the estimation of pulse pressure variation and Stroke volume variation.

To derive Stroke Volume Variation, specially designed minimally invasive monitors are required.

Compared to pulse pressure variation, the Stroke volume variation is a direct measure of stroke volume not influenced by arterial compliance, it should characterise the modification in cardiac output with respiration and better than PPV.(2)

Calculation of SVV

$$SVV = \frac{(SV \max - SV \min)}{\frac{1}{2} \times (SV \max + SV \min)} \times 100$$

Pleth Variability Index

Analogous to the pulse pressure variation phenomenon, the cardiopulmonary interactions induces changes in the amplitude of phlethysmographic wave.

The INFRA-RED rays are absorbed both by pulsatile (designated as AC) and non-pulsatile tissues (designated as DC).

The perfusion index (PI) is the percentage ratio estimated by the formula

$$(PI = [AC/DC] \times 100).$$

The perfusion index reflects pleth trace amplitude.

The Pleth Variability Index is calculated from the change in perfusion over an entire respiratory cycle.(5)

Evidence has found that PVI is a totally Non-Invasive, reliable means of assessing fluid responsiveness.(6)

$$PVI = \frac{(PI_{max} - PI_{min})}{PI_{max}} \times 100$$

Monitors to assess adequacy of tissue perfusion

Determining the preload dependency state in the vulnerable group of critically ill and those who are subjected to major surgeries associated with marked hemodynamic fluctuations such as massive haemorrhage and administration of vasoactive agents is a challenge.

Organ dysfunction can happen, either due to diminished tissue oxygenation, arising out of deficient intravascular volume or as a consequence of excessive extravascular fluid resulting from oedema due to surplus fluid administration.

Incorrect usage of vasopressor or inotrope in patients who are dependent on preload, in fact exacerbates the perfusion impairment.

Patients are considered fluid responsive when the myocardial stroke volume is improved by increasing the intravascular volume, in other words by influencing the preload.

Appropriate hemodynamic monitoring and management are indispensable for reducing morbidity and mortality.

Bedside assessment

Clinical valuation is inaccurate to conclude the requirement for fluid replacement. It is insensitive in the initial stages of hypovolemia.

Passive leg raising test

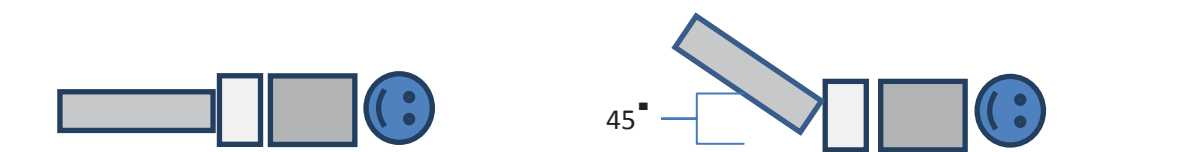
Redistribution of blood in the lower extremities to the central compartment, utilising patient's own blood enables us to estimate whether the patient is dependent on preload is a simple non-invasive method.

It can be performed in the bedside without the need for any additional equipment.

The recommendation is to raise the leg end by 45 degrees. Besides shift of blood from the legs it also causes blood present in the splanchnic circulation to enter the central compartment.(7)

Even in Septic patients Passive leg raising test has shown decent relationship.(7)

Although commonly applied in the intensive care setup, it has limited applicability in the intraoperative period since it can hinder the surgical process.



Non dynamic measures /static measures

Central venous pressure

Central venous pressure assessed during the termination of expiration denotes the right heart pressure, with the phlebostatic axis as the zero reference level.

Characterised by three positive (a, c and v) and two negative waves (x and y).

Presence of central venous catheter provides an access for sampling central venous oxygen saturation.

The sepsis guidelines recommend to consider both CVP and central venous oxygen saturation.(6)

Absolute numbers in CVP are obsolete, only the trend has been used in combination with other modalities.

Magder et al, stated that only 4.5% of the patients with CVP of over 10 mmHg responded to volume infusion .(8)

The conventional measures such as central venous pressure, arterial oxygen tension are imprecise.(9)

Current recommendation in the intensive care setup is to employ a combined approach involving both a non-invasive system alongside one of the downstream markers such as Base excess, Mixed venous oxygen tension, Serum lactate levels. etc.(9)

Invasive techniques

Until the availability of minimally invasive cardiac monitoring devices, cardiac output estimation with Swan-Ganz Pulmonary Artery Catheter (PAC) was considered the Gold Standard.

Pulmonary artery catheter

Flow directed positioning of the catheter enables us to measure pressures of right and left side of heart.

Ideally Pulmonary artery catheters should be positioned in zone 3 of lung.

Pulmonary artery catheterization allows measurement of a variety of hemodynamic parameters, such as cardiac output, mixed venous oxygen saturation and pulmonary artery diastolic and wedge pressure.

If the pulmonary vascular pressure is normal pulmonary arterial diastolic pressure indicates pulmonary capillary wedge pressure. In the absence of mitral valve disease pulmonary capillary wedge pressure reflects left atrial pressure.

We can also study the effect of vasopressors and inotropic therapy using PAC.

Sandham et al, showed reported higher frequency of nonfatal pulmonary embolism secondary to PAC.(10)

Recent studies identified that there is questionable improvement in the outcome with the use of Pulmonary Artery Catheter.(11)

Present role of invasive monitors

Even though the utilisation of Pulmonary Artery Catheters as a primary modality for cardiac output has decreased the Thermo-dilution technique using Pulmonary Artery Catheter is the reference standard against which minimally invasive Cardiac output devices are compared.

It is also helpful in calibrating and comparing the accuracy of various newer modalities.

Pulmonary Artery Catheters are indicated when there is a necessity for measuring the Pulmonary artery pressure and for sampling mixed venous blood.

The clinical application of Pulmonary artery catheter has declined significantly as the Risks outweigh the Benefits.

The nature and the incidence of complications favours selection of less invasive monitoring techniques.(11)

Non-invasive monitors

Minimally -invasive monitors are Categorized Depending on the principle they use for measuring cardiac output.

Thus the minimally-invasive cardiac output devices are classified as system devices operating on the principle of,

- Pulse contour analysis,
- Pulse Doppler technique,
- Bio-impedance / Bio-reactance,
- Applied Fick's principle.

Pulse contour analysis is further divided as

- Devices requiring calibration
- Un-calibrated devices.(11)

For accurate analysis a proper arterial waveform is mandatory.

PICCO

Estimates Stroke volume from the Area under the systolic portion of the arterial wave.

PICCO demands femoral arterial catheter which houses a thermistor at the tip.

For uninterrupted measurement of Stroke Volume (SV) it necessitates insertion of central venous line for calibration.(11)

The calibration is achieved by the way of Tran pulmonary thermo dilution.

In a stable patient calibrating every 8 hourly is sufficient, but in an unstable patient hourly calibration is crucial.

Calibration using trans-pulmonary dilution technique provides values for aortic impedance and systemic vascular resistance.

Even during periods of hemodynamic unsteadiness PICCO is accurate.(12)

Pulse contour analysis by PICCO precisely recognised volume responsiveness in Studies conducted in cardiac surgery patients.(13)

PICCO derives GEDV (global end-diastolic volume) which helps to discriminate acute respiratory distress syndrome from pulmonary oedema.(14)

Patients with lesser EVLW (extravascular lung water) showed superior survival.(15)

SVV was utilised for identifying fluid dependency state in bariatric surgery patients.(16)

LIDCO plus

LIDCO also operates on the same principle of PICCO.

It is based on the Law of conservation of Power.

Hence it is also referred as Pulse Power Analysis Technique.(11)

LIDCO is calibrated by Trans-pulmonary lithium dilution,where Lithium serves the role of indicator.

Usage of lithium for trans-pulmonary calibration facilitates estimating pulse power analysis instead of pulse contour analysis.

LIDCO doesn't warrant central major arterial line.

FloTrac

Marketed by Edward's life sciences

Requires Vigileo monitor.

Connected to peripheral arterial line and patients particulars such as age, sex, height and weight are entered.

It operates an algorithm which derives arterial compliance and Systemic vascular resistance by evaluating the pulse wave contour.

FloTrac estimates Cardiac output, Cardiac Index, Stroke volume (SVV)

Computes Cardiac Output every 20 seconds.

Uses privately owned transducers and exclusive unrevealed formula for computing.

Calculation of Systemic vascular resistance necessitates insertion of central line.

The advantage of FloTrac is it doesn't require external calibration.

Arterial pulsatility $CO = PR * SD (AP) * (X)$.

PR- Pulse Rate

SD (AP) – Standard Deviation of pressure wave over 20 seconds.

X constant which reflects patient's arterial compliance and Peripheral vascular resistance, which is upgraded every minute.(17)

X is calculated using individual patient's Age, Sex, Height, Shape of the wave and it estimates peripheral vascular resistance by means of the rate of rise of slope of the wave (The average variation in mean arterial pressure).

Derives SVV from arterial pressure waveform.

SVV derived from FloTrac has been shown to be moderately correlating with SVV derived from other Cardiac output monitoring devices.

Even though FloTrac derived SVV is not the gold standard, SVV was found to have the ability to predict fluid responsiveness, which is suitable in normal and hypodynamic circulatory state, but not in hyperdynamic state like septic shock which has major reduction in Systemic vascular resistance.

Comparing the accurateness of LIDCO, PICCO and FloTrac has found that LIDCO and PICCO are superior to FloTrac.(18)

PRAM (pressure recording analytical method)

Requires both arterial and central line Un-calibrated device calculates Stroke volume.

Insufficient evidence supporting its accuracy.(17)

Descending Aortic Doppler

By inserting an Oesophageal probe for quantifying descending aortic blood flow by Doppler assessment.(17)

Stroke volume is measured from Descending Aortic Cross Sectional Area acquired using M mode and Velocity time integral measured from the area under the flow Doppler curve as the stroke distance.

Probe Inserted 35cm into the oesophagus.(19)

Flow time is corrected to heart rate FTc.(19)

The cross sectional area of the descending aorta is computed using the M mode

Limitations:

Measurement of Stroke volume will not always reflect actual Stroke volume in hemodynamically unstable patient with disproportionate distribution of blood flow.(11)

Prone for frequent dislodgment.

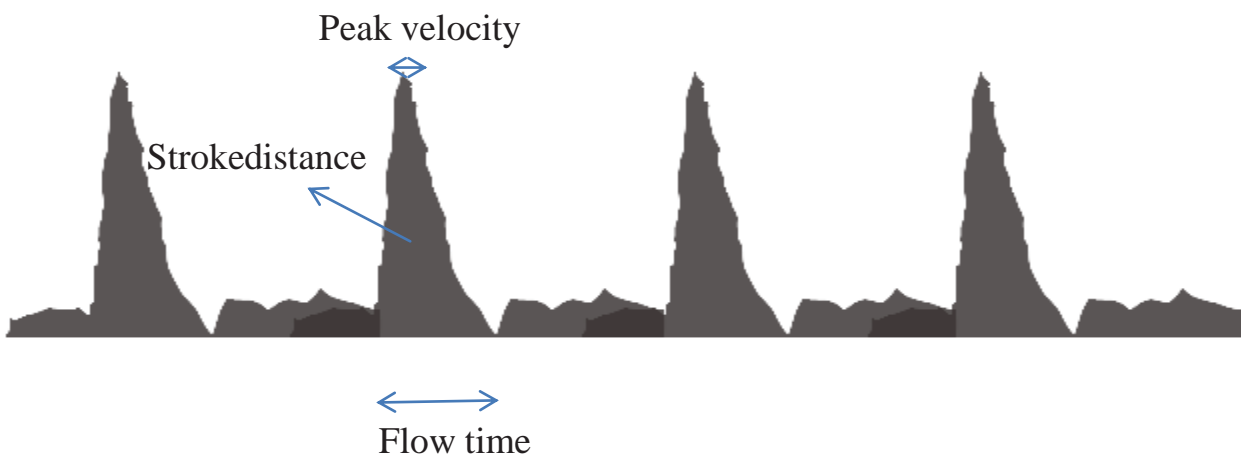


Fig.3. Oesophageal Doppler waveform.

Echocardiography

Fundamental principle is based Flow measurement

It also offers insights on various structural defects.

Info on Myocardial contraction,Valvular motion and Pericardial spaces.

Transthoracic echocardiography

Determining the Inferior Venacava diameter with reference to the respiratory phase gives an indication of preload condition of the right ventricle.

IVC diameter is measured using a 2-4 MHZ frequency curved probe.

The long axis of the IVC is visualised.

IVC Dimensions are taken during Inspiration and Expiration.

The diameter is measured 1 cm inferior to the confluence of Hepatic vein and IVC.

It is entirely non-invasive.

Under hypovolemic conditions the IVC appears narrow and displays exaggerated collapsing.

Nagdev et al, demonstrated that IVC index is a non-invasive measure of CVP.(20)

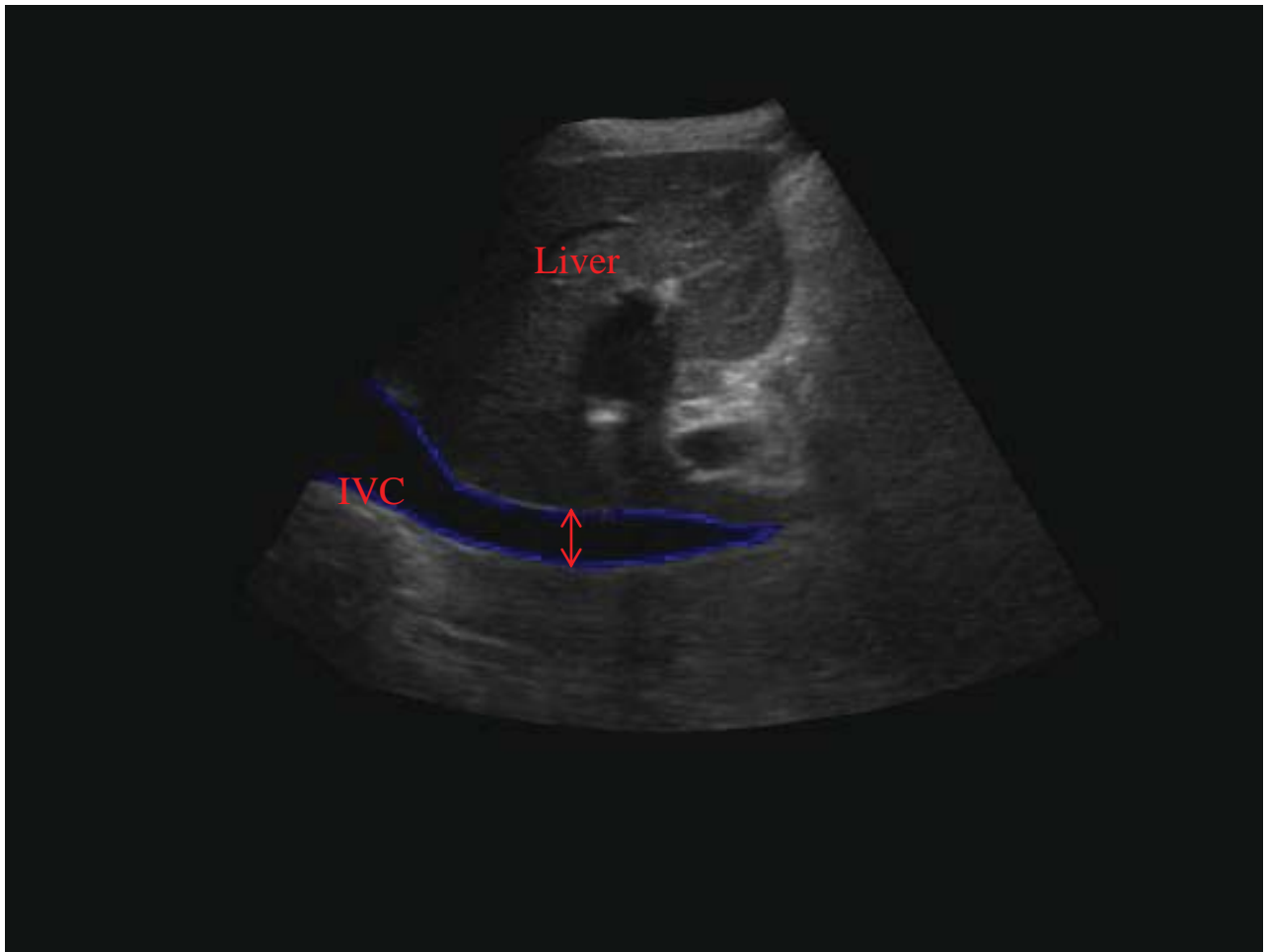


Fig.4. Transthoracically acquired image of the Inferior Venacava.

The IVC dimension is measured both during inspiration and expiration.

