COMPARISON OF HAEMODYNAMICS AND CARDIAC FUNCTION BEFORE AND AFTER NEUROSURGERY IN PATIENTS WITH AND WITHOUT RAISED INTRACRANIAL PRESSURE: A PILOT OBSERVATIONAL STUDY WITH TRANSTHORACIC ECHOCARDIOGRAPHY

Thesis submitted for the partial fulfilment for the requirement Of

The degree of

DM Neuroanaesthesia

Of SCTIMST

Dr NEERAJA AJAYAN

DM Neuroanaesthesia Resident

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM

KERALA 695011, INDIA

AUGUST 2020

DECLARATION

I hereby declare that this thesis entitled **"Comparison of haemodynamics and cardiac function before and after neurosurgery in patients with and without raised intracranial pressure: A pilot observational study with Transthoracic Echocardiography"** has been prepared by me under the able guidance of Prof. Manikandan S, Division Of Neuroanaesthesia& Neurocritical care , Department Of Anaesthesiology, Sree Chitra Tirunal Institute For Medical Sciences & Technology, Thiruvananthapuram.

Trivandrum ,

24/08/2020

Dr Neeraja Ajayan

DM Neuroanesthesia Resident,

Division Of Neuroanaesthesia& Neurocritical care ,

Department Of Anaesthesiology,

SCTIMST, Thiruvananthapuram.

CERTIFICATE

This is to certify that this thesis entitled "**Comparison of haemodynamics and cardiac function before and after neurosurgery in patients with and without raised intracranial pressure: A pilot observational study with Transthoracic Echocardiography**" has been prepared by Dr Neeraja Ajayan, DM Neuroanaesthesia Resident, Division of Neuroanaesthesia& Neurocritical Care, Department of Anaesthesiology at Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram. She has been sincere in efforts and has shown keen interest in the clinical and research aspect of the project and final submission.

Place : Thiruvananthapuram

Date : 27.08.2020

Prof. Manikandan S.,
Professor and Incharge,
Division of Neuroanaesthesiology
and Neurocritical Care,
Department of Anaesthesiology,
SCTIMST, Thiruvananthapuram

CERTIFICATE

This is to certify that this thesis entitled "**Comparison of haemodynamics and cardiac function before and after neurosurgery in patients with and without raised intracranial pressure: A pilot observational study with Transthoracic Echocardiography**"has been prepared by Dr Neeraja Ajayan, DM Neuro Anaesthesia Resident, Division of Neuroanaesthesia, Department of Anaesthesiology at Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram.This thesis was done under the able guidance of Prof. Manikandan S. She has shown keen interest in preparing this project.

Place: Thiruvananthapuram

Date: 27/8/20

Prof. Thomas Koshy,

Professor (Senior Grade) and Head,

Department of Anaesthesiology,

SCTIMST,

Thiruvananthapuram

CERTIFICATE

This is to certify that this thesis entitled "**Comparison of haemodynamics and cardiac function before and after neurosurgery in patients with and without raised intracranial pressure: A pilot observational study with Transthoracic Echocardiography**" has been prepared by Dr Neeraja Ajayan, DM Neuro Anaesthesia Resident, Division of Neuroanaesthesia, Department of Anaesthesiology at Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram. This thesis was done under the able guidance of Prof. Manikandan S. She has shown keen interest in preparing this project.

Place: Thiruvananthapuram

Date: 28/8/2020

Dr Unnikrishnan P,

Assistant Professor,

Department of Anaesthesiology,

SCTIMST,

Thiruvananthapuram

ACKNOWLEDGEMENT

Preparation of this thesis has been an invaluable and extremely rewarding experience for me. I would like to extend my gratitude to all those who have contributed towards the study in umpteen ways:

To commence with, I pay my obeisance to GOD, the almighty who has bestowed upon me everything I have in my life and of which I give utmost value to faith.

After GOD, I express my sincere and deepest gratitude to my guide, Dr. Manikandan S, Professor and Head, Division of Neuroanaesthesia and Neurocritical care, Department of Anesthesiology, SCTIMST who has taken great efforts in not just teaching me echocardiography but also ploughing through several preliminary versions of my text, posing challenging questions, providing creative and critical suggestions in the writing of the dissertation . His expertise, invaluable guidance, constant encouragement, affectionate attitude, understanding and patience is something I will truly be indebted for. This work would never have seen the light of the day without his constant support and inspiration .

I owe my special thanks to Dr Thomas Koshy, Professor (Senior Grade), Head, Department of Anaesthesiology, SCTIMST for guiding me in every step and boosting my morale. I take this opportunity to express my gratitude and respectful regards to Dr. Smita V for her suggestions and encouragement during my study. I thank Dr Ajay Prasad Hrishi for his timely motivation, constant support ,inspiration and unfailing help in completing this project. I extend my gratitude to Dr Unnikrishnan P who found time to clarify my doubts and gave valuable insights. Special thanks to Dr. Ranganatha Praveen for providing constant motivation.