Transesophageal echocardiography

The Left ventricular end diastole area (LVEDA) in the Mid-Esophageal Transgastric short axis view is a dependable measure of left ventricular end diastolic volume.(21)

The SVC collapsibility is similar to the estimation of TTE IVC collapsibility.(22)

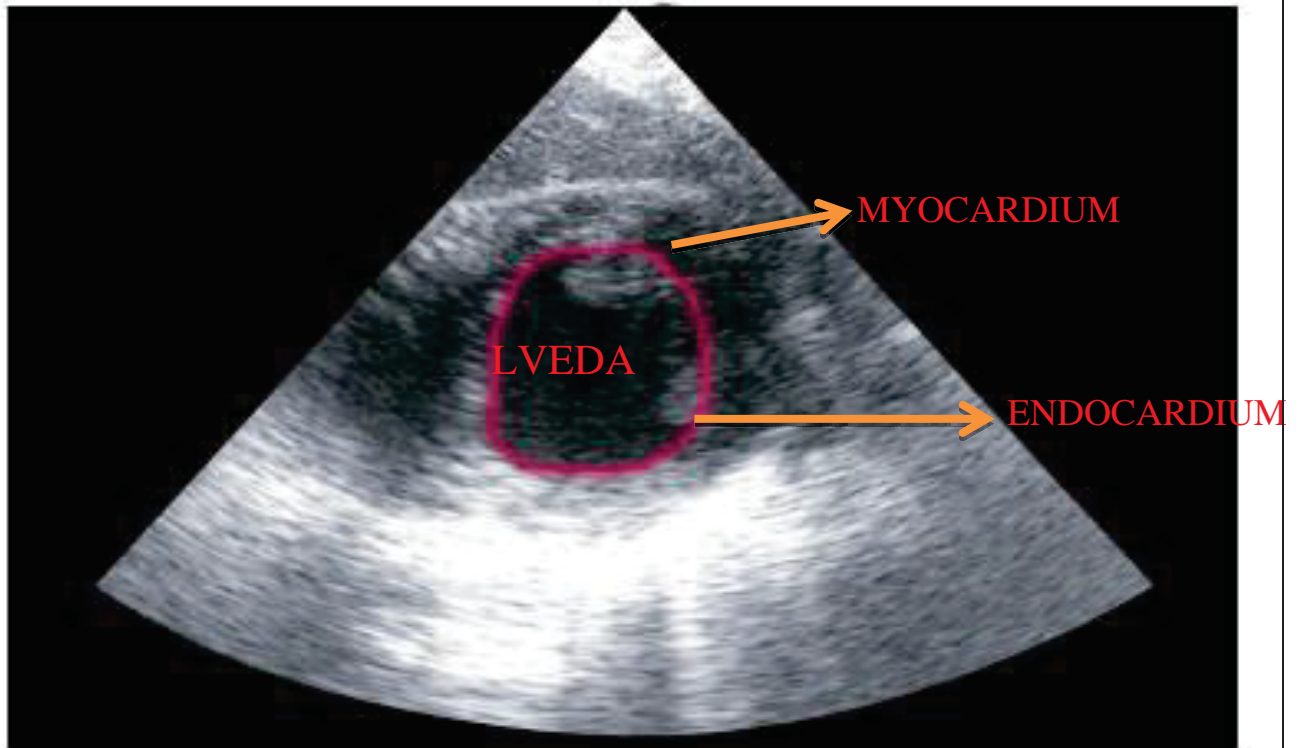


Fig.5.Mid Esophageal Transgastric short axis view during diastole.

LVEDA-Left ventricular end diastole area.

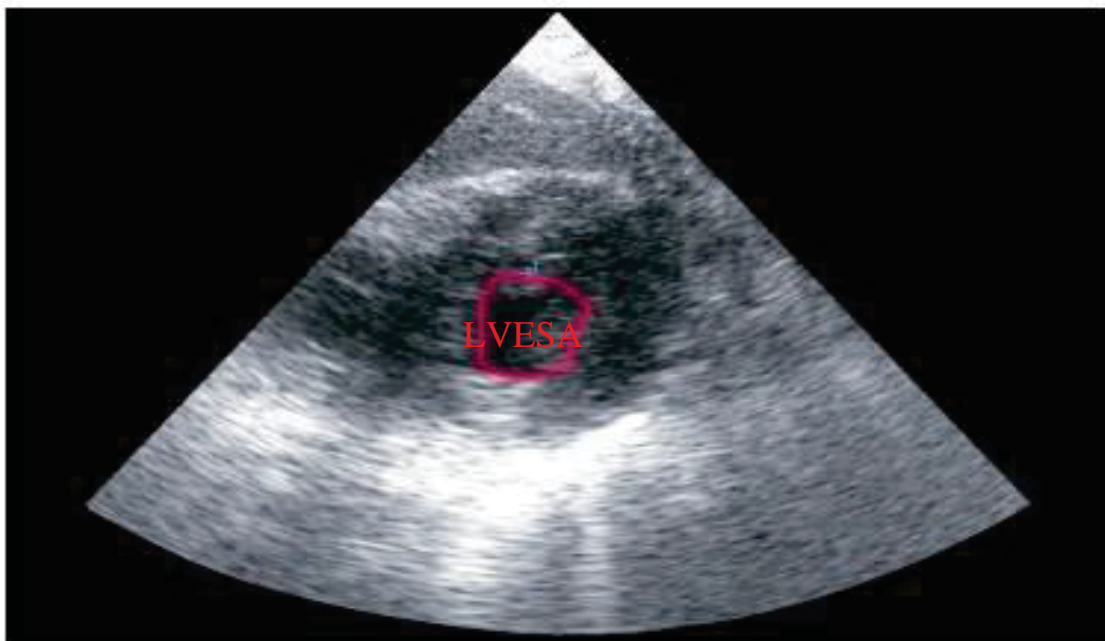


Fig.6.Mid Esophageal Transgastric short axis view during diastole.

LVESA -Left ventricular end systole area.

Derives Cardiac output from partial carbondi-oxide rebreathing technique

NICO (Nova metrix medical systems) comprises of rebreathing circle, Infra-red sensor for Carbondioxide measurement, an flow sensor and pulse oximeter.(18)

Artificially induces a state of partial rebreathing.

It determines cardiac output by subjecting the patient to a short duration of rebreathing,using Fick' principle yields cardiac output from the variation in End-tidal carbondioxide concentration and carbondioxide removal.(18)

But this method is inaccurate.(18)

Thoracic bio-impedance.

The impedance (Z_o) presented by the thorax to direct current depends on the quantity of fluid in the thorax.

The rate of change of impedance (dZ_o/dt_{max}) is considered to be related to aortic blood flow.(18)

The cardiac output is proportional to the speed of increase of (dZ_o/dt_{max}) and the duration of ejection.

But this method is inaccurate when there is too much of ambient noise,excessive extravascular lung water (EVLW) and during patient movement.(18)

BIO-REACTANCE

To overcome the constraints of Bio-impedance, Bio-reactance was introduced.

It employs the Resistor (R) and Capacitor (C) characteristic of the thorax.

NICOM Bio-reactance device , estimates the impedance (Z_o) from pulsatile flow of blood which causes alterations in Resistor (R) and Capacitor (C) generating phase shifts.

It is a totally Non-Invasive method.

Cardiac output obtained from Bio-reactance has got good correlation with the standard systems.(18)

Pulse dye densitometry

Performs intermittent Cardiac output measurement by means of Indigo-cyanine green dye.(11)

There is no single device suitable for different clinical settings and patient disorders.

Overzealous fluid administration predisposes to perioperative complications and delay discharge.

Recent studies identified that nearly half of the patients with hemodynamic instability are not responsive to volume expansion.

With superior understanding of pathophysiology of shock, it is recommended to accurately estimate cardiac output since measurement of stroke volume provides additional relevant information pertaining to the need for volume loading or indication for vasopressors.

Although the correctness of each discrete value is important, while assessing the reliability of Non-Invasive cardiac output devices the capability of the method to constantly sense the change

in the stroke volume and cardiac output before and after any intervention is considered more important.(18)

The magnitude of the issue

Both diabetes and hypertension are well recognised clinical predictors of adverse cardiovascular incidents.(23)

There is an uptrend in the incidence of Hypertension and diabetes with increasing prevalence. The Joint National Committee classification of hypertension which included pre hypertension state in the seventh report emphasising the impending raised cardiovascular jeopardy.

25% to 50% of patients undertaken for surgical procedure were on longstanding medicines, wherein Anti-hypertensives predominate. Which explains the magnitude of the problem and the frequency at which we encounter such patients for perioperative management?

The perioperative risks in hypertensives are determined by the presence of concurrent cardiovascular illness.

Undoubtedly patients with hypertension with end organ damage (Left ventricular hypertrophy or renal involvement) undergoing cardiovascular procedure are associated with adverse perioperative events like left ventricular dysfunction and renal failure.

Presence of Left Ventricular Hypertrophy raises this risk even in non-cardiac surgery.

Absence of accepted conclusive evidence regarding the continuation and discontinuation of different Anti-hypertensives increases the risk of perioperative adverse cardiovascular incidence.

Pathophysiology of HTN

In hypertensive patients pulse pressure is used as a prognosticator of mortality and morbidity.(24)

It has been proposed that vascular endothelial dysfunction is the primary pathology behind essential hypertension. (21)

The vascular endothelium is responsible for regulating normal vascular tone by means of modifying the release of vaso-active products.

Two major classes of Vaso-active agents were categorised as Endothelium dependent Relaxing Factor (EDRF) and Endothelium Independent Relaxing Factor.

Nitric oxide is the most important EDRF with major influence on the normal vascular tone.

Nitric oxide was implicated in the pathogenesis of Atherosclerosis. (21)

Hypertensive patients have endothelial dysfunction accompanying reduction in the production Nitric oxide and also with amplified destruction of Nitric oxide.

Untreated hypertension induced endothelial dysfunction results in diminished Vaso-dilatory response to Acetylcholine (Ach).(24)

HTN associated change in pulse pressure

Decreased Nitric oxide bioavailability is associated with increased vascular resistance and increased vascular tone because of the disproportion of vaso-dilatory and vaso-constrictory mediators.

Reduced Nitric oxide also leads to a pro-inflammatory state, hastened smooth muscle and fibroblast proliferation, accelerated platelet adhesiveness resulting in sclerotic vessels.

Pulse pressure is determined by stroke volume (ventricular ejection) and peripheral vessel stiffness.

Insufficient concentration of nitric oxide is attributed to widened pulse pressure.(24)

As the study by Ceravolo et al, in 262 hypertensive patients has shown that raised pulse pressure results in reduced forearm blood flow in untreated hypertensives.

Anaesthetic implications of Hypertension

Patients with pre-existing Hypertension are susceptible to significant hemodynamic fluctuations.

Hypertensives are vulnerable for adverse cardiac events.

Intubating a normal person produces a 20 -30 mmHg rise in systolic blood pressure, the heart rate rises by 15-20 beats per minute.

During the intraoperative period secondary to the effects of anesthetic agents, hypertensives exhibit more episodes of hypotension.

Once the anaesthetic agents are discontinued the blood pressure rises again.

Hence hypertensives are at risk of myocardial ischemia.

When compared to Non-hypertensives, the peri-operative risk is three folds higher.

The cerebral Auto-regulation curve is shifted to the right in patients with chronic arterial hypertension, Hence swings in blood pressure Compromise spinal cord perfusion and deteriorate neurologic outcome.

Careful pre-operative assessment and selection of best treatment can prevent marked hypotension or hypertension during anaesthesia.

The recommendation is to preserve the mean arterial pressure between 70-100% of the pre-anaesthetic value.

Perioperative risks with Anti- hypertensives

Regardless of the antihypertensive drug used Hypertensives on treatment are predisposed to intraoperative hypotension, secondary to constricted blood volume and concealed ventricular diastolic dysfunction. Besides these effects extended periods of fasting worsens hypotension.

Hypertensive patients getting beta blockers should continue the drug.

Recent meta-analysis in patients on calcium channel blockers has shown that calcium channel blockers have Reno-protective effects hence not discontinued during the perioperative period.(25)

But patients on either angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers have predilection for substantial hypotension current consensus is to withhold the morning dose of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers.(25)

Review of perioperative use of antihypertensive by Smith and Jackson propose that Patients on anti-hypertensive therapy are more susceptible to undue drop in blood pressure often observed with Angiotensin-converting enzyme (ACE) inhibitors , Angiotensin receptor blockers and calcium channel blockers, particularly those who are on di-hydropyridine group of drugs.(25)

Pathophysiology of DM

It is not surprising to find diabetes in the early forties with the current fast track lifestyle. Diabetes is one of the foremost aetiology of vasculopathy and rapid evolution of atherosclerosis as a consequence of Micro and Macro-angiopathy, We often encounter patients with concomitant hypertension adding fuel to the fire.

Hyperglycemia by formation of advanced Glycation end products and Ribosylation of PolyADP, increase the oxidative stress and free radical generation.(26)

Autonomic dysfunction

The oxygen derived free radicals leads to the development of neural damage and compromise neural blood supply eventually terminating in Autonomic neuropathy.

Chronic Hyperglycemia is implicated in the pathogenesis of Autonomic neuropathy, which in the preliminary phase is characterised by sympathetic over activity because of the loss of normal parasympathetic fibres activity resulting in resting tachycardia.

Diabetes is associated with dominant sympathetic activity during sleep and Nocturnal Hypertension resulting in increased occurrence of Left ventricular Hypertrophy.

The earliest manifestation of diabetic autonomic neuropathy is impaired Heart Rate Variation (HRV)(26)

Reduced Exercise tolerance occurs since they have attenuated cardiovascular responses to exercise due to the Autonomic dysfunction.

Myocardial Mitochondrial oxidative stress develops as sequelae of the disequilibrium between parasympathetic and sympathetic neurons.

Cardiac Autonomic Dysfunction (CAN) is responsible for failure to appreciate pain of myocardial ischemia (SILENT MI).

Cardiac Autonomic Neuropathy is involved in the increased incidence of perioperative adverse cardiac events.(26)

Surgery provokes a stress response resulting in augmented counter-regulatory hormones concentration and elevated serum glucose even in Non - diabetics, which is undesirable in diabetics.

Evidence indicates a strong association with Increase in morbidity and mortality arises as a consequence of both hypoglycaemia and hyperglycemia.

The objective is to minimize excessive fluctuations in serum glucose.

Patients often require insulin infusion for optimising the glucose concentration which necessitates close monitoring to prevent iatrogenic hypoglycaemia.

Perioperative Stress causes an upsurge in the serum level of stress hormones such Epinephrine, Nor-adrenaline, Glucagon, Cortisol, and Growth Hormone culminating in accelerated hepatic gluconeogenesis and reduced insulin-mediated glucose uptake (IMGU) in skeletal muscle which causes attenuated response to insulin.

How our study is different from pre-existing similar studies

Pulse pressure variation is dependent on the arterial compliance.

PPV is undependable in paediatric population which has been shown by several studies conducted in paediatric group.

The reason being reduced Arterial Elastance in children when related to an adult's Arterial Elastance.(27)

Former researches have convincingly proved the capability of PPV and SVV to evaluate the preload status during major spine procedures.

Most of the studies have experimented either in the normal population or in a population where patients with co-morbidities are part of the total sample.

All these studies have witnessed the response to volume loading by exposing the patient to a fixed dose of volume expanders.

Biais et al,(28) evaluated the ability of pulse pressure variations and stroke volume variations to predict fluid responsiveness in prone position during scoliosis surgery .

They subjected the patients to volume expansion (VE) with 500 ml of Hetastarch 6%] and in supine and prone position. Volume Responders exhibited a percentage increase in cardiac index at least by 15%.

Both PPV and SVV correlated with VE- induced changes in CO, but defined an greater threshold in prone posture (15%) compared to supine position threshold of 11%).(28)

By what means our study is dissimilar from pre-existing similar studies

- Exclusively ASA II and III.
- Major procedure in terms of the average duration and blood loss.
- Unpredictable abrupt hypotension.

Our concern is about patients with altered vascular compliance arising secondary to common diseases and the drugs which affect the regular function of the autonomic system.

Our emphasis is principally during occasions of sudden significant intraoperative hypotension.

In patients with longstanding Diabetes or Hypertension, the systemic vascular resistance is reduced and hence there is a theoretical probability that the measure affected by arterial compliance (Pulse Pressure Variation [PPV]) is unreliable.

Materials and methods

- Study Design and study population
- Study Setting
- objective
- Sample size calculation
- Anaesthesia protocol
- Premedication
- Pre-induction period
- Induction and maintenance
- Protocol
- Results
- Statistical analysis

Methods

Study Design:

With the authorisation of the IRB, we conducted a prospective observational study in adults with ASA (American Society of Anaesthesiologist) physical status 2 and 3 subjected to elective major spine procedures.

To ascertain , whether PPV correlates with cardiac output changes as a predictor of fluid status , fluid responsiveness and the need for inotropic / vasopressor support as compared to SVV when abrupt haemodynamic fluctuations which are observed during major spine surgeries.

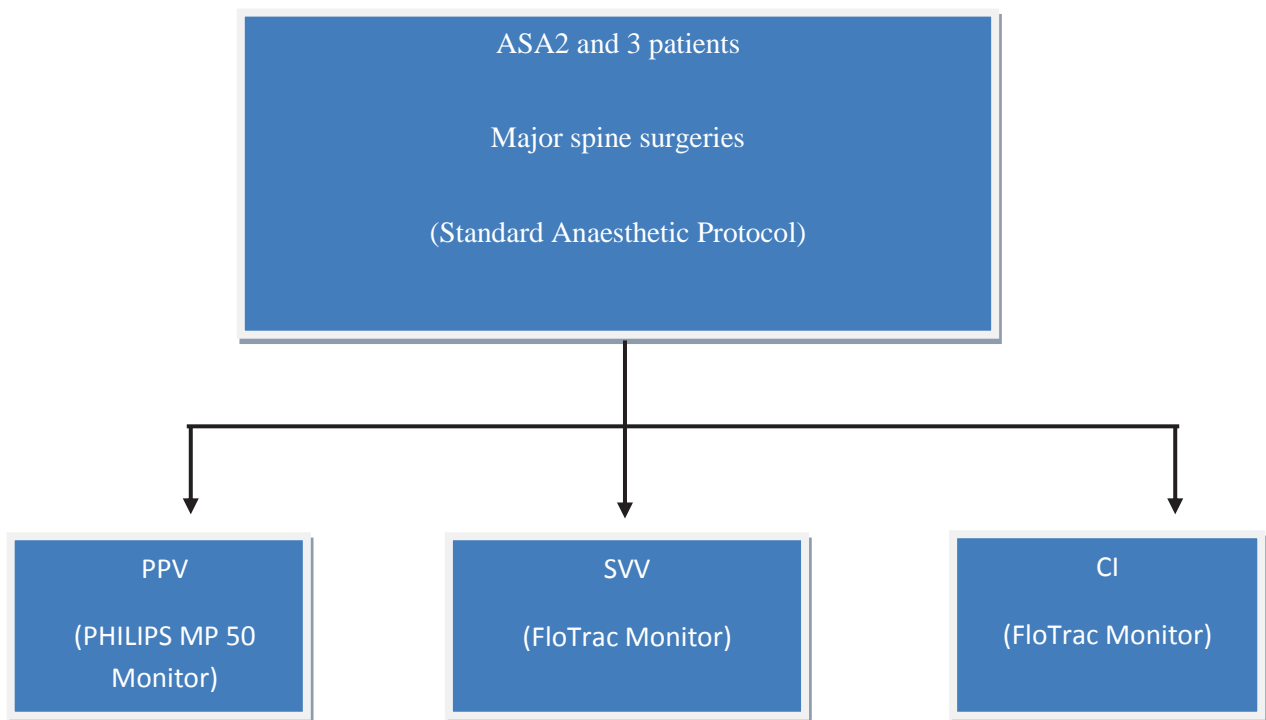
Our study is focused only on ASA 2& 3 patients (controlled or uncontrolled

Diabetics and Hypertensives and IHD (Ischemic heart disease patients with normal LV function.