I am extremely grateful to Prof. (Dr) Asha Kishore, Director, SCTIMST ,academician of international acclaim and custodians of novel ideas, for kindly permitting me to work in my project, in this esteemed institution. There have always extended generous help whenever I needed.

I am grateful and express my sincere thanks to the honourable members of the Institute Ethics committee and Technical Advisory committee for approval of my research protocol.

I sincerely value the contribution of all my fellow residents especially Dr Keta Thakkar and Dr Nagmoti Shilpa Vikasrao, for extending their unstinted support throughout. I am thankful to all my seniors, friends and colleagues of SCTIMST, Trivandrum, in general and Department of Anaesthesiology in particular for their relentless support, love and affection.

I am obliged to Mr Jayakumar P for his assistance during the statistical analysis of this research work.

I shall fail in my duties if I do not acknowledge my deep gratitude to all those patients who had volunteered themselves as subjects for this study.

I am thankful to all anaesthesia technicians of SCTIMST for their cooperation and help.

I feel a deep sense of gratitude to my parents for providing unconditional love and persistent inspiration for my journey in this life.

I am also indebted to my beloved husband Mr Anoop Ramanujam for providing me invaluable love and inexplicable support throughout, which has made this work possible. Last but never the least, my son , Ishaan Shankar Anoop .. words prove a meagre media to write down my feelings for him!

List of Abbreviations

A vel	:	A velocity (velocity during atrial contraction)
ABP	:	Arterial blood pressure
AHA	:	American Heart Association
AF	:	Atrial fibrillation
Ao VTI	:	Aortic velocity time integral
AIS	:	Acute ischaemic stroke
ANS	:	Autonomic nervous system
ASE	:	American Society of Echocardiography
ATP	:	Adenosine Triphosphate
AV	:	Atrio ventricular
A4C	:	Apical 4 chamber
BBB	:	Blood brain barrier
BIS	:	Bi-spectral index
BNP	:	B-type natriuretic peptide
BSA	:	Body surface area
BMI	:	Body Mass Index
CAN	:	Central autonomic network
CAD	:	Coronary artery disease
CBF	:	Cerebral blood flow
CBN	:	Contraction band necrosis

CBV	:	Cerebral blood volume
CI	:	Cardiac index
CO	:	Cardiac output
COPD	:	Chronic obstructive pulmonary disease
CPP	:	Cerebral perfusion pressure
CNS	:	central nervous system
CSA	:	Cross sectional area
CSF	:	Cerebro-spinal fluid
CT	:	Computed tomography
CWD	:	Continuous wave Doppler
DD	:	Diastolic dysfunction
DMH	:	Dorsomedial
DMNX	:	Dorsal motor nucleus of the nervus Vagus
LH	:	Lateral hypothalamus
Dec T	:	Deceleration time
E vel	:	E velocity (velocity during early diastole)
e’	:	e prime
EF	:	Ejection fraction
ECG	:	Electrocardiogram
Et	:	End Tidal
FAC	:	Fractional area change

FS	:	Fractional shortening
GCS	:	Glasgow coma scale
GEDV	:	Global End Diastolic Volume
GLS	:	Global longitudinal strain
HR	:	Heart rate
IC	:	Insular cortex
ICP	:	Intra cranial pressure
ICH	:	Intracerebral haemorrhage
ICU	:	Intensive care unit
IVSd	:	Interventricular septum thickness end-diastole
IVSs	:	Interventricular septum thickness systole
IWIDd	:	Inferior wall internal diameter end diastole
IWIDs	:	Inferior wall internal diameter end-systole
LA	:	Left atrium
LAD	:	Left atrium diameter
LVMI	:	Left ventricular mass index
LVOT	:	Left ventricle outflow tract
LAP	:	Left atrial pressure
LAVI	:	Left atrial volume index
LV LAX	:	Left ventricular long axis view
LV	:	Left ventricle

LH	:	Lateral hypothalamus
LVIDd	:	LV internal diameter at end diastole
LVIDs	:	LV internal diameter at end systole.
LVOT	:	Left ventricular outflow tract
LVEDA	:	Left Ventricular End Diastolic Area
LVESA	:	LV end-systolic area
LVEDV	:	Left ventricular end-diastolic volume,
LVESV	:	Left ventricular end-systolic volume
MAC	:	Minimum alveolar concentration
MAP	:	Mean arterial pressure
MCA	:	Middle cerebral artery
MRI	:	Magnetic resonance imaging
MRN	:	Median raphe nucleus
MSNA	:	Muscle sympathetic nerve activity
MV	:	Mitral valve
NA	:	Nucleus ambiguous
NSC	:	Neurogenic stress cardiomyopathies
NTS	:	Nucleus tractus solitarius
PaCO2	:	Partial pressure of carbon-di-oxide
PLAX	:	Parasternal long axis
PSAX	:	Parasternal short axis