Since the ability of PPV& SVV to predict the fluid responsiveness to fluid boluses has already been proved in ASA 1 patients.

Our patients either had long-term disease or recent onset disease on irregular medications and fluctuating serum glucose and blood pressures.

We have also included ischemic heart disease patients on several vasoactive drugs.



Analysis:

PPV vs. SVV

PPV vs SVV

Correlation between PPV and SVV with CI were studied.

Study Setting

We restricted this analysis to ASA 2 & 3 patients undergoing major spine surgeries

- Posterior Lumbar Interbody Fusion,(PLIF),
- Trans-foraminal Lumbar Intervertebral Fixation(TLIF) and
- Multilevel (>3) laminectomies with or without tumour excision and
- EPCD (extended posterior circumferential decompression).

Study population

Inclusion criteria :

- Age : > 18years < 70 yrs.
- ASA (American Society of Anaesthesiologists) 2 and 3 (Diabetics, Hypertensives and Ischaemic heart disease with normal left ventricular function)
- BMI: 18 – 40.

Exclusion criteria

- LV dysfunction / regional wall motion abnormality.
- ASA-1/4/5 patients.
- Valvular heart diseases or arrhythmias /conduction abnormalities.
- Chronic Obstructive Lung Disease Patients.
- Emergency Surgeries
- Inabilities of the patient to understand for giving the consult.

Sample size calculation:

- Biais et al, (2010) have reported that significant correlation between Pulse pressure variation (PPV) and Cardiac output (CO) in prone position was (0.77).
- However, we expected a poor correlation in Diabetes and HT patients.
- Hence we estimated the size with the correlation of around (0.4) to (0.5). We Kept the Alpha and Beta errors at 5% and 20% respectively; hence we have studied 30 subjects.

Table: 1 Calculation of the sample size

Regression methods-Sample size for correlation coefficient analysis (Testing against population value)			
Sample correlation coefficient	0.4	0.5	0.3
Population correlation coefficient	0	0	0
Power(1-beta)%	80	80	80
Alpha Error (%)	5	5	5
1 or 2 Sided	2	2	2
Required sample size	47	29	85

Anaesthesia protocol

30 patients in the age group of (40 to 70 yrs.) who suffered either from diabetes or hypertension or both were recruited.

Procedure

We described about the benefits and disadvantages related to arterial cannulation, to

Every single patients and a written consent was obtained.

All our patients received a uniform premedication of Diazepam (5 -10 mg).

Standard hemodynamic monitors such as Electrocardiogram, No- invasive blood pressure, Pulse-oximetry were applied).

The study involved insertion of a 20 G arterial cannula in the Radial artery for observing the changes in PPV, SVV and cardiac output.

The transducer was sited at the level of phlebostatic axis.

Pulse pressure variation (PPV) was obtained from the Phillips Intellivue MP50

Module incorporated into the Phillips Monitor).



Fig.7 Photograph of Phillips Intellivue MP50 for PPV measurement.

Stroke volume variation (SVV) and cardiac index(CI) were derived from the minimally invasive cardiac output module - FloTrac transducer system, Vigileo, Edwards Life Sciences)



Fig.8 The FloTracVigileo monitor for deriving Stroke volume variation and Cardiac index.

Anaesthesia was induced using (Fentanyl 1-2 mcg/kg, propofol 2-3 mg/kg,

Vecuronium 1.5mg/kg and maintained with intermittent doses of Vecuronium.

The End-tidal Isoflurane was maintained between of (0.8-1).

Ventilation was controlled with a tidal volume of 8ml/kg to maintain ETCO₂(End tidal Carbondioxide) of 35- 40 mmHg at Fractional Inspired Oxygen of 40%.

All patients were pre-emptively given a Crystalloid bolus of 10ml/kg before turning to prone to counteract the relative hypovolemia induced by prone position.

Analgesia provided with additional dose of fentanyl, Paracetamol and Morphine up to 0.1 mg/kg. Morphine was given after prone positioning.

A baseline, Heart rate, Systolic Blood Pressure (SBP), Mean Blood Pressure (MBP), Diastolic Blood Pressure (DBP), Pulse Pressure Variation (PPV), Stroke volume variation (SVV), cardiac output (CO), cardiac index (CI) and Pulmonary compliance were recorded in supine position after intubation.

Similar sets of readings were obtained with the patient in prone position, which was considered as the baseline for our study.

Any incident of significant hemodynamic alteration (20% from baseline cardiac index and mean arterial pressure) throughout the entire course of the surgery and the Pressure Variation (PPV), stroke volume variation (SVV) during such occasion were noted.

The event was treated appropriately with the administration of either fluids or vasoactive agents depending on the clinical correlation, the values of cardiac index and mean arterial pressure, Pressure Variation (PPV) and stroke volumes (SVV) were noted after the treatment.

Our aim was to assess whether PPV predicts the changes in cardiac output at the same time as SVV does and whether PPV is as reliable as SVV in prone position.

Results

We enrolled 30 patients, because of technical error; we could not acquire data for one of the patient which we have excluded.

Out of 29 patients, 26 patients belong to ASA class 2 and three were ASA class 3 patients.

More than 50% of our patients belong to the age group of 50 to 60 years.

In our study females predominated the sample.

Majority of the procedures involved lumbar spine of which posterior lumbar inter-body fusion was the most common procedure.

Nearly 90% of the procedures were performed using Relton-Hall support.

Over 80% of our patients were hypertensives, while more than 50% were diabetics.

25% of our patients were on ACE inhibitors.

All our patients received gradual volume expansion with 10ml per kg of crystalloid solution (Ringer Lactate), to compensate for relative hypovolemia.

Invariably all the required administration of vasopressors (phenylephrine and, or ephedrine) for treating the hypotension accompanying prone position.

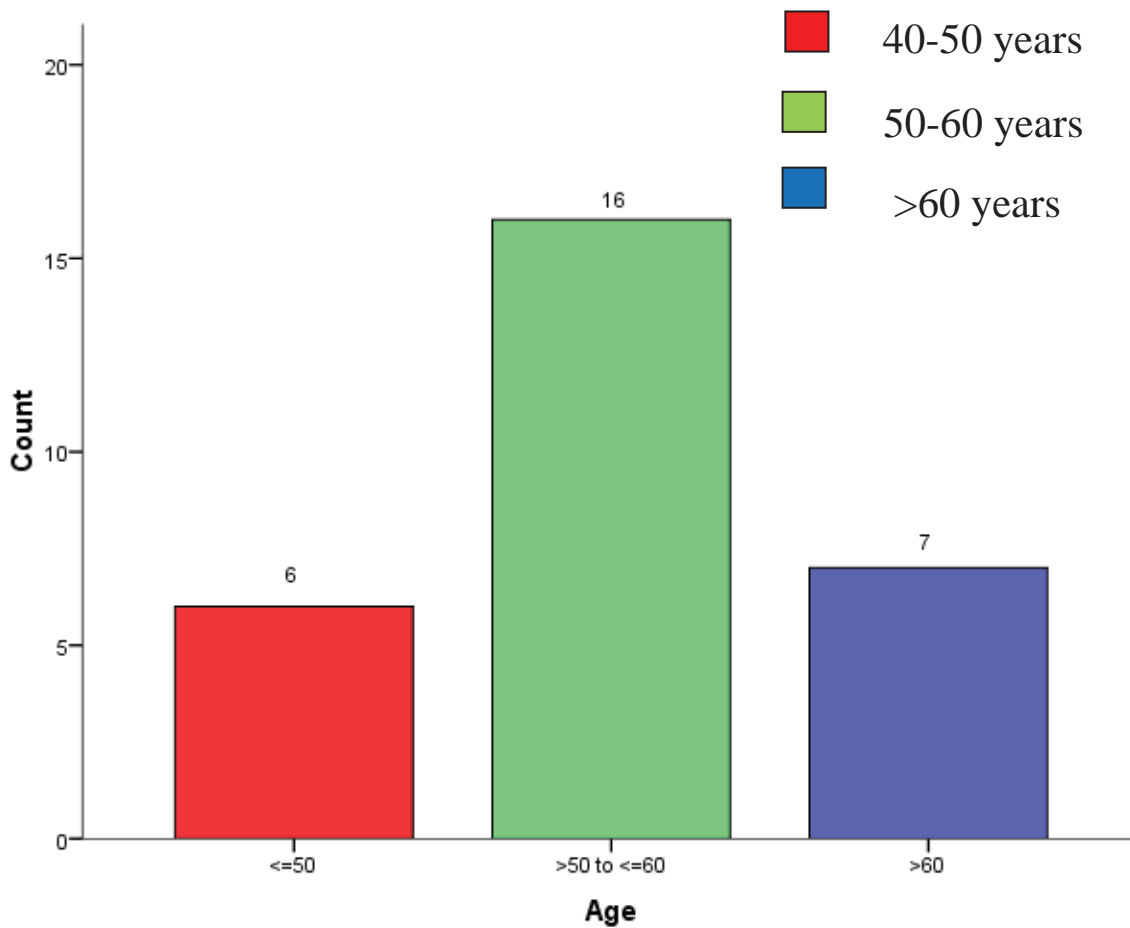


Fig.9. Bar chart expressing the age distribution of our study population

Age in years along the horizontal axis.

Number of persons along vertical axis.

Table: 2. Distribution of the Gender in our study.

Sex	Number of patients
Male	11
Female	18

Table: 3 Distribution of the co-morbid diseases.

Co-morbidity	Number of patients
Hypertension	24
Diabetes mellitus	15
Ischemic Heart Disease (IHD)	3
Obesity	3
Hypothyroid	4
Both Diabetes mellitus and Hypertension	10
Multiple Co-morbidities	15

Table: 4 Type of diabetic medication taken by our study population

Diabetic medication	Number of patients
Insulin	4
Oral Hypo-glycaemic Agents	13

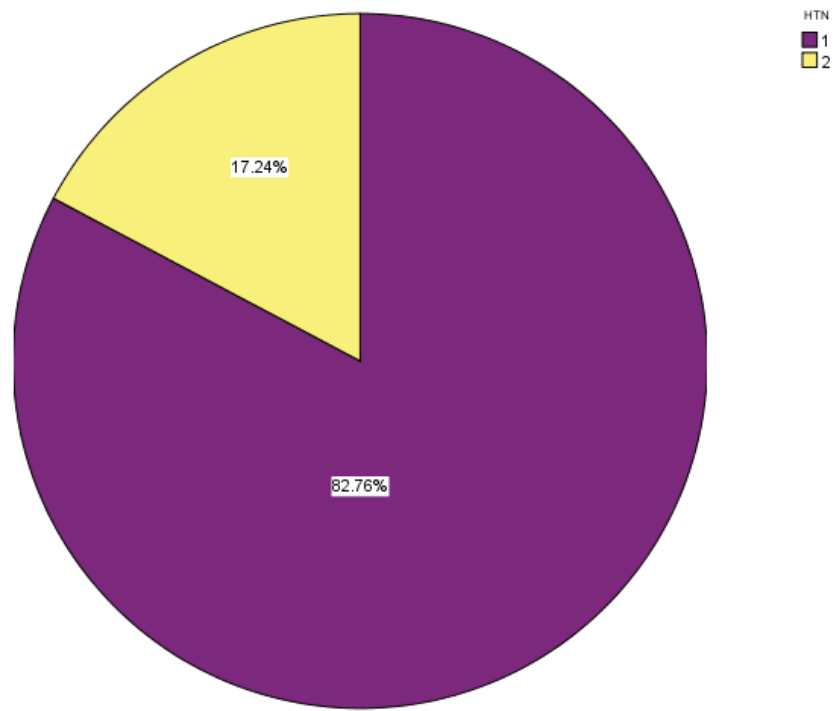


Fig.10 Pie diagram displaying the percentage of Hypertensives in our study population.

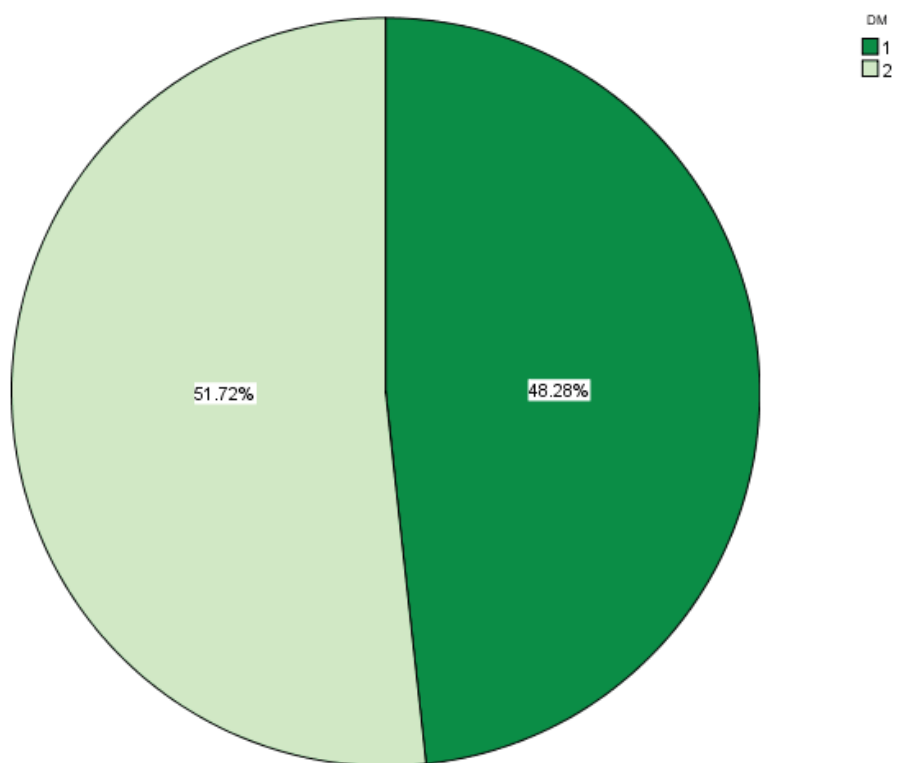


Fig.11 Pie diagram displaying the percentage of Diabetics in our study population.

Table: 5 Type of Surgical procedures performed in our study.

Location the surgical site	Number of patients
Cervical	4
Thoracic	3
Lumbar	22

Table: 6 Type of patient support utilised in our study.

Type of support	Number of patients
Relton–Hall position	26
Foam bolster support	3

Table:7 Description of the study characteristics. Expressed in terms of mean and the range.

Characteristics	Values Mean(Range)
Age	56.4 (42-70)
Sex (male/female)	11/18
ASA classification (II/III) (number)	26/3
Anaesthesia duration (minutes)	226 (120-330)
Blood loss (millilitres)	667 (150-2000)
Levels operated (number)	2.5 (2-6)

Table: 8 Particulars of individual patients

Serial no:	AGE	SEX	COMORBIDITY	CO-MOB (YEARS)	DRUG	ANAESTHESIS A DURATION	SURGERY	BLOOD LOSS(ml)	SUPPORT	EVENT OF SIGNIFICANCE
1	55	F	Hypertension Diabetes	10 10	AMLODIPINE INSULIN	3.5	PLIF	150	RH	REQUIRED NOR ADRENALIN
2	54	F	Hypertension Diabetes	10 10	RAMIPRIL INSULIN GLYCIPHAGE	4	D11-D12 EPCD	200 0	RH	REQUIRED BLOOD TRANSF
3	42	F	Hypertension Diabetes	3	NICARDIAPINE DIURETICS	5.5	PLIF	100 0	RH	
4	58	M	Hypertension Hypothyroid	4	AMLODIPINE THYROX	4	L2 EPCD	180 0	RH	REQUIRED BLOOD TRANSF
5	56		Hypertension	5	AMLODIPINE ATENOLOL	4	PLIF	150	RH	REQUIRED NOR ADRENALIN
6	62	M	Hypertension	10	OLMESARTAN AMLODIPINE	2.5	PLIF	300	RH	
7	48	F	Hypertension Diabetes	2	GLYCIPHAGE AMLODIPINE	4.5	PLIF	100 0	RH	ON IRREGULAR MEDICATIONS
8	57	F	Hypertension	10	LOSARTAN HYDROTHIAZIDE	5.5	D12-L1 EPCD	200 0	RH	REQUIRED BLOOD TRANS
9	49	F	Diabetes	5	GLYCOMET GLIMIPIRIDE	3.5	PLIF	300	RH	
10	60	F	Diabetes	10	GLYCIPHAGE	2	L4-L5 DECOM	150	RH	NO SIGNIFICANT HEMODYNAMIC CHANGE

Table: 8Patient's particulars continued

Serial no:	AGE	SEX	COMORBIDITY	CO-MOB (YEARS)	DRUG	ANAESTHESIA DURATION	SURGERY	BLOOD LOSS(ml)	SUPPORT	EVENT OF SIGNIFICANCE
11	67	M	DIABETES	5	OHA	5.5	L2-L5 FUSION	1100	RH	ON IRREGULAR MEDICATION
12	57	F	HYPERTENSION HYPOTHYROID	10	LOSARTAN AMLODIPINE THYROXINE	4	PLIF	400	RH	NO SIGNIFICANT HEMODYNAMIC CHANGE
13	70	M	HYPERTENSION DIABETES	RECENT 30YRS	AMLODIPINE OHA	4.5	PLIF	300	RH	NO SIGNIFICANT HEMODYNAMIC CHANGE
14	59	M	IHD	20	RAMIPRIL BETA BLOC NITRATES	4	C3-C6 LAMNECTOMY	1500	RH	REQUIRED BLOOD TRANSF
15	LOSS OF DATA									
16	51	M	IHD HYPERTENSION DIABETES HYPOTHYROID	RECENT 2 >10	ENALAPRIL OHA THYROX	5	D5-D8 FUSION	700	RH	REQUIRED NOR ADRENALIN
17	55	M	IHD HYPERTENSION DIABETES OBESE	3YRS	RAMIPRIL CARVIDILOL GLIMIPRIDE ALDACTONE TORSEMIDE	5	L1-L5 LAMINECTOMY	1000	RH	REQUIRED NOR ADRENALIN
18	70	F	HYPERTENSION HYPOTHYROID	20	ATENOLOL THYROXINE	3.5	PLIF	700	PILLOWS	REQUIRED NOR ADRENALIN
19	52	F	HYPERTENSION DIABETES OBESE	4	ARB INSULIN	2	PLIF	200	RH	
20	50	M	DIABETES	4	METFORMIN GLIMIPRIDE	3.5	PLIF	400	RH	

Table: 8 Patient's particulars continued

Serial	AGE	SEX	COMORBIDIT	CO-MOB (YEARS)	DRUG	ANAESTHESIS ADAPTATION	SURGERY	BLOOD LOSS(ml)	SUPPORT	EVENT OF SIGNIFICAN CE
21	53	M	HYPERTENSION DIABETES	5	ATENOLOL INSULIN METFORMIN	3	C3-C6 LAMINECTOMY	300	PILLOW S	REQUIRED NOR ADRENALIN
22	69	F	HYPERTENSION	15	LOSARTAN HYDROTHIAZID E	2.5	L4-S1 DECOMPRESSIO N	150	RH	
23	47	F	HYPERTENSION OBESE	RECENT	AMLODIPINE	4.5	L5-S1 TLIF	750	PILLOW S	ON IRREGULAR MEDICATION
24	52	F	HYPERTENSION DIABETES	10	LOSARTAN OHA	4	PLIF	400	RH	
25	69	F	HYPERTENSION	15	LOSARTAN HYDROTHIAZID E NEBIVIOL	3.5	PLIF	400	RH	NO SIGNIFICANT HEMODYNAMI C CHANGE
26	55	M	HYPERTENSION	20	AMLODIPINE	3	C3-C6 LAMINECTOMY	500	RH	
27	64	F	HYPERTENSION DIABETES	RECENT 2	AMLOPIDINE GLYCIPHAGE	4.5	L4-L5 PLIF	120 0	RH	
28	41	F	HYPERTENSION	2	ATENOLOL AMLODIPINE	4	L5-S1 PLIF	100	RH	NO SIGNIFICANT HEMODYNAMI C CHANGE
29	58	F	HYPERTENSION	2	TELMISARTAN	4	L1-L2 PLIF	150	RH	
30	56	M	HYPERTENSION	3	AMLODIPINE	4.5	C3-C6 LAMINECTOMY	200	RH	

Statistical Methods

Mean and Standard Deviation, Median and Percentiles were provided for all the continuous variables and frequencies and percentages for categorical variables. However, Histogram and Box plots were done for continuous variables to study the distribution.

The outcome variables were compared between pre and post measurements using Paired t-test, if they are normally distributed.

For variables which were not normally distributed Wilcoxon Signed Rank Test was used to compare the medians between pre post measurements.

The correlation between variables was quantified using Pearson's product moment correlation coefficient, for normally distributed data and using Spearman's Rank Correlation Coefficient, for non-normal outcomes.

P-values below 0.05 are considered statistically significant.

All statistical analysis was done using SPSS 18.0.

Interpretation

We considered the hemodynamic change in Cardiac Index as significant if it had fluctuated by 20% from baseline value in prone.

We have obtained a maximum of five pairs (T1 to T5) of readings categorised each pair as during and after the significant hemodynamic incident.

We analysed the correlation between Pulse Pressure Variation and Cardiac Index during three time points.

We acquired the correlation co-efficient and p-values for these three pair of readings which was given in the table (8).

The pictorial representation was provided by the corresponding scatter plots.(values for correlation co-efficient and p value are given below each scatter plot).

We obtained a statistically significant strong correlation between PPV and SVV consistently ($P < 0.05$) during all three time points (both before and after each significant hemodynamic change).

We obtained a consistent negative correlation between Pulse Pressure Variation and Cardiac Index, but it was not statistically significant.

Since we obtained a poor correlation, we did further analysis using the Change in Pulse Pressure Variation and Cardiac Index derived from before and after observations at each individual time points.

Even the modified analysis failed to show a statistically significant correlation between PPV and CI.

Further we did a modified sub analysis by eliminating the time factor.

We estimated the changes occurred in cardiac index from the Baseline value (taken in prone position) with each significant hemodynamic event, similar values for changes in pulse pressure variation from baseline and with each significant hemodynamic event were acquired.

We categorised the percentage difference in Cardiac Index into two groups,

Group-1 with <30% change in cardiac index from baseline, the other group being >30% change in cardiac index from baseline.

We assessed the correlation between the change in Cardiac Index and change in Pulse Pressure Variation for the two groups.

The modified analysis failed to show a statistically significant correlation between Pulse Pressure Variation and Cardiac Index.

Table: 9 Descriptive paired test analysis results of hemodynamic parameters during significant hemodynamic change (20% reduction in cardiac index from baseline) and after correction of the incident.

HR-Heart rate, MAP - Mean arterial pressure, PPV-Pulse Pressure Variation, SVV-Stroke Volume Variation, CI-Cardiac Index.

T1-first incident, T2-second incident, T3-third incident.

Variable	Time	Before Median (Percentile, 25 th – 75 th)	After Median (Percentile, 25 th – 75 th)	p-value
HR	T1	81.0 (68.5 - 91.8)	76.0 (66.3 – 95.0)	0.958
	T2	79.5 (59.3 – 93.0)	70.5 (62.0 – 83.5)	0.130
	T3	68.0 (58.0 – 85.5)	67.0 (59.0 – 87.5)	0.282
MAP	T1	58.0 (52.0 – 65.0)	78.0 (69.3 – 92.0)	0.000
	T2	59.0 (52.3 – 65.0)	75.5 (72.0 – 81.8)	0.047
	T3	55.0 (50.5 – 63.5)	73.0 (67.5 – 82.0)	0.007
PPV	T1	14.0 (9.8 – 24.5)	13.5 (10.3 – 21.0)	0.014
	T2	14.0 (10.0 – 22.5)	12.0 (11.0 – 17.8)	0.062
	T3	15.0 (12.0 – 21.5)	15.0 (7.5 – 19.0)	0.012
SVV	T1	15.5 (11.5 – 20.8)	14.0 (10.0 – 18.5)	0.033
	T2	16.5 (13.3 – 20.0)	14.5 (12.0 – 18.0)	0.130
	T3	15.0 (12.0 – 19.5)	13.0 (11.0 – 17.5)	0.077
CI	T1	2.2 (1.6 – 2.7)	3.0 (2.5 – 3.3)	0.000
	T2	1.9 (1.5 – 2.6)	2.8 (2.2 – 3.4)	0.003
	T3	2.0 (1.6 – 2.8)	2.9 (2.2 – 3.4)	0.019

Table: 10 Correlation between difference in Cardiac Index and difference in Pulse Pressure Variation acquired during and after correction of the first significant hemodynamic incident.

T1_PPV_diff –Cardiac Index difference between during the incident and after correction of the first hemodynamic incident.

T1_CI_diff –Cardiac Index difference between during the incident and after correction of the first hemodynamic incident.

		T1_PPV_diff	T1_CI_diff
Spearman's rho	T1_PPV_diff	1.000	-.186
	Correlation Coefficient		
	Sig. (2-tailed)	.	.344
	N	28	28
	T1_CI_diff	-.186	1.000
	Correlation Coefficient		
	Sig. (2-tailed)	.344	.
	N	28	28

** . Correlation is insignificant at the 0.3 level (2-tailed).

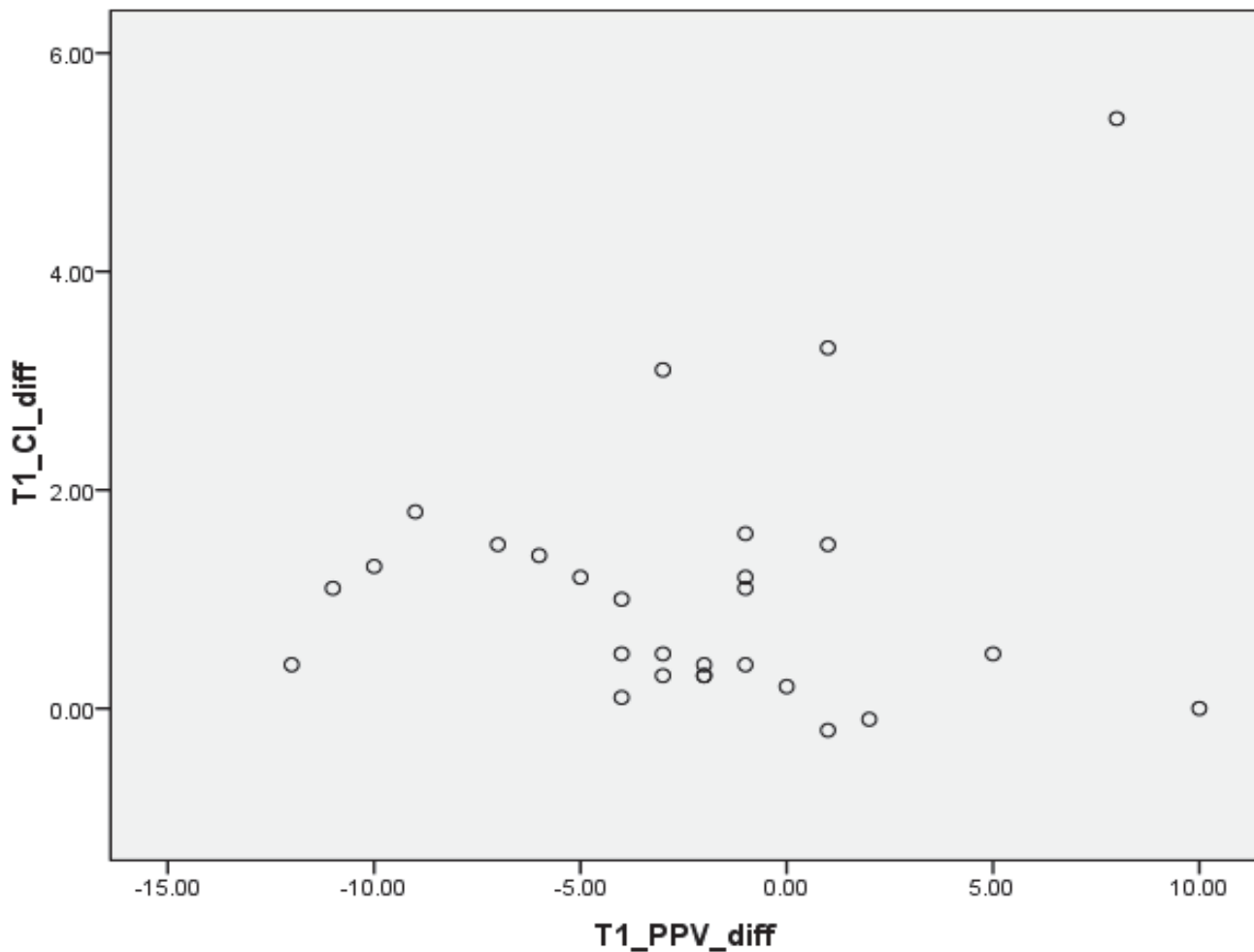


Fig.12 Scatter plot illustrating the relationship between difference in Cardiac Index and difference in Pulse Pressure Variation acquired during and after correction of the first significant hemodynamic incident.

T1_PPV_diff –Pulse Pressure Variation difference between during the incident and after correction of the first hemodynamic incident.

T1_CI_diff –Cardiac Index difference between during the incident and after correction of the first hemodynamic incident.

“The Spearman's Rank Correlation Coefficient value is (- 0.186), which is not significant ($p > 0.3$). This suggests a weak relationship between PPV and CI”.

The scatter plot gives the pictorial representation of the relationship between CI and PPV”.

Table: 11 Correlation between difference in Cardiac Index and difference in Pulse Pressure Variation acquired during and after correction of the second significant hemodynamic incident.

T2_PPV_diff –Pulse Pressure Variation difference between during the incident and after correction of the second hemodynamic incident.

T2_CI_diff –Cardiac Index difference between during the incident and after correction of the second hemodynamic incident.

	T2_PPV_diff	T2_CI_diff
Spearman's rho T2_PPV_diff Correlation Coefficient	1.000	-.217
Sig. (2-tailed)	.	.308
N	24	24
T2_CI_diff Correlation Coefficient	-.217	1.000
Sig. (2-tailed)	.308	.
N	24	24

** . Correlation is insignificant at the 0.3 level (2-tailed).

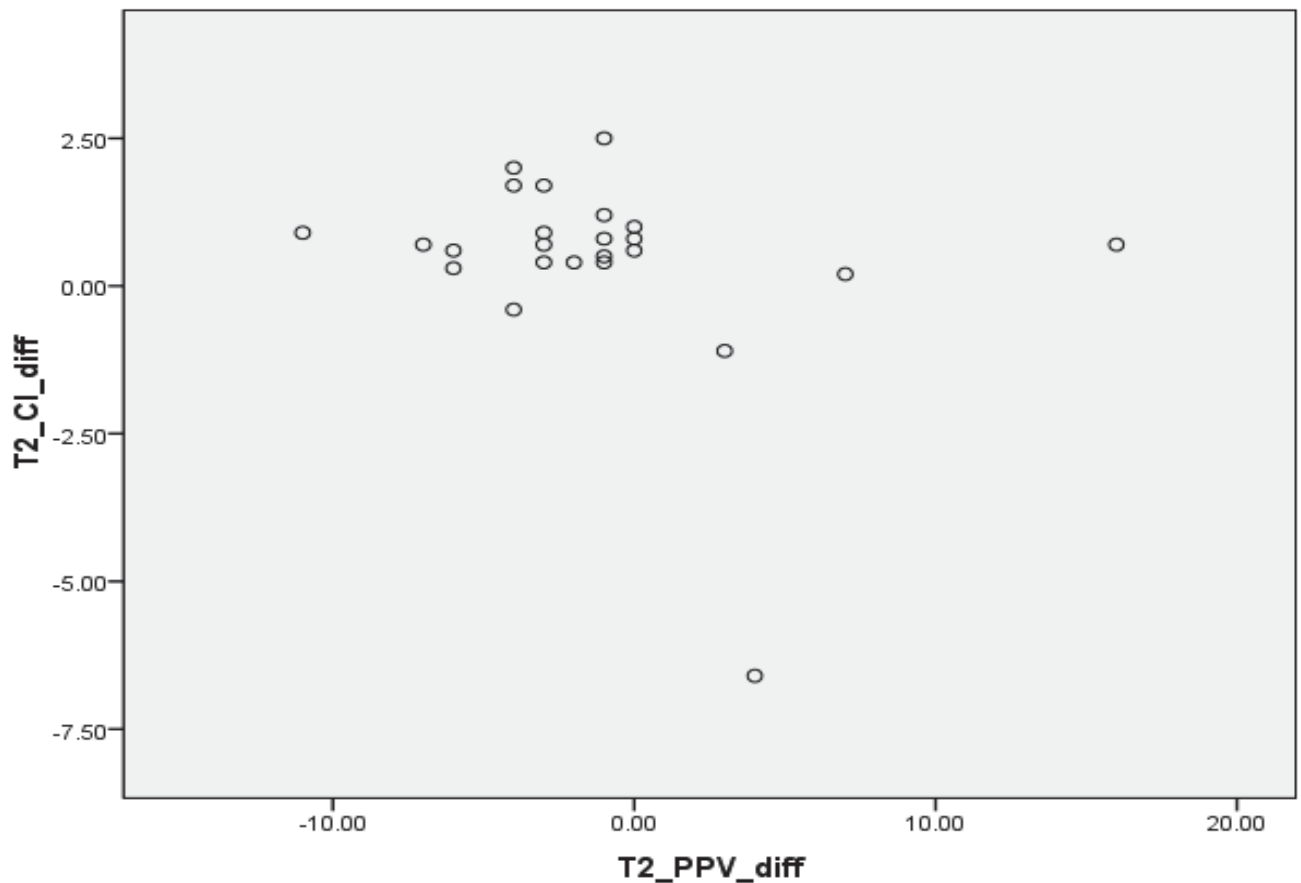


Fig.13 Scatter plot illustrating the relationship between difference in Cardiac Index and difference in Pulse Pressure Variation acquired during and after correction of the second significant hemodynamic incident.

T2_PPV_diff –Pulse Pressure Variation difference between during the incident and after correction of the second hemodynamic incident.

T2_CI_diff –Cardiac Index difference between during the incident and after correction of the second hemodynamic incident.