PeFH	:	Perifornical hypothalamus
PWD	:	Pulsed wave Doppler
RAP	:	Right atrial pressure
RCT	:	Randomized Control Trial
RR	:	Respiratory Rate
RV	:	Right ventricle
RVEDP	:	Right ventricular end diastolic pressure
RVEDV	:	Right ventricular end diastolic volume
RVLM	:	Rostral ventrolateral medulla
RWMA	:	Regional wall motion abnormalities
RWT	:	Relative wall thickness
SNS	:	Sympathetic nervous system
STE	:	Speckle tracking echocardiography
SA	:	Sino atrial
SAH	:	Subarachnoid Haemorrhage
SBP	:	Systolic blood pressure
SCTIMST	:	Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum
SPN	:	Sympathetic preganglionic neurons
SUDEP	:	Sudden unexplained death in epilepsy
SV	:	Stroke volume

TAPSE	:	Tricuspid annular plane systolic excursion
TBI	:	Traumatic brain injury
TDI	:	Tissue Doppler imaging
TOF	:	Train of four count
TTE	:	Transthoracic Echocardiography
TV	:	Tricuspid valve
UO	:	Urine output
VT	:	Ventricular tachycardia
VF	:	Ventricular fibrillation
2D	:	Two dimensional
3D	:	Three dimensional

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES:

Abstract

Introduction

In patients presenting with primary brain tumours, the ICP rises gradually. Acute rise in ICP has been shown to affect the cardiac functions due to brain ischemia and the associated increased sympathetic activity or in severe cases sympathetic storm. However in situations like slow progressive increase in ICP, the effects of ICP on cardiac function have not been studied. We hypothesized that in patients presenting with primary brain tumours, with features of gradual increase in ICP, there will be impairment of cardiac function ; which will be reversed once ICP is normalized after the neurosurgical procedure. We aimed to assess and compare the cardiac functions using transthoracic echocardiography in patients with brain tumors presenting with and without raised ICP for neurosurgery.

Materials and methods:

In this prospective observational study, we included 60 patients; Group 1 (30 patients without features of raised ICP) and Group II (30 patients with features of raised ICP). Transthoracic echocardiography was performed on the day before the surgery and the seventh postoperative day. Hemodynamic, electrocardiographic and echocardiographic parameters were collected during pre, intra and postoperative period and was used for statistical analysis.

Results:

We found increased left ventricular wall thickness, increased incidence of systolic (22%) and diastolic dysfunction (33. 3%) along with ECG and hemodynamic changes in Group II compared to Group I patients. There was an increased incidence of

intraoperative adverse events such as post-induction hypotension and vasopressor use in patients with raised ICP. Post neurosurgery, there was an improvement in the systolic function, whereas chamber dimensions and diastolic dysfunction did not improve significantly.

Conclusions:

Our study suggests that raised ICP might contribute to the pathophysiology of sympathetic over-activity and sympathetically-driven cardiac dysfunction, which does not entirely revert in the immediate postoperative period.

Introduction

Brain injury or alterations in the cerebral physiology can result in multi-organ dysfunction. This is due to the influence of the brain on the control of various organ systems of the body. The effects of the injured brain on alterations in the cardiovascular system has gained significant attention in the emerging field of Neurocardiology. (1) It represents an example of organ cross-talk or neurovisceral damage in general wherein the nervous system causes pathological influences on various systems of the body. There has been extensive literature on the complex heart-brain relation in the background of various neurological catastrophes such as aneurysmal subarachnoid haemorrhage (SAH), acute ischaemic stroke (AIS), intracerebral haemorrhage (ICH) and status epilepticus or epilepsy in relation to sudden unexplained death in epilepsy (SUDEP). (1–5) The impact of resultant cardiac dysfunction as a deleterious secondary insult to the brain could adversely affect the prognosis of neurosurgical patients.

There is substantial evidence which signposts towards sympathetic overactivity as the common phenomenon which links various cardiac manifestations seen in neurological catastrophes. Shivalkar et al. studied canine models of increased intracranial pressure and demonstrated a 1000-fold increase in serum levels of epinephrine after brain death. The same study explored the variable effects of rapid Vs slow rise in ICP on the myocardium. Cardiac histology in the dogs that had an acute rise in ICP revealed substantial pathologic myocardial ischemia. In contrast, canines that had a gradual increase in intracranial pressure showed a lesser increase in serum epinephrine levels. (6) Similarly, transmurally scattered foci of myocardial injury were found in patients dying from acute intracranial lesions large enough to produce acute increases in ICP such as intracranial bleeding and massive ischaemic oedema. These cardiac lesions weren't found in slowly progressive tumours, unless additional factors such as

haemorrhage into a tumour or inflammatory oedema, superimposed an acute rise in ICP. It is generally perceived that in patients whom ICP raises slowly, significant clinical cardiac effects are not seen. Only when the intracranial compliance is reduced, acute rises in ICP is commonly manifested as bradycardia or hypertension. (2,7,8)

The research on heart-brain interactions in the setting of pathological conditions producing an acute rise in ICP such as SAH, AIS, ICH is overwhelming; but, there is a lacuna of literature in the setting of raised ICP in brain tumours. Patients with chronically raised ICP, especially with primary brain tumours undergo surgery for the removal of the lesion. Any subtle cardiac dysfunction can adversely affect the perioperative course and hence is of utmost relevance for the neuro anaesthesiologists managing the patients. Thus, it is pertinent to understand the brain-heart interactions in conditions like brain tumours causing an increase in ICP, so as to enable us to manage these conditions effectively. A well-planned study will address this issue to fill up the existing lacuna in literature. Hence, we decided to conduct a prospective observational study to assess the impact of raised ICP on cardiac function, in patients with primary brain tumours presenting for tumour decompression.