“The Spearman's Rank Correlation Coefficient value is(- 0.217), which is not significant ($p>0.3$). This suggests a weak relationship between PPV and CI”.

The scatter plot gives the pictorial representation of the relationship between CI and PPV”.

Table: 12 Correlation between difference in Cardiac Index and difference in Pulse Pressure Variation acquired during and after correction of the third significant hemodynamic incident.

T3_PPV_diff – Pulse Pressure Variation difference between during the incident and after correction of the third hemodynamic incident.

T3_CI_diff – Cardiac Index difference between during the incident and after correction of the third hemodynamic incident.

	T3_PPV_diff	T3_CI_diff
Spearman's rho T3_PPV_diff Correlation Coefficient	1.000	-.064
Sig. (2-tailed)	.	.784
N	21	21
T3_CI_diff Correlation Coefficient	-.064	1.000
Sig. (2-tailed)	.784	.
N	21	21

** . Correlation is insignificant at the 0.7 level (2-tailed).

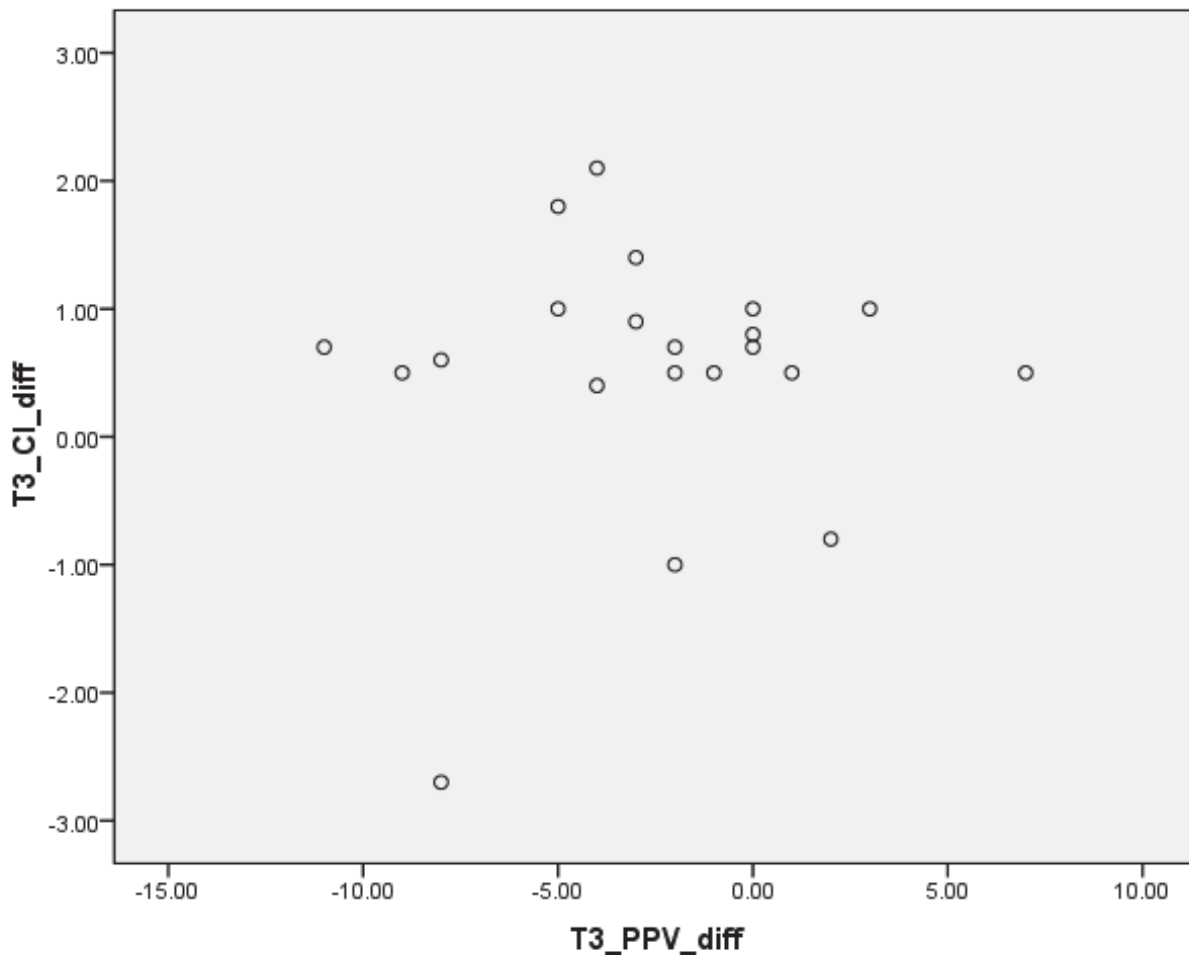


Fig.14 Scatter plot illustrating the relationship between difference in Cardiac Index and difference in Pulse Pressure Variation acquired during and after correction of the third significant hemodynamic incident.

T3_PPV_diff –Pulse Pressure Variation difference between during the incident and after correction of the third hemodynamic incident.

T3_CI_diff –Cardiac Index difference between during the incident and after correction of the third hemodynamic incident.

“The Spearman's Rank Correlation Coefficient value is(- 0.64), which is not significant ($p>0.7$).

This suggests a weak relationship between PPV and CI”.

The scatter plot gives the pictorial representation of the relationship between CI and PPV”.

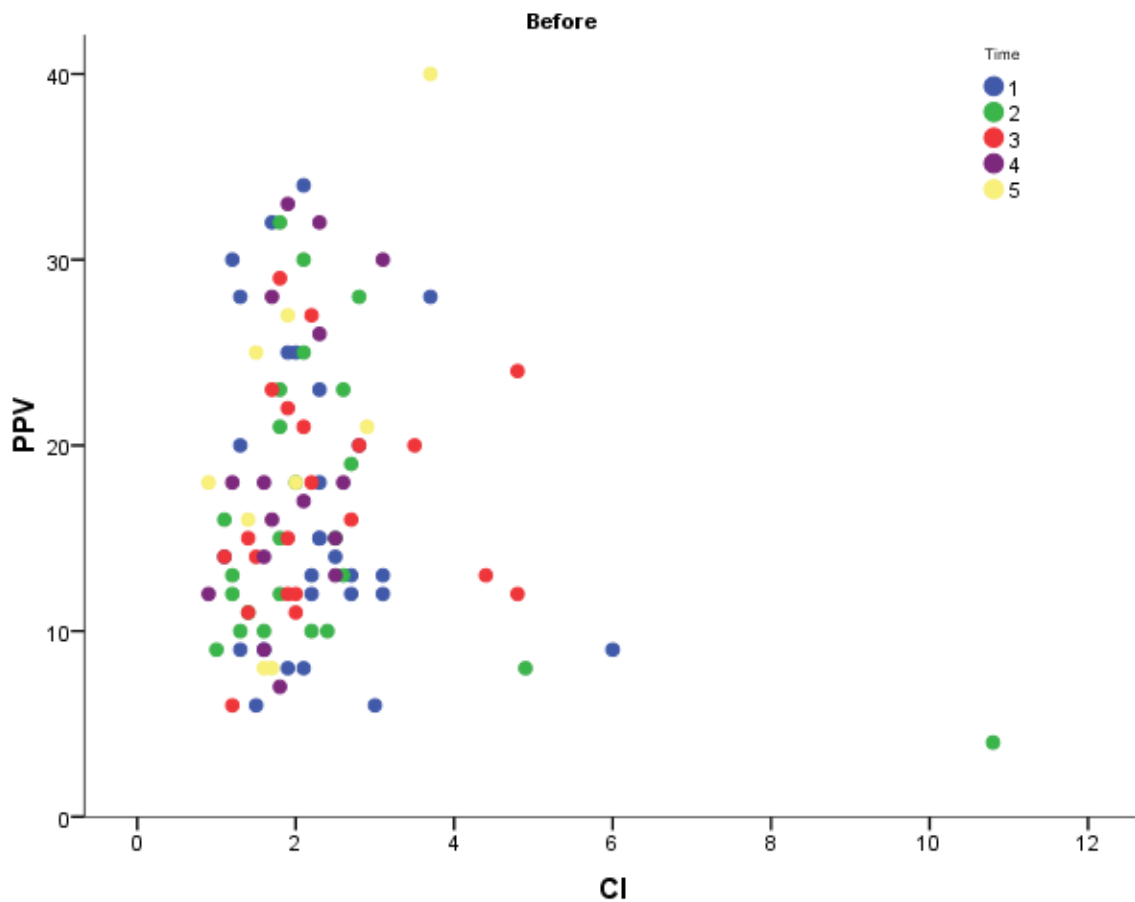


Fig.15 Scatter plot pictorial representation of all five significant hemodynamic incidents illustrating that there is weak statistically significant relationship between Cardiac Index and Pulse Pressure Variation during significant hemodynamic incident.

PPV- Pulse Pressure variation. CI – Cardiac Index.

Table: 13 Correlation between the Pulse Pressure Variation and Stroke Volume Variation values acquired during the first significant hemodynamic incident.

T1_PPV before - Pulse Pressure Variation during the first hemodynamic incident.

T1_SVV before - Stroke Volume Variation during the first hemodynamic incident.

		T1_PPVbefore	T1_SVVbefore
Spearman's rho	T1_PPVbefore	1.000	.871**
	Correlation Coefficient		
	Sig. (2-tailed)	.	.000
	N	28	28
	T1_SVVbefore	.871**	1.000
	Correlation Coefficient		
	Sig. (2-tailed)	.000	.
	N	28	28

** . Correlation is significant at the 0.01 level (2-tailed).

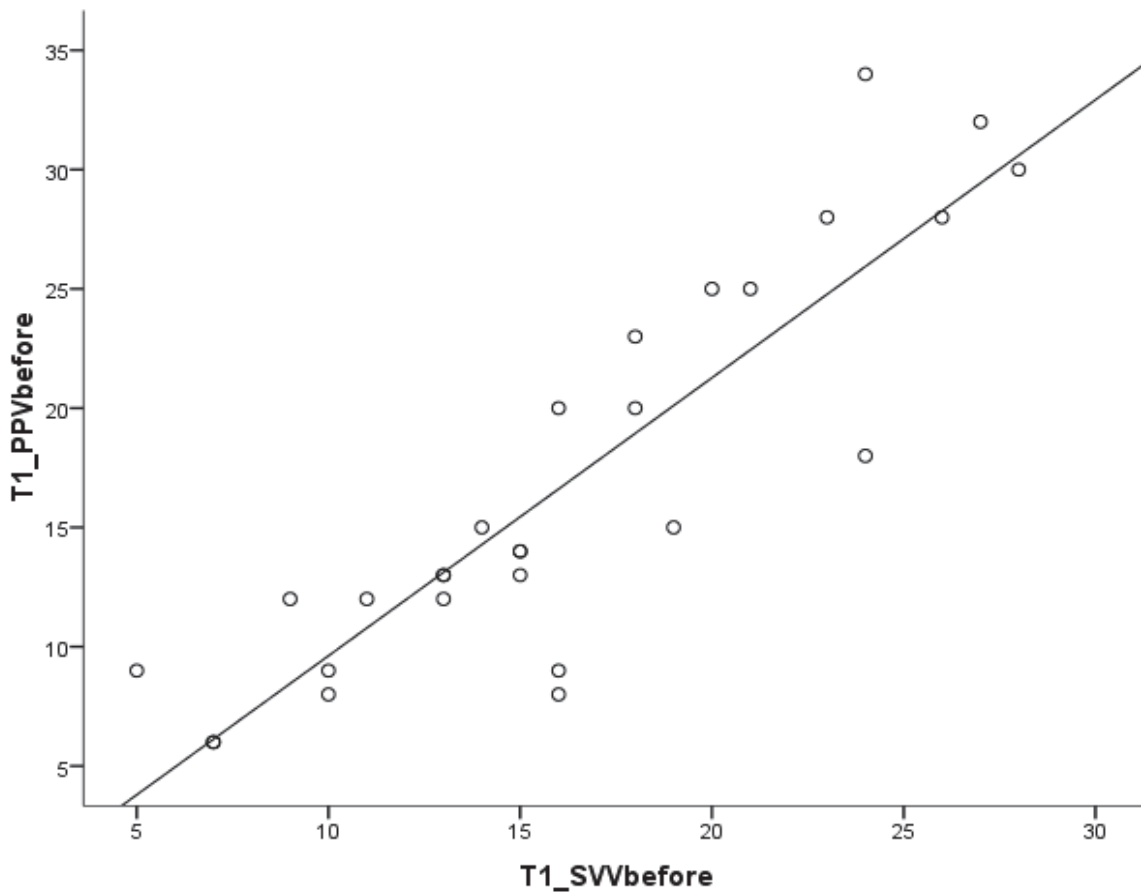


Fig.16 Scatter plot illustrating the relationship between Pulse Pressure Variation and

Stroke Volume Variation during the first significant hemodynamic incident.

T1_PPVbefore- Pulse Pressure variation during the first hemodynamic incident

T1_SVVbefore -Stroke Volume Variation during the first hemodynamic incident.

“The Spearman's Rank Correlation Coefficient value is 0.871, which is highly significant ($p < 0.0001$). This suggests, a strong positive linear relationship exists between PPV and SVV”.

The scatter plot gives the pictorial representation of the relationship between SVV and PPV”.

Table: 14 Correlation between the Pulse Pressure Variation and Stroke Volume Variation values acquired after correction of the first significant hemodynamic incident.

T1_PPVafter - Pulse Pressure Variation after correction of the first hemodynamic incident.

T1_SVVafter -Stroke Volume Variation after correction of the first hemodynamic incident.

			T1_PPVafter	T1_SVVafter
Spearman's rho	T1_PPVafter	Correlation Coefficient	1.000	.906**
		Sig. (2-tailed)	.	.000
		N	28	28
	T1_SVVafter	Correlation Coefficient	.906**	1.000
		Sig. (2-tailed)	.000	.
		N	28	28

** . Correlation is significant at the 0.01 level (2-tailed).

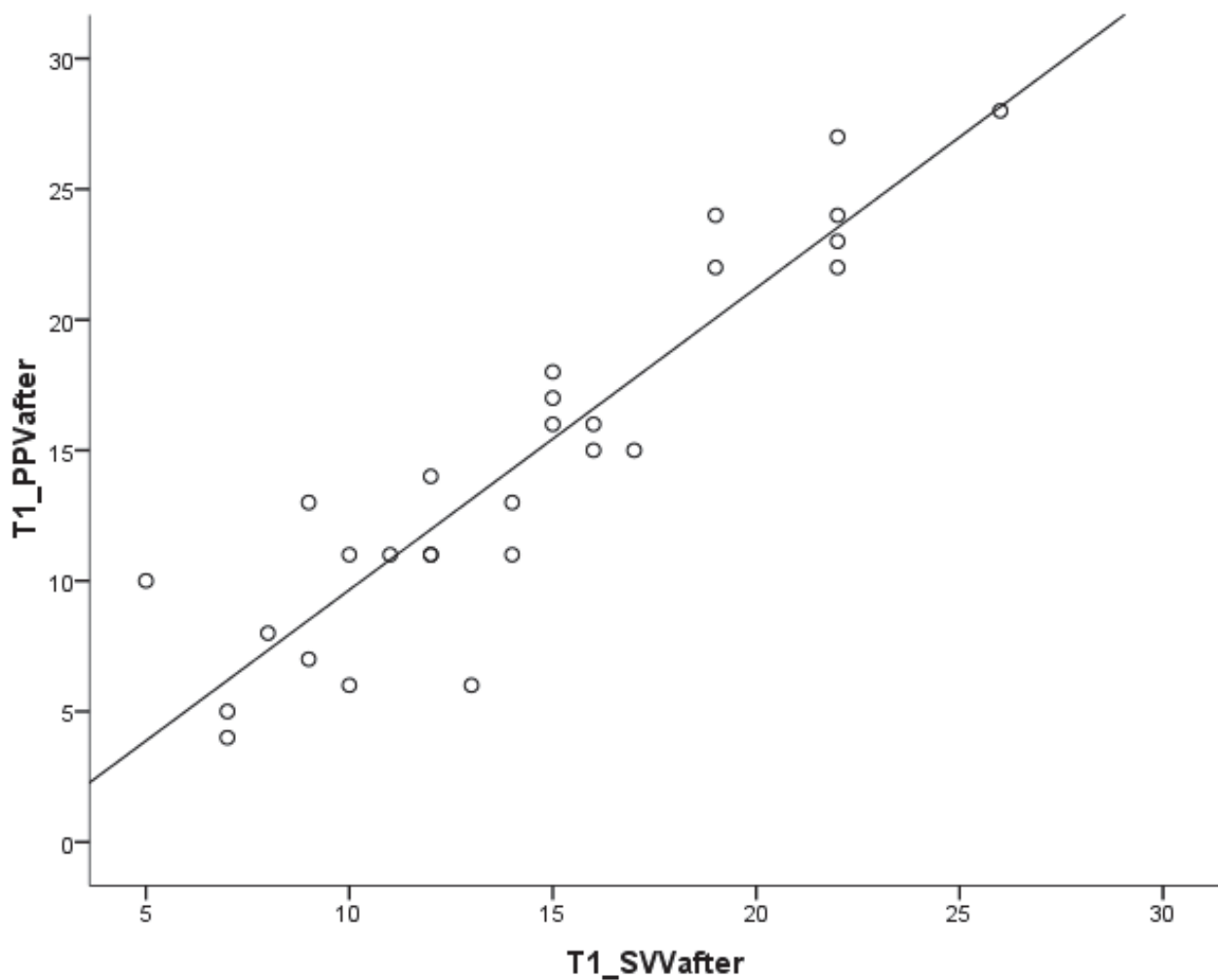


Fig.17 Scatter plot illustrating the relationship between Pulse Pressure Variation and Stroke Volume Variation after correction of the first significant hemodynamic incident.
 T1_PPVafter - Pulse Pressure variation after correction of the first hemodynamic incident
 T1_SVafter - Stroke Volume Variation after correction of the first hemodynamic incident.

“The Spearman's Rank Correlation Coefficient value is 0.906, which is highly significant ($p < 0.0001$). This suggests, a strong positive linear relationship exists between PPV and SVV”.

The scatter plot gives the pictorial representation of the relationship between SVV and PPV”.

Table: 15 Correlation between the Pulse Pressure Variation and Stroke Volume Variation values acquired during the second significant hemodynamic incident.

T2_PPV before - Pulse Pressure Variation during the second hemodynamic incident.

T2_SVV before - Stroke Volume Variation during the second hemodynamic incident.

			T2_PPVbefore	T2_SVVbefore
Spearman's rho	T2_PPVbefore	Correlation Coefficient	1.000	.774**
		Sig. (2-tailed)	.	.000
		N	24	24
	T2_SVVbefore	Correlation Coefficient	.774**	1.000
		Sig. (2-tailed)	.000	.
		N	24	24

** . Correlation is significant at the 0.01 level (2-tailed).

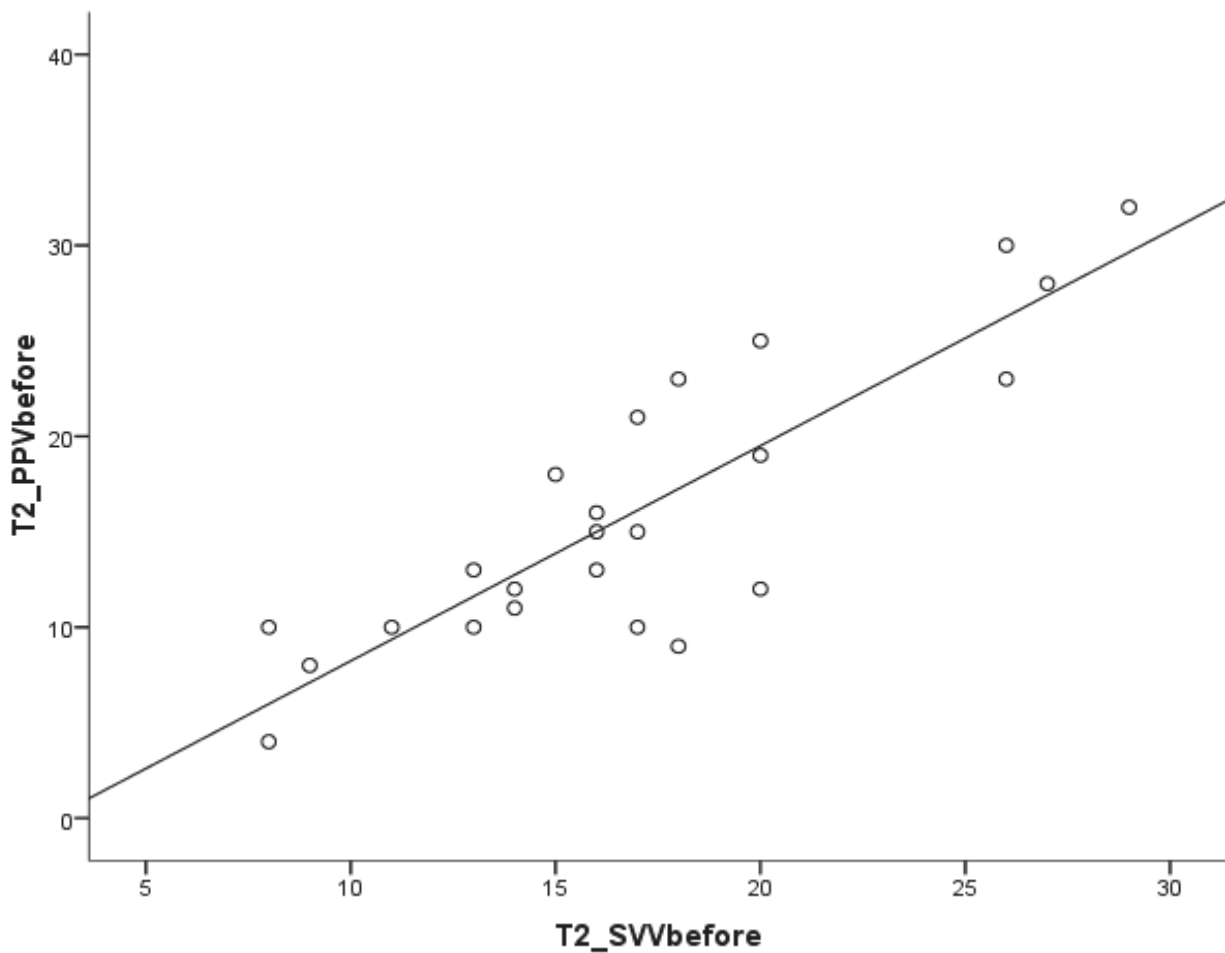


Fig.18.Scatter plot illustrating the relationship between Pulse Pressure Variation and Stroke Volume Variation during the second significant hemodynamic incident.
T2_PPV before - Pulse Pressure Variation during the second hemodynamic incident.
T2_SVV before -Stroke Volume Variation during the second hemodynamic incident.

“The Spearman's Rank Correlation Coefficient value is 0.774, which is highly significant ($p < 0.0001$). This suggests, a strong positive linear relationship exists between PPV and SVV”.

The scatter plot gives the pictorial representation of the relationship between SVV and PPV”.

Table: 16 Correlation between the Pulse Pressure Variation and Stroke Volume Variation values acquired after correction of the second significant hemodynamic incident.

T2_PPVafter - Pulse Pressure Variation after correction of the second hemodynamic incident.

T2_SVVafter - Stroke Volume Variation after correction of the second hemodynamic incident.

			T2_PPVafter	T2_SVVafter
Spearman's rho	T2_PPVafter	Correlation Coefficient	1.000	.710**
		Sig. (2-tailed)	.	.000
		N	24	24
	T2_SVVafter	Correlation Coefficient	.710**	1.000
		Sig. (2-tailed)	.000	.
		N	24	24

** . Correlation is significant at the 0.01 level (2-tailed).

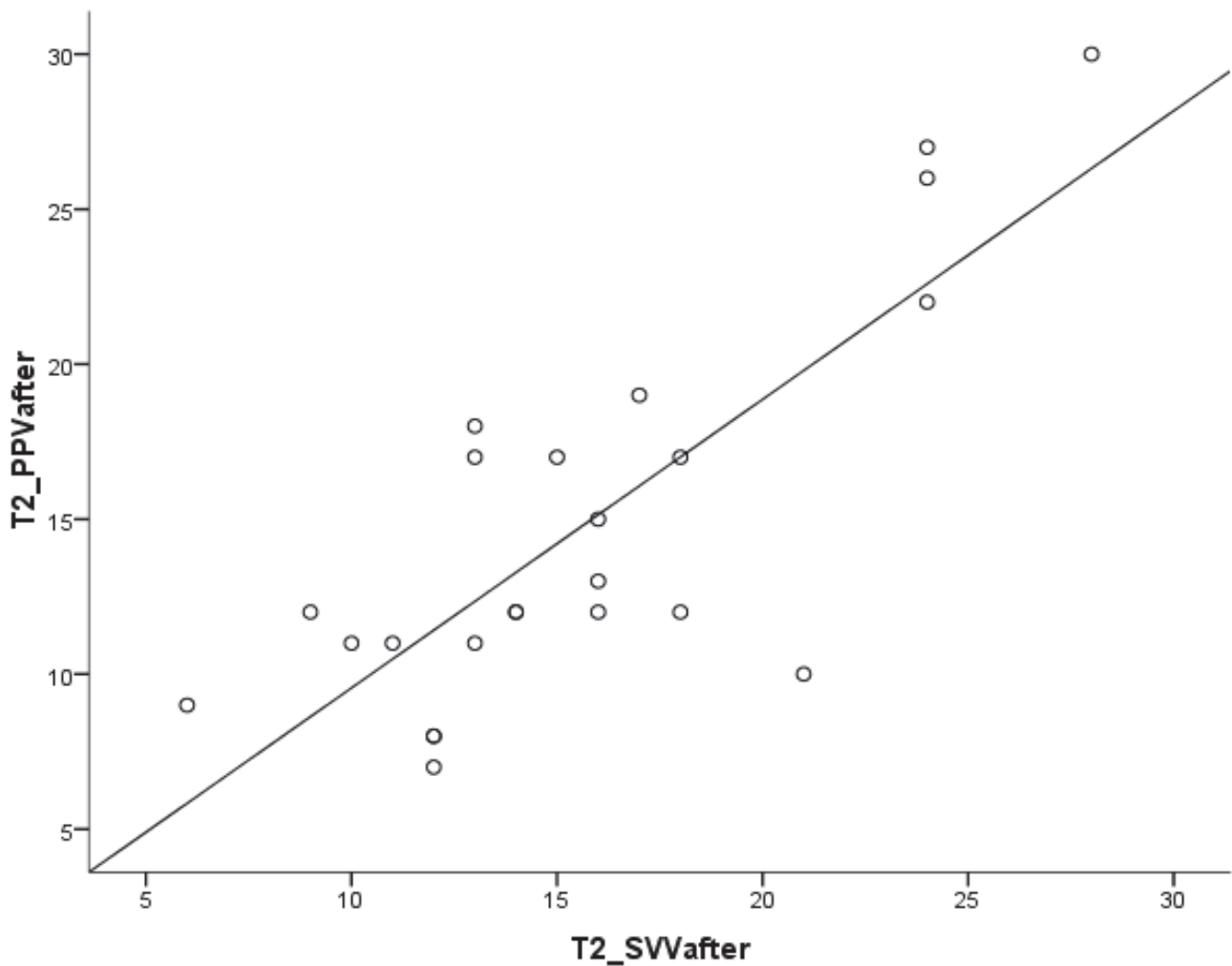


Fig.19 Scatter plot illustrating the relationship between Pulse Pressure Variation and Stroke Volume Variation after the correction of the second significant hemodynamic incident.

T2_PPV after - Pulse Pressure Variation after the correction of the second significant hemodynamic incident.

T2_SVV after -Stroke Volume Variation after the correction of the second significant hemodynamic incident.

“The Spearman's Rank Correlation Coefficient value is 0.710, which is highly significant ($p < 0.0001$). This suggests, a strong positive linear relationship exists between PPV and SVV”.

The scatter plot gives the pictorial representation of the relationship between SVV and PPV”.

Table: 17 Correlation between the Pulse Pressure Variation and Stroke Volume Variation values acquired during the third significant hemodynamic incident.

T3_PPV before - Pulse Pressure Variation during the third hemodynamic incident.

T3_SVV before - Stroke Volume Variation during the third hemodynamic incident.

	T3_PPVbefore	T3_SVVbefore
Spearman's rho T3_PPVbefore Correlation Coefficient	1.000	.702**
Sig. (2-tailed)	.	.000
N	21	21
T3_SVVbefore Correlation Coefficient	.702**	1.000
Sig. (2-tailed)	.000	.
N	21	21

** . Correlation is significant at the 0.01 level (2-tailed).

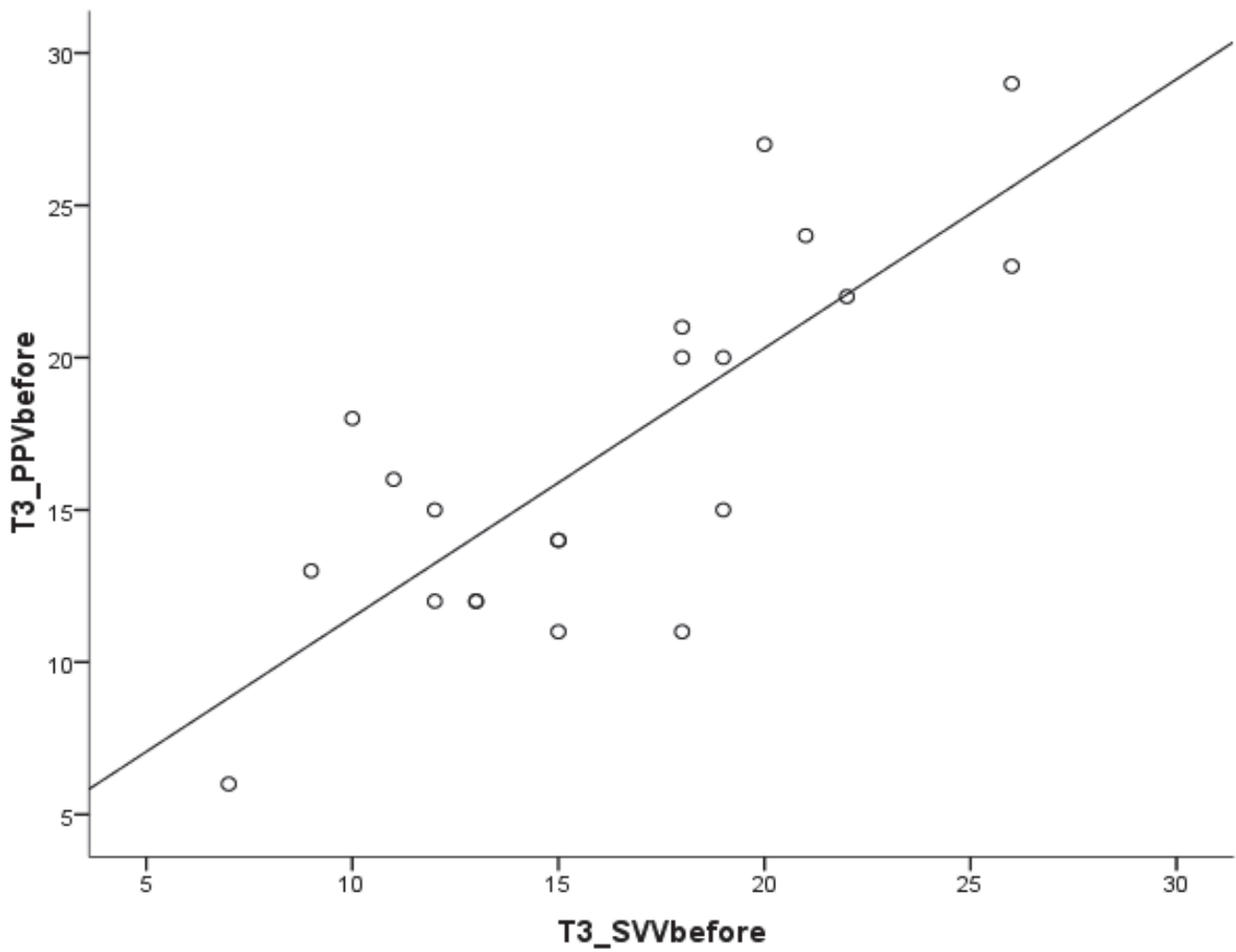


Fig. 20 Scatter plot illustrating the relationship between Pulse Pressure Variation and Stroke Volume Variation during the thirdsignificant hemodynamic incident.

T3_PPV before - Pulse Pressure Variation during the thirdsignificant hemodynamic incident.

T3_SVV before -Stroke Volume Variation during the thirdsignificant hemodynamic incident.

Table: 18 Correlation between the Pulse Pressure Variation and Stroke Volume Variation values acquired after correction of the third significant hemodynamic incident.

T3_PPVafter - Pulse Pressure Variation after correction of the third hemodynamic incident.

T3_SVVafter - Stroke Volume Variation after correction of the third hemodynamic incident.

			T3_PPVafter	T3_SVVafter
Spearman's rho	T3_PPVafter	Correlation Coefficient	1.000	.830**
		Sig. (2-tailed)	.	.000
		N	21	21
	T3_SVVafter	Correlation Coefficient	.830**	1.000
		Sig. (2-tailed)	.000	.
		N	21	21

** . Correlation is significant at the 0.01 level (2-tailed).

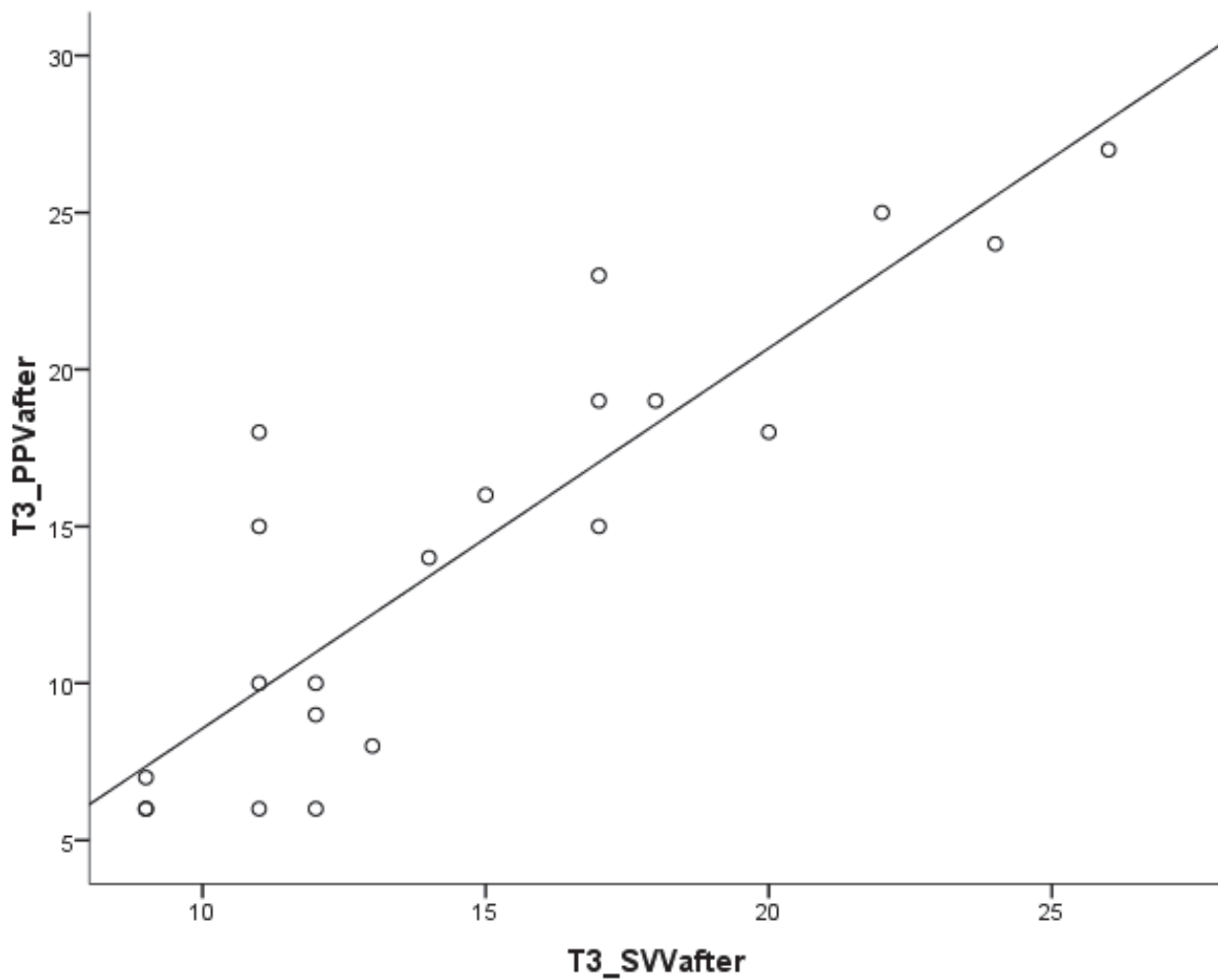


Fig. 21 Scatter plot illustrating the relationship between Pulse Pressure Variation and Stroke Volume Variation after the correction of the third significant hemodynamic incident.