Reversibility of cardiac dysfunction has been studied in the context of heart transplantation after brain death. (8) Many studies show evidence of improvement of cardiac function after the heart was removed from this environment and transplanted. (7–10)This gives us insight into the mechanisms of reversible forms of cardiac injury wherein removing the initiating neurological insult can result in the recovery. We hypothesized that similarly, if the milieu of intracranial hypertension is removed by neurosurgical procedures, the cardiac dysfunction seen in such conditions will resolve. This study to our best knowledge is the first one which has evaluated the

cardiac function in patients with supratentorial brain tumours who had evidence of intracranial hypertension.

Review Of Literature

Intracranial pressure (ICP): Background and pathophysiology

Monroe and Kellie, centuries ago, proposed the concept of intracranial pressure as a function of the volume and compliance of each component of the intracranial compartment. (11) It states that, once the fontanelles have closed, the incompressible intracranial contents, comprising the brain tissue,blood, and cerebrospinal fluid(CSF)are contained within the rigid skull, and they create a mildly positive pressure called Intracranial pressure(ICP). (12)

The contents are in a state of volume equilibrium where a volume change in one component should be compensated by the volume change in the other. When decompensation occurs, an increase in ICP ensues. In this context, the interaction of the intracranial components in the clinical setting of an expanding, intracranial tumour. This formed the basis for the description of the clinical stages of raised ICP [Table 1] [Figure1]. As previously described, an initial increase in tumour volume is compensated for by a reduction in the volume of blood and CSF, resulting in no increase in ICP. This phase is the stage 1. However, as these compensatory mechanisms become exhausted ICP starts to rise slowly. This phase, called stage 2 is where clinical symptoms begin to manifest [Table 1]. In stage 3, the compensatory mechanisms are exhausted such that even a small increase in the volume results in a substantially large rise in ICP. When the intracranial pressure increase to the values of mean blood pressure, there is a drastic reduction in cerebral perfusion pressure, ultimately resulting in ischemia which can manifest clinically as coma and, ultimately, death.

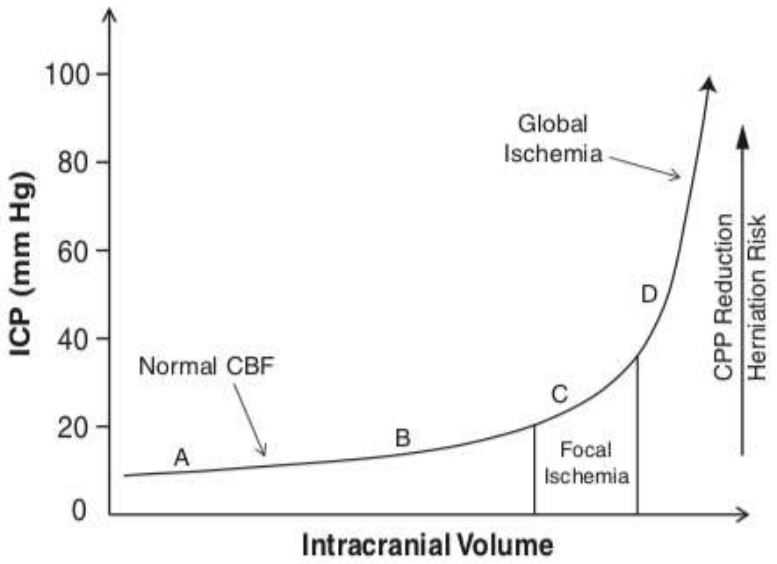


Figure 1: Schematic diagram of the intracranial pressure (ICP)–volume relationship (elastance). An initial increase in intracranial volume (A to B) is compensated by a minimal increase in ICP, but as elastance decreases there is a transition from minimal increase to a marked increase in ICP (C to D) for even small increases in intracranial volume. Any further increases in ICP result in decreased cerebral perfusion pressure (CPP), global ischemia, and herniation.

Stages	Intracranial response	Clinical symptoms and signs
1	Compensation phase	None
2	Exhausted buffering mechanisms; slow increase in ICP; cerebral perfusion maintained	Headache, nausea, vomiting
3	Fast and large increase in ICP ; compromised cerebral perfusion	Altered sensorium, Cushings response
4	Cerebral vasomotor paralysis, ICP increase to values of MAP.	Dilated fixed pupils, deeply comatose and ultimately death

Table 1: Stages of development of intracranial hypertension

The causes of raised ICP can be summarised by the 'four lump' concept. The intracranial pathologies precipitating the rise can cause an increase in the volume of brain tissue, CSF and blood along with cerebral oedema [Table 2]. If we take the example of a supratentorial mass lesion, in the majority of cases the pathology is localized and, together with surrounding cerebral oedema, it produces the compression and distortion of the adjacent brain which ultimately leads to herniation and pressure gradients between CSF spaces. Coincident with this, the cerebral perfusion may be compromised by direct compression of cerebral blood vessels. This exacerbates the vascular compromise as a consequence of a decrease in cerebral perfusion pressure subsequent to increased ICP. Hence the ultimate consequence of increased ICP is both localized and diffuse ischaemic damage of the brain.

Intracranial compartment	**Mechanism**	**Example**
Brain tissue	Mass effect	Brain tumour, intracranial hemmorhage
	Cerebral edema	Vasogenic edema by brain tumours, Traumatic brain injury(TBI)
Blood volume	Cerebral venous hypertension	Cerebral venous sinus thrombosis
Cerebrospinal fluid	Obstruction of cerebrospinal pathways	Obstructive hydrocephalus by tumour, congenital anomaly
	Increased CSF production	Meningitis, choroid plexus papilloma

Table 2 : Causes of raised intracranial pressure

Effects of raised Intra Cranial Pressure on sympathetic activity and cardiac function:

The Cushing response:

The Cushing response/phenomenon is a physiological response to acute and large increase in ICP. The response elicits the Cushings triad of hypertension, bradycardia and irregular breathing. It is traditionally believed to be due to ischemia of the brain-stem inducing sympathetic overactivity. The massive intrinsic activation of the sympatho-excitatory neurons of the ventrolateral medulla is believed to be the mechanism of this terminal response. (2,13–15) Fitch et al. described the sequence of events from the start of a rise in ICP. The hypertensive component was identified as the last of six events which included bradycardia, arrhythmia, pupillary constriction, unilateral pupillary dilatation and systemic hypertension. The traditional school of thought was that it was an agonal and terminal event followed by circulatory failure. (16)

The recent evidence of physiological role of Cushing response:

It is recently postulated that the systemic vascular response, rather than being a reflex, is a “last ditch” protection for maintaining cerebral perfusion. Plets et al in their study found that a drop in the cerebral perfusion precedes the development of plateau waves in the setting of rising ICP. After the reduction in CPP, the Cushings response was then observed 5 to 15 seconds following which there was abolition of these plateau waves. They concluded that the Cushings response is beneficial in restoring cerebral perfusion. (17)

Schmidt et al. , induced intracranial hypertension in patients with normal pressure hydrocephalus, and demonstrated that the increase in ICP was followed by systemic hypertension which diminished the magnitude of the drop in cerebral perfusion pressure. They also found that there was an increase in heart rate variability indicating change in sympathetic nervous system(SNS)(15).

Mechanisms of Cushing response:

Cushing response may result either from a baro-sensitive or a chemo-sensitive mechanism.

The baro-sensitive mechanism is supported by the presence of pressure- sensitive areas in the brainstem which is identified as the rostroventral medulla. Mechanical stimulation of the same yields a systemic vascular response like Cushings response. (15,18,19) This pressure-sensitive mechanism is also consistent with the concept of "neurogenic" origin of hypertension since mechanical compression of the lateral part of the medulla can play a role in ABP elevation. The fact that Cushing response is rapid, with latency of only one second between the onset of direct intracranial compression and systemic vascular response. The chemo-sensitive hypothesis postulates that hypoxia activates sympathetic outflow through direct effects on the brainstem.

In the clinical setting of brain tumours, the causality of raised Intracranial pressure causing autonomic dysfunction has not been extensively studied. Recently, Koszewicz et al assessed the autonomic dysfunction profile of patients with primary brain tumors. (20) Besides conducting neurological examinations and the Low's autonomic disorder questionnaire; electro- physiological autonomic tests were

performed in patients with recognized primary brain tumours. The averaged Low's Questionnaire score, SBP and HR was increased in the tumour group compared to control. Interestingly, HRV was severely low with higher LF/HF ratio in the patients. The results of the study indicates that in patients with primary brain tumours, sympathetic overactivity was present. The authors suggested that high intracranial pressure could be a plausible factor in the pathogenesis of dysautonomia.

The effects of acute rise in intracranial pressure on cardiac function has been evaluated in experimental and clinical settings. Shivalkar et al induced brain death in dogs by inflating saline into epidural Foley catheters at different rates that produced an explosive rise in ICP or a gradual rise in ICP. A sudden rise in ICP yielded a 1000-fold increase in level of epinephrine and more area of myocytolysis and necrosis whereas a gradual rise in ICP yielded only a 200-fold increase. (6)

Novitzky et al. , inflated an intracranial Foley catheter balloon in the baboon animal model,to produce an increase in ICP which is associated with catecholamine surge and brain death. The total study population was divided into three groups: group A (control), group B (total denervation of the heart), and group C (incomplete denervation of the heart). The results were similar in the control and incomplete heart denervation group, but the complete heart denervation group showed a modified hemodynamic response and normal myocytes. (21)An intact vagal supply to the heart did not appear to have a role, since myonecrosis still occurred following vagotomy, but can be completely blocked by cardiac sympathectomy or denervation. Since myonecrosis still occurred following bilateral adrenalectomy, circulating catecholamines do not appear to be the crucial mediator of neurogenic cardiac injury,

but rather suggest that local release of norepinephrine from myocardial sympathetic nerve terminals is key in the pathogenesis of cardiac dysfunction.