T3_PPV after - Pulse Pressure Variation after the correction of the third significant hemodynamic incident.

T3_SVV after -Stroke Volume Variation after the correction of the third significant hemodynamic incident.

The modified analysis

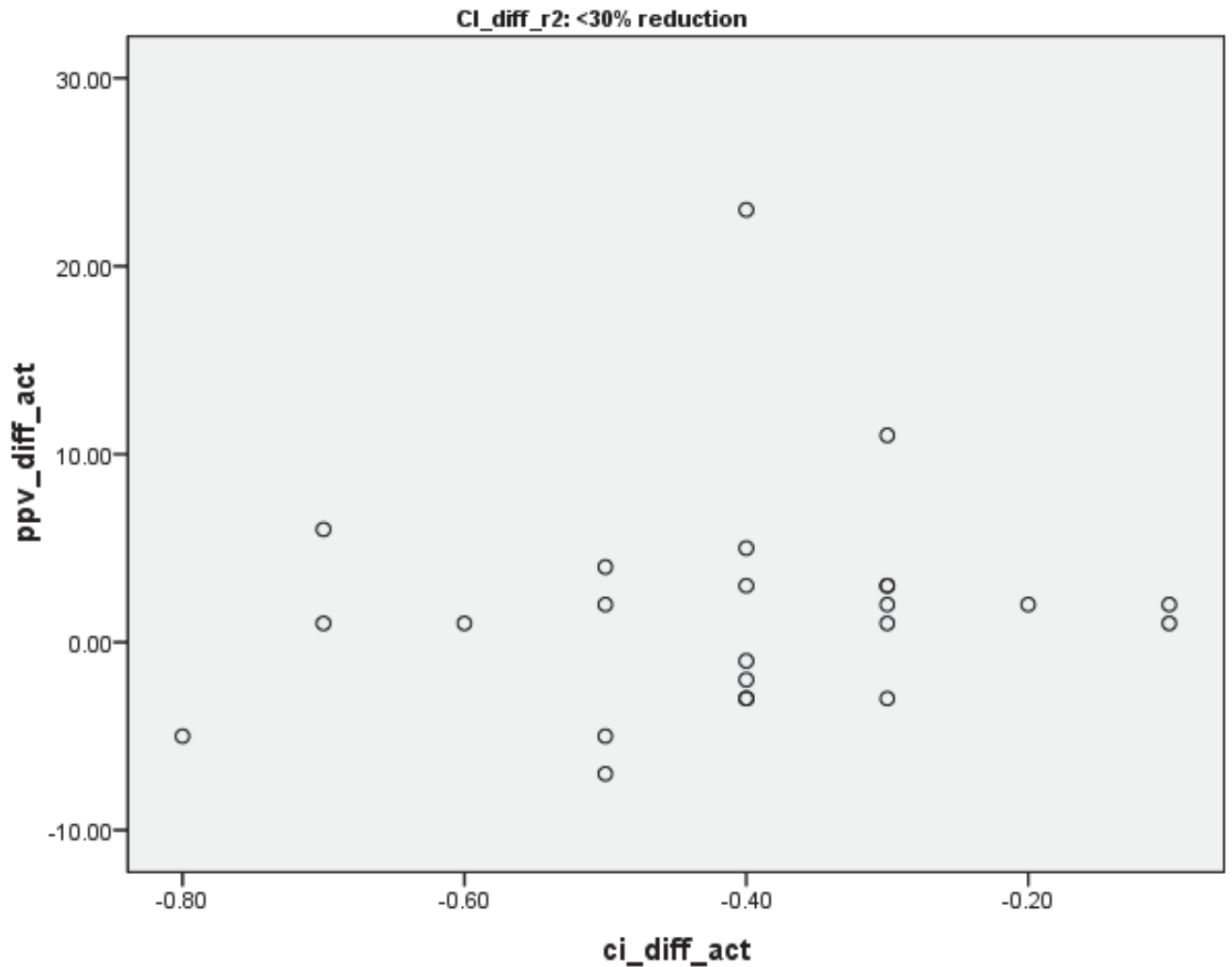


Fig.22 Scatter plot illustrating the relationship between Cardiac Index and the Pulse Pressure Variation for less than 30% difference between the baseline value and during significant hemodynamic incident

ppv_diff_act –Difference in Pulse Pressure Variation between the baseline value and the significant hemodynamic incident.

ci_diff_act - Difference in Cardiac Index between the baseline value and the significant hemodynamic incident.

“The Spearman's Rank Correlation Coefficient value is not significant ($p>0.2$).

This suggests a weak relationship between PPV and CI”.

The scatter plot gives the pictorial representation of the relationship between CI and PPV.

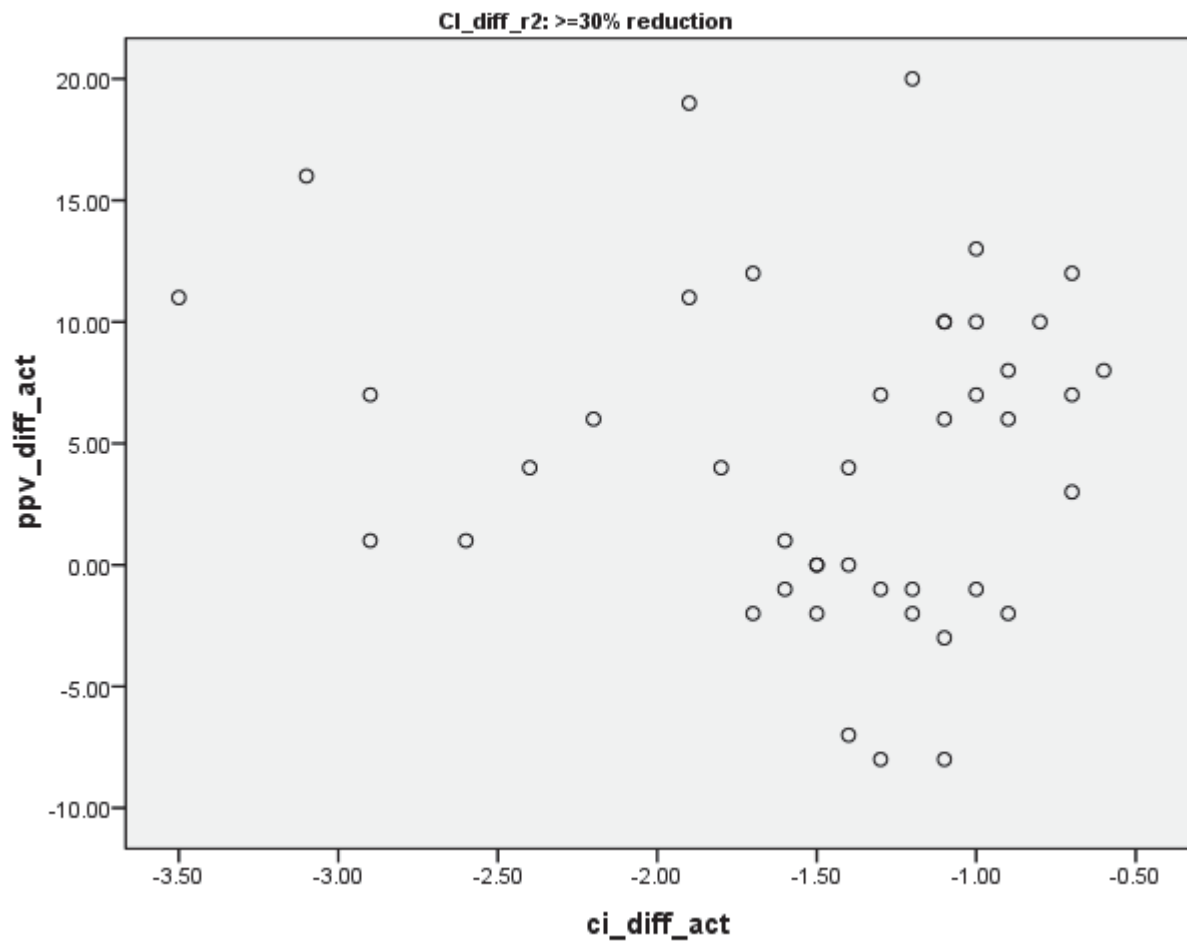


Fig.23 Scatter plot illustrating the relationship between Cardiac Index and the Pulse Pressure Variation for more than 30% difference between the baseline value and during significant hemodynamic incident

ppv_diff_act – Difference in Pulse Pressure Variation between the baseline value and the significant hemodynamic incident.

ci_diff_act - Difference in Cardiac Index between the baseline value and the significant hemodynamic incident.

“The Spearman's Rank Correlation Coefficient value is not significant ($p > 0.7$).

This suggests a weak relationship between PPV and CI”.

The scatter plot gives the pictorial representation of the relationship between CI and PPV.

Trends in the hemodynamic variables throughout the procedure

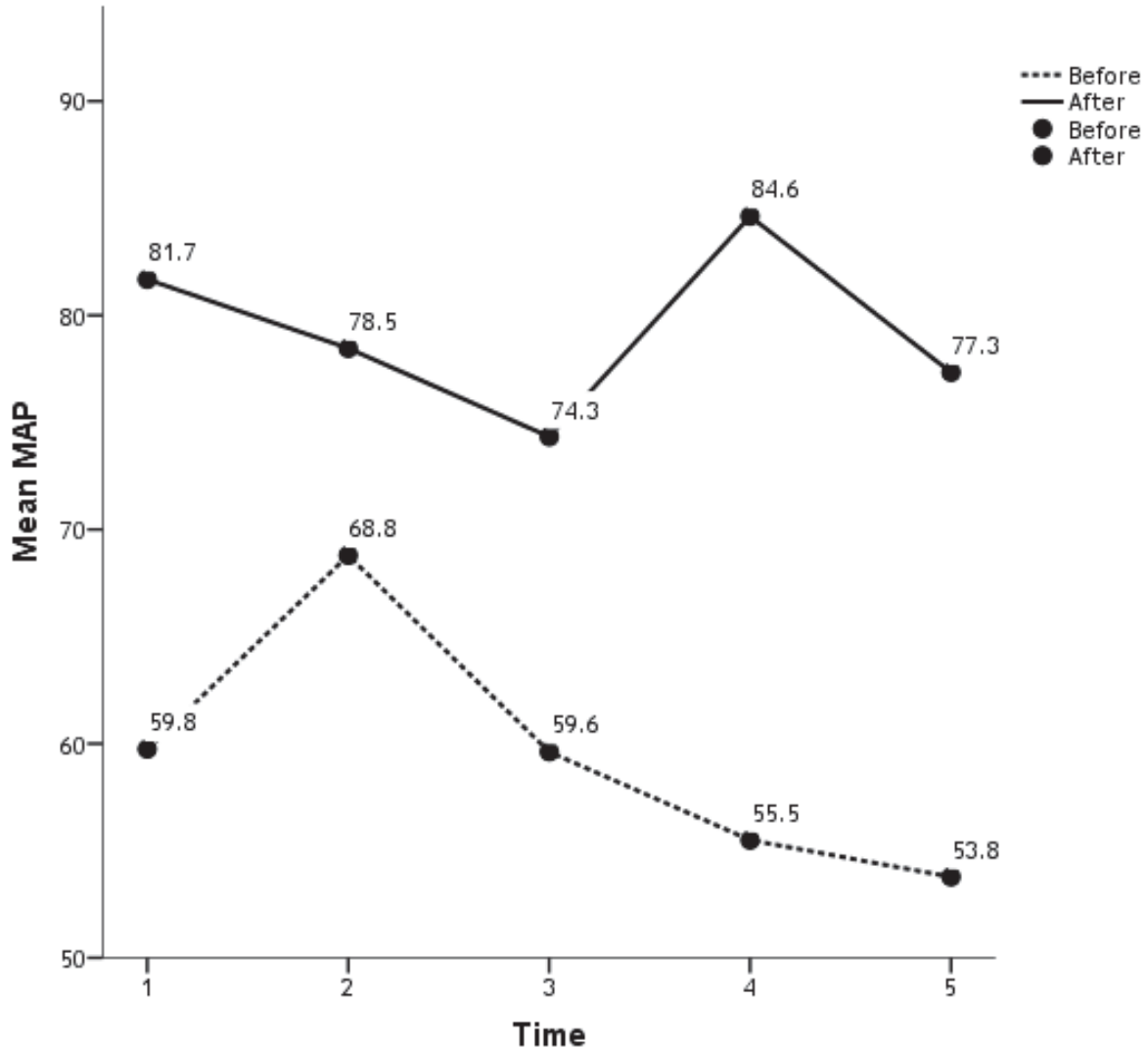


Fig.24 Graph showing the trends in the mean value of Mean arterial pressure, obtained during and after all five significant hemodynamic incidents.

Mean MAP- Mean arterial pressure.

Time- five different significant hemodynamic incidents.

Before-during significant hemodynamic incidents.

After- after significant hemodynamic incidents.

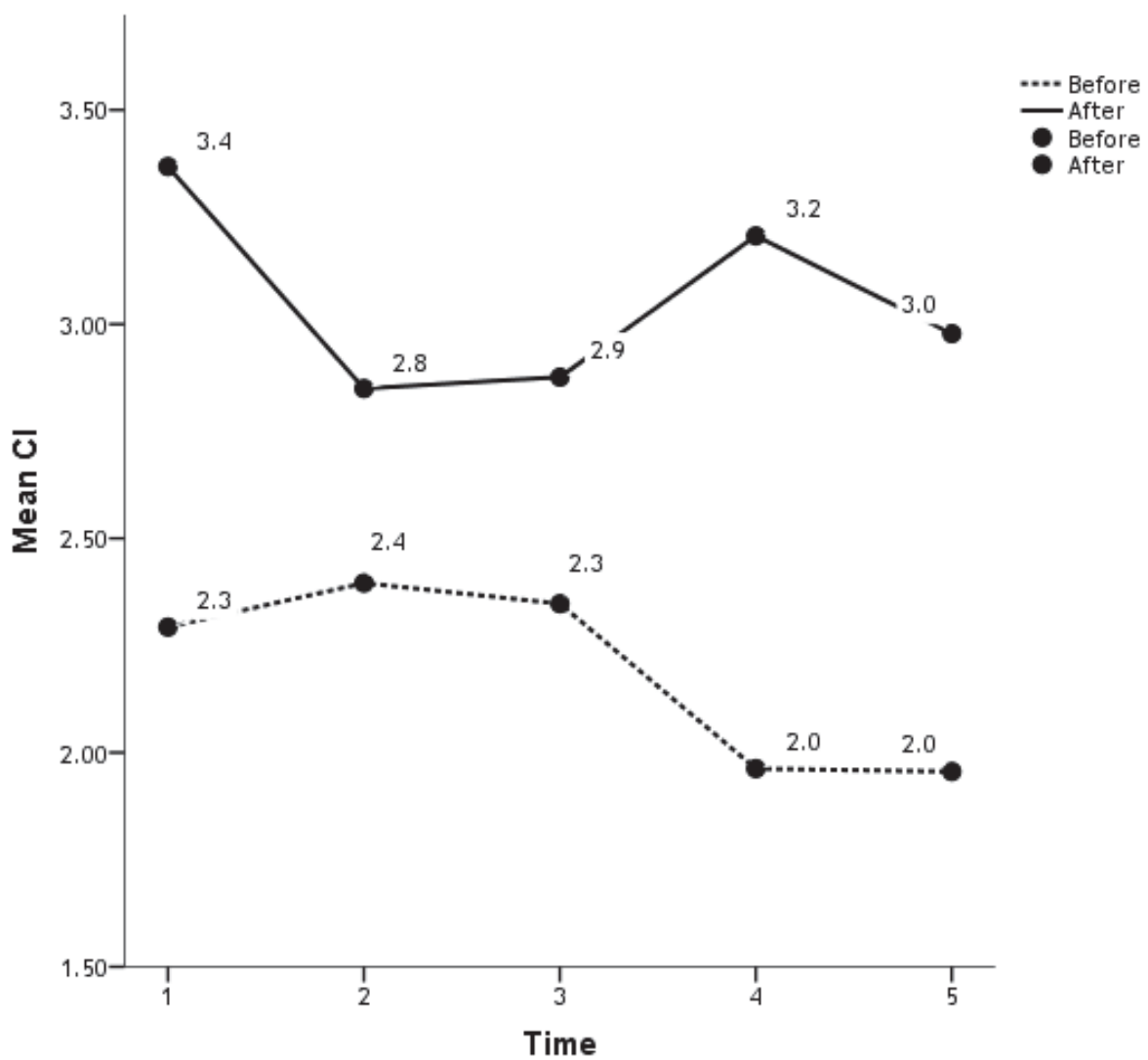


Fig.25 Graph showing the trends in the mean Cardiac Index, obtained during and after all five significant hemodynamic incidents.