Ferrera et al. , who evaluated the acute changes in myocardial function of Wistar rats with raised ICP. (22) LV chamber dimensions and fractional shortening at baseline, during and after BD induction was measured with echocardiography. In control group, an increase in wall thickness and a decrease in LV cavity dimension was noted. This was completely prevented in the group treated with beta-blockers, but not in other groups. Extensive myocardial interstitial edema was also found in all groups, except in the beta-blocker group. The echocardiographic results of their study is well explained by the finding of myocardial interstitial edema in histology. They concluded that brain death associated autonomic storm is associated with interstitial myocardial edema leading to myocardial wall hypertrophy. Schmidt et al. , demonstrated that a modest 7 mmHg ICP rise significantly increases sympathetic activity by 17% without any change in arterial blood pressure[Figure 2]. (18)

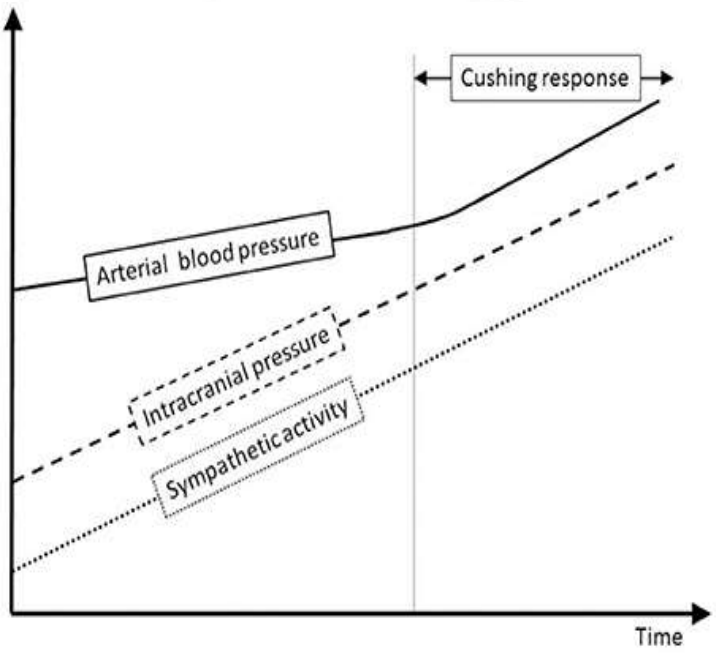


Figure 2: The schematic figure to display hypothesis proposed by Schmidt et al, about the interplay between ICP and sympathetic activity and ABP. Modest ICP increase augments pari passu sympathetic activity that parallels the ICP rise, but has a mild influence on ABP. For higher ICP values, the increase in sympathetic activity yields the Cushing response.

Similar or higher ICP increases are encountered in various pathological conditions such as head trauma, hydrocephalus, stroke and subarachnoid haemorrhage. After neurological injury, sympathetic over-activity is reported with increased risk of cardiovascular complications and poor outcome(detailed description in following paragraphs). Takotsubo cardiomyopathy, an acute heart failure attributed to a surge in catecholamine levels, is reported after intracranial haemorrhage with intracranial hypertension. (23,24) In chronic conditions, the exact role of ICP rise on sympathetic overdrive has to be addressed. (5)There is a paucity of studies regarding same.

Neuro-cardiology

"Neurocardiology," which is a relatively recent interdisciplinary field, examines the interaction between the cardiovascular and autonomic nervous systems in pathological states. (1) Neuro-cardiology with its many facets can be divided into three major categories: the heart's effects on the brain (for e. g. , an embolic stroke due to atrial fibrillation), the brain's effects on the heart (e. g. , neurogenic cardiomyopathy after primary brain injury), and neurocardiac syndromes such as Friedreich disease. (4,5,24)

History of the evolution of neuro-cardiology:

Since 1942 when Walter B. Cannon narrated about death from fright in his paper' Voodoo Death', the learning about the brain-heart connection has taken giant leaps. (25) Richter, in his experiments to elucidate the mechanism of "voodoo" death, made an incidental discovery of an epidemic of sudden death in rats whose whiskers were clipped. Their assumption was that intense stress had resulted in the sudden death. (26)

Electrocardiogram(ECG) is an easily available window into autonomic activity. Byer and colleagues reported six patients whose ECGs showed large upright T waves and long QT intervals and they concluded that these ECG changes were caused by subendocardial ischemia. (27) Burch and colleagues in their report on patients with stroke showed that patients had ECG abnormalities which were long QT interval, inverted T waves and U waves. (28) Cropp reported on the ECG abnormalities in patients with subarachnoid haemorrhage, and they concluded that ECG changes in patients' with the neurological disease are due to autonomic dysregulation rather than a manifestation of ischemic heart disease. (29)

By this time, the assumption made was that cardiac effects due to neurological conditions are due to autonomic dysregulation. In rats, cardiac lesions were produced with either fluorocortisol, calciferol, or thyroxine and the animals were restrained or stressed with cold. The agents that inhibited catecholamine-mobilizing reflex arc at the hypothalamic level or the ones which blocked only the circulating catecholamines were not protective of cardiac muscle, wherein ganglion blockers or direct intramyocardial catecholamine depletors were effective. The concept that catecholamines released directly into the heart via neural connections causing catecholamine toxicity were supported by data. (30) Adrenaline, when infused inside the coronary vessels, produced the characteristic ECG pattern of neurocardiac lesions and subendocardial ischemia, though no ischemic lesion could be found. (31)In the following years, reports of cardiac repolarization abnormalities in the backdrop of brain injury came from around the world.

The involvement of the autonomic nervous system was further elucidated by many studies. Melville et al. found that stimulation of the hypothalamus of cats produced ECG changes and myocardial necrosis. (32) Anterior hypothalamic stimulation

produced parasympathetic responses in the form of bradycardia, and lateral hypothalamic stimulation caused sympathetic responses in the form of tachycardia and ST-segment depressions. Intense bilateral and repeated lateral stimulation caused contraction band necrosis.

The fact that myocardial damage could occur not just in animals but also humans was shown by Koskelo et al. , in the 1960's who reported ECG changes and subendocardial petechial haemorrhages in patients with subarachnoid haemorrhage. (33) Focal myocytolysis, especially in patients who suffered fatal intracranial haemorrhages, was further reported by Connor. (34)

Greenshoot et al. also reported similar cardiac lesions in patients with SAH but also found that adrenalectomy did not protect the heart which corroborated the assertion that the ECG changes and cardiac lesions are due to direct intracardiac release of catecholamines. (35)

The next scientific question was how we could prevent or modify cardiac lesions. Hunt, who pre-treated a group of rats with propranolol found a decreased incidence in the treated rats, which suggested that the effect of ANS via catecholamines may be responsible for cardiac cell death. (36) Studies have found a correlation of myocardial necrosis with Hunt-Hess grading system for subarachnoid haemorrhage with higher grades being more prone for cardiac effects. (37)

BASIC ANATOMY, PHYSIOLOGY AND PATHOLOGY OF NEUROCARDIOLOGY

The relevant anatomy and physiology of the structures in the CNS and its connections to the cardiovascular system prior to the discussion of pathologic processes are

presented here. The importance of ANS, which modulates heart rate, conduction velocity and cardiac contractility is profound.

Heart to the brain: Cardio-regulatory sympathetic pathways (the hypothalamic-pituitary-adrenocortical and sympatho-adrenomedullary axes) enable the cardiovascular function to adapt to different challenges that result in neuroendocrine changes, including an increase in epinephrine and norepinephrine levels. (38)

The cardiovascular system has afferent connections which begin with chemo & baroreceptors and the ascending information transmitted by glossopharyngeal and vagus nerves. The information relays on the nucleus of the solitary tract(NTS), dorsal vagal nucleus, and the parabrachial nucleus. The afferent pathways continue to the central nucleus of the amygdala, hypothalamus, prefrontal cortex, as well as ventral basal thalamus. the paraventricular nucleus of the thalamus and The prefrontal cortex and have connections to the insular cortex of both hemispheres. (2)

Brain to heart: The insula has significant efferent projections which project to the infralimbic cortex, medial dorsal nucleus of the thalamus, NTS and the amygdala and ultimately to the sympathetic preganglionic neurons in the spinal cord via the ventral lateral medulla. The descending pathway continues finally to the cardiac plexus along with the SA node and AV node[Figure 3]. (4)