Mean CI- Cardiac Index.

Time- five different significant hemodynamic incidents.

Before-during significant hemodynamic incidents.

After- after significant hemodynamic incidents.

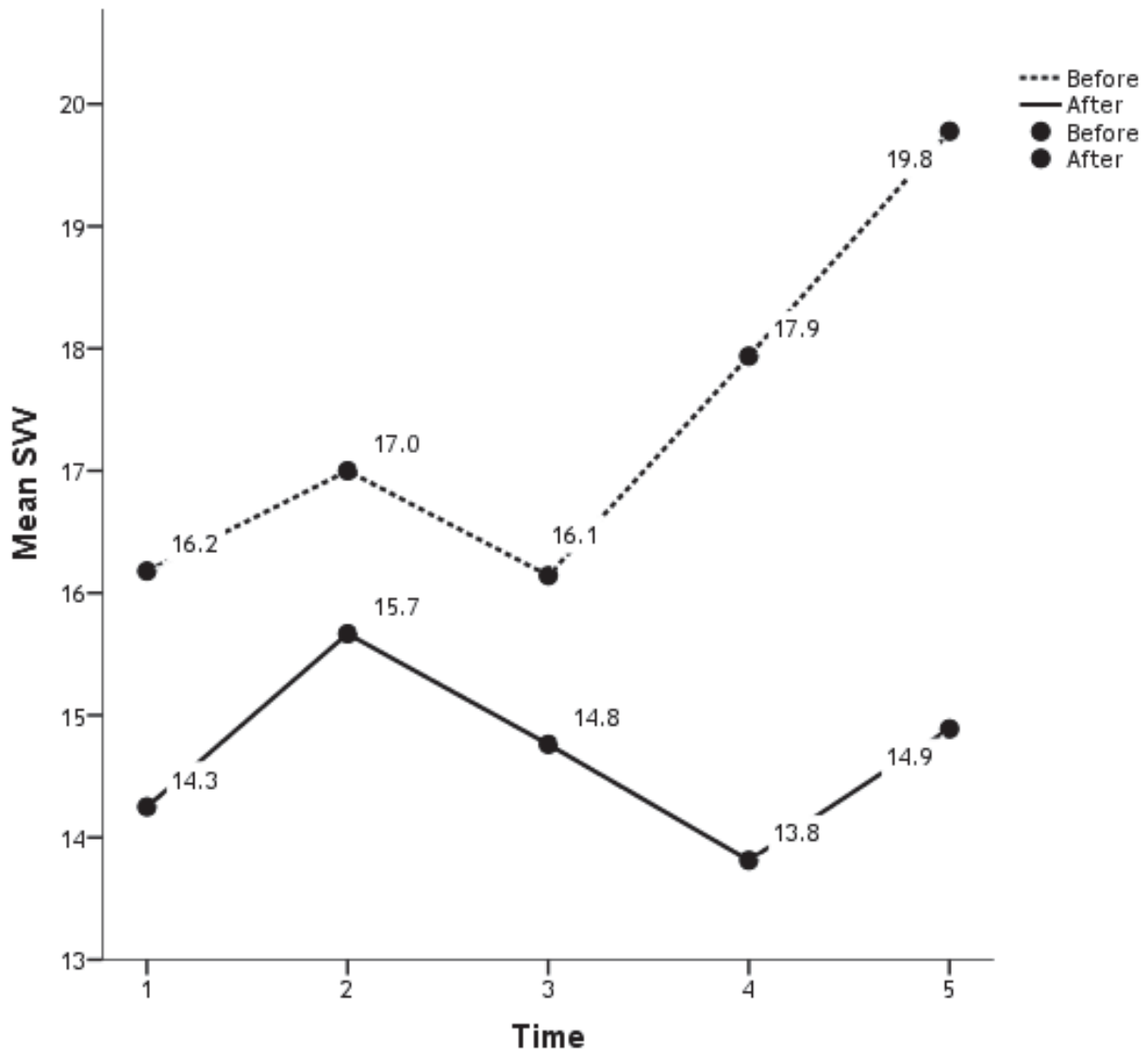


Fig.26 Graph showing the trends in the mean Stroke Volume Variation, obtained during and after all five significant hemodynamic incidents.

Mean SVV- Percentage of Stroke Volume Variation.

Time- five different significant hemodynamic incidents.

Before-during significant hemodynamic incidents.

After- after significant hemodynamic incidents.

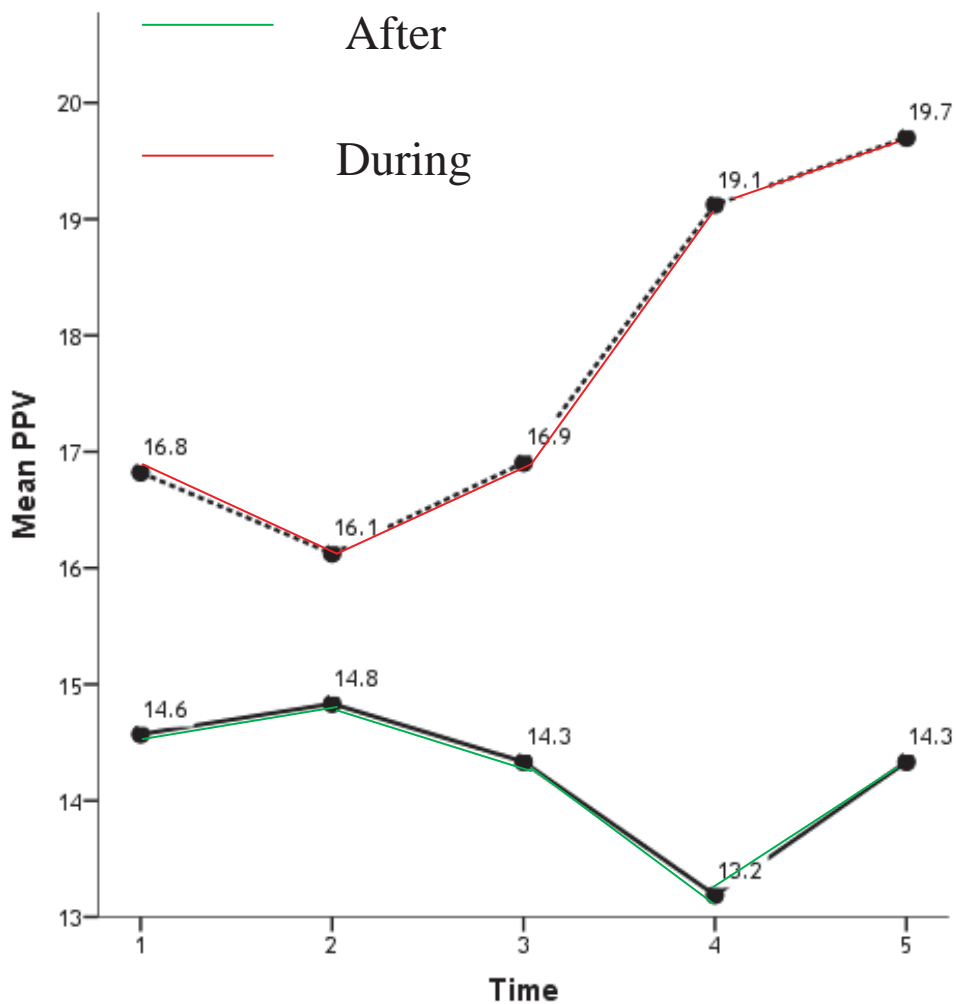


Fig.27 Graph showing the trends in the mean Pulse Pressure Variation, obtained during and after all five significant hemodynamic incidents.

Mean PPV- Percentage of Pulse Pressure Variation.

Time- five different significant hemodynamic incidents.

Before-during significant hemodynamic incidents.

After- after significant hemodynamic incidents.

Discussion

Intraoperative optimization of cardiac function and the systemic organ perfusion is important in all major surgeries. This is of significant concern in patients with altered Arterial Elastance, such as patients with long standing Diabetes mellitus, Hypertension and those on drugs which alter the sympathetic tone.

In such patients major surgeries performed in prone position requires extreme vigilance regarding the fluid management so as to optimize the cardiac output.

It is a fine balance between the judicious use of vasopressors and fluid administration for preload optimization.

The objective of our study is to compare the reliability of alterations in Pulse Pressure Variation with regard to the variation in Stroke Volume and Cardiac Index in patients with altered Arterial Elastance in the prone position.

It has been shown that the static indices of fluid responsiveness such as central venous pressure and pulmonary capillary wedge pressure are neither accurate nor reliable in extremely labile hemodynamic alteration.

Further mechanical ventilation induces certain changes in the intrathoracic and transpulmonary pressures that transiently affect the Left Ventricular preload resulting in cyclic changes in Stroke Volume which are reflected by the arterial pulse pressure.

Hence the Dynamic indices of fluid responsiveness such as the Systolic pressure variation, Pulse Pressure Variation and Stroke Volume Variation are preferred for evaluating the fluid responsiveness.(28)

Mark et al, have found that in patients undergoing spine procedures in the prone position, Systolic Pressure Variation has the similar predictive value as compared to the supine posture.(29)

However, Bias and colleagues in their study on patients undergoing, Kypho-Scoliosis repair have shown that in the prone position, there is a significant increase in PPV and SVV, but both are able to predict fluid responsiveness. They have suggested that PPV is able to predict fluid responsiveness at a threshold of 15% as compared to 11% in the supine position.(28)

In a porcine model, by Jenner et al, the effect of increased intra-abdominal pressure was evaluated and it was shown that the optimal threshold of PPV for predicting fluid responsiveness increased dramatically (20.5% vs. 11.5%)(30)

In our study, we have considered of 3-5 pairs of events in each patient, where there has been a significant hemodynamic change (i.e. a decrease or increase of cardiac index by more than or equal to 20%), which after treatment with vasopressors or fluids returned the Cardiac Index to its baseline. As part of the protocol in the study, we have preloaded the patients adequately, to compensate for relative hypovolemia (10 ml/kg).

We found that in all instances where the cardiac index has dropped significantly, the most common intervention has been administration of vasopressors to optimize the cardiac output. This is probably because, we expect the altered vasomotor tone to be further exaggerated in the presence of anaesthesia and prone position.

Hence the changes in the CI observed in these patients responded favourably to vasopressors.

We also found that the correlation between the PPV and SVV was quite significant (correlation coefficient of (0.87) with a p value of (0.001) in such circumstances both before and after intervention. (Refer table: 13)

Though there was a strong clinical correlation between CI and the dynamic indices of fluid responsiveness (SVV and PPV), there was only a weak statistical correlation (correlation coefficient of (-0.21) with a p value of (0.3). (Refer table: 11)

Bias et al, have also shown that the prone position induced changes in cardiac output were not only preload dependent. but other mechanisms such as decreased RV preload due to blood sequestration and increase in inspiratory pressure are responsible for the changes in cardiac out. Our study also confirms the above observation; where in the prone position changes in the cardiac output has got a weak correlation with changes in the PPV or SVV.(31)

Pulse pressure Variation is the difference between the arterial systolic and diastolic pressure. This difference is influenced by the Stroke volume and the arterial compliance.

SVV examines the difference between the Stroke Volume during inspiratory and expiratory phase of ventilation measures Stoke Volume either directly or indirectly and independent of arterial compliance.

FloTrac sensor utilizes pulse contour analysis through a proprietary formula to measure Cardiac output and SVV.

Because the Arterial Elastance is not a factor in measuring the CO and SVV, it should accurately reveal changes in the cardiac output during respiration and should theoretically serve as a better predictor of volume responsiveness.

In our study, we found that both SVV and PPV were reflective of changes in the CI to the same extent, both during the fall in cardiac index and after optimizing CI to the baseline.

Although, we expect SVV as a better predictor than PPV, we found that both groups were correlating to the same extent in this group of patients, where the changes in cardiac Index are attributable to a change in Systemic Vascular Index. Even though PPV is dependent on the Arterial Elastance, it closely reflects the changes in SVV.

It has been shown in animal models that in the absence of volume expansion PPV is reliable when blood pressure is augmented by vasoconstrictors.(32)

In addition to being less expensive, PPV proves to be less invasive and reliable indicator of fluid responsiveness, even in those with altered Arterial Elastance.

Hence PPV may be safely used as a dynamic predictor of fluid responsiveness.

In the absence of volume expansion PPV is reliable when blood pressure is augmented by vasoconstrictors in the prone position.

In patients with impaired Arterial Elastance vasopressors are preferred to volume expansion for the restoration of the cardiac index

Further evaluation of these patients in terms of estimation of the Systemic Vascular Resistance Index (SVRI) would be highly valuable in analysing the underlying explanation for the reduction in CI and its effect on the dynamic Indices.

Jens Kubitz et al, had observed changes in Systolic pressure variation and Pulse pressure variation in twelve pigs. They have maintained cardiac output primarily with vasopressors during reduction in hemodynamics, they found that both Systolic pressure variation and Pulse pressure variation correlated with changes in Stroke volume variation.(32)

Similarly in our study Cardiac Index was restored with the use of vasopressors instead of volume expansion during periods when there was no clinically significant blood loss.

Table: 19 Comparison of similar studies.

Study	Methodology	Inference
Bias.et.al,(31)	<p>Studied 27 humans. Underwent scoliosis. Study population: ASA 1 & 2 Used volume expansion with colloids Utilised FloTrac.</p>	<p>Prone position induced significant increase in both PPV & SVV, The absolute threshold is increased.PPV-15%) &SVV (14%) PPV and SVV correlated significantly with volume induced changes in cardiac output.</p>
Khwannimit et al,(33)	<p>Studied 42 septic patients, Used volume expansion using 500ml of colloid in Supine position Utilising FloTrac.</p>	<p>Both SVV and PVV perform well in septic patients in prediction of fluid response. Threshold for SVV (10%) PPV (12%)</p>
Derichad et al,(34)	<p>11 patients, underwent major abdominal surgeries. Intervention : during hemodynamic instability volume expanded with colloids Utilised FloTrac.</p>	<p>Both PPV & SVV accurately predict fluid responsiveness during major abdominal surgeries.Threshold for SVV (13%) PPV (12%).</p>
Yang et al,(35)	<p>Studied44 humans, underwent lumbar posterior fusions. ASA 1 & 2 Used volume expansion. (6ml/kg colloid) twice (one in supine and second in prone) Utilised esophageal Doppler.</p>	<p>PPV and has higher predictability in prone position than FTc (corrected flow time), both PPV &FTc are useful predictors for guiding fluid therapy.</p>

Limitations of our study

Our study has pitfalls in that change in SVV and PPV with respect to intravascular volume expansion has not been studied.

It is primarily because in this subset of patient volume loading in the absence of clinical hypovolemia may be more deleterious than beneficial.

In contrast to experimental studies in animals where it is possible to induce hypovolemia and thereby assess fluid responsiveness, we have studied the effects of change in cardiac indices which has been restored with vasopressors and its effects on PPV and SVV.

We were not able to measure the Systemic Vascular Resistance due cost constraints.

Conclusion

We conclude that Pulse Pressure Variation (PPV) and Stroke Volume Variation (SVV) correlate with each other even in patients with altered Arterial Elastance in the prone position, although PPV doesn't show a strong correlation with Cardiac Index.

The primary reason for the fall in Cardiac Index in patients who have been adequately volume replaced is a fall in Systemic Vascular Resistance.

We also suggest that the measurement of Systemic Vascular Resistance Index (SVRI) will provide better understanding of the underlying physiology for the reduction in the CI in patients with altered Arterial Elastance subjected to major prone procedure.

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Appendices

INFORMED CONSENT DOCUMENT

Relationship of pulse pressure variation and stroke volume variation with cardiac output changes during mechanical ventilation in ASA 2 & 3 patients, undergoing major spine surgeries in prone position.

Study number-

Participant's name-

Hospital Number-

I /guardian of give my consent to include me in this study. It has been explained to me that an arterial catheter will be inserted to me during the surgical procedure. This test is accepted universally at the moment but not used as a protocol. This test which will be done is not of any harm to me. Further I have been told that this will not incur any additional expense. I understand that this is a clinical study done to know more about the need for intravenous fluid administration.

It has been explained to me that I am free to withdraw myself from the study any time I want and will not in any way compromise the treatment. I understand that my identity and participation will not be revealed in any information released to third parties. I am giving this consent on my own free will. I have been explained about the study in a language familiar to me.

Name of the patient

Signature / Thumb impression

Name of relative (guardian/parent)

Signature

Name of witness

Signature.

Signature of the person taking consent.

Proforma

Relationship of pulse pressure variation and stroke volume variation for predicting hemodynamic changes during mechanical ventilation in ASA 2 & 3 patients, undergoing major spine surgeries in prone position.

Serial Number:

Date of Surgery:

Hospital Number:

Age:

Sex:

Ht:

Wt:

BMI:

BSA:

ASA Status:

Co-morbid illness:

Diagnosis:

Duration:

Surgery:

HbA1C:

Type of support used:

Drugs:

Levels operated:

Duration of Anaesthesia:

Use of Vasopr/ Inotr:

Urine output:

Blood loss:

Lactate