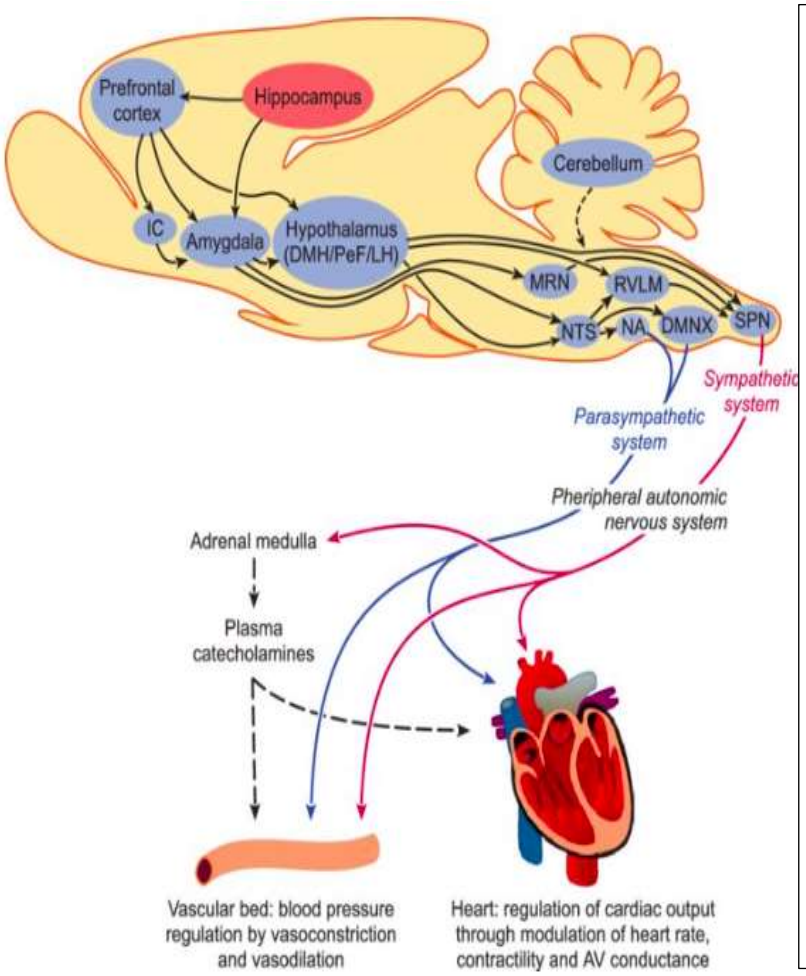


Figure 3: Central autonomic network(CAN); Blue ellipses denote brain areas that are part of the central autonomic network, whereas the hippocampus (red ellipse) is implicated in cognitive modulation of the CAN. The blue line indicates parasympathetic system to the vascular bed. Besides fast neural regulation via central and peripheral autonomic pathways, slower stress hormone release (catecholamines from the adrenal medulla) also contributes to cardiovascular regulation. AV: atrioventricular; DMNX: dorsal motor nucleus of the nervus vagus; DMH/PeF/LH: dorsomedial/perifornical lateral hypothalamus; IC: insular cortex; MRN: median raphe nucleus; NA: nucleus

The parasympathetic system via the vagus nerve and the neurotransmitter acetylcholine causes bradycardia and decreased contractility, whereas the sympathetic system via noradrenaline causes tachycardia and increased contractility.

Studies have demonstrated a component of laterality in arrhythmias and repolarization abnormalities as well as troponin elevations. (39) For example, stellate (sympathetic) blockades on the right cause bradycardia, which does not occur when the left is blocked. Also, right insular stimulation causes tachycardia and hypertension, whereas the opposite has been observed in a case of left insular stimulation. (40) Patients with neurovascular lesions such as stroke and haemorrhage often have elevated systemic

levels of catecholamines, especially so when the right insula is involved. Oppenheimer demonstrated that patients with right-hemisphere stroke have a higher incidence of cardiac arrhythmias and electrocardiogram (ECG) changes compared to left hemispheric stroke. (41)The increased parasympathetic tone in the left insular stroke-causing bradycardia and asystole. The insula is involved in approximately half of the middle cerebral artery (MCA) stroke and additionally close anatomic relationship to the insula in mesial temporal lobe epilepsy may in part explain why it is posited that some cases of sudden death in patients with MCA stroke and epilepsy have a cerebral arrhythmogenic origin.

A dysautonomic imbalance between the parasympathetic and sympathetic nervous systems and catecholamine toxicity occurs with the neurologic insult and may predispose patients to repolarization abnormalities as well as premature ventricular beats and other arrhythmias which could lead to malignant arrhythmias, with SCD as a potential outcome. (5) Pathologic disruption of neurocardiac axis causes various manifestations such as subendocardial ischemia, malignant arrhythmias and neurogenic stress cardiomyopathies(NSC) which are most commonly described in aneurysmal SAH, ICH and AIS. (2)

MANIFESTATIONS OF CARDIAC DYSFUNCTION IN NEUROCRITICALLY ILL PATIENTS

ECG changes:

Common cardiac manifestations include arrhythmias and repolarization abnormalities. Lavy et al. , prospectively followed patients with stroke with and without comorbid cardiac disease and described new-onset sinus bradycardia, nodal bradycardia,

supraventricular extra- systolic beats and tachycardia, atrial fibrillation (AF), atrial flutter, and complete AV block. (42) Goldstein reported rates of ECG abnormalities and arrhythmias in stroke patients (IS, ICH, and SAH) and most common were prolonged QTc, tachycardia, and other arrhythmias. (43) Kallmuenzer et al. reported that approximately 25% of patients admitted with a diagnosis of acute stroke had an arrhythmia of which AF was the most prevalent arrhythmia detected in 11% of patients, focal atrial tachycardia in 3%, supraventricular tachycardia in 2%, type II AV block in 2%, SA block in 2 patients, ventricular ectopy in 1%, nonsustained VT in 1%, atrial flutter in under 1%, and complete AV block in less than 1%. (44)

The prognosis of patients with acute neurovascular diseases has been demonstrated to be significantly worsened by the presence of an arrhythmia. Mortality in all patients was increased by 80% when a "malignant" ventricular arrhythmia was detected. Other ECG changes such as prolonged QTc and ventricular extrasystolic beats have also been demonstrated to lead to worse outcomes. (45)

In the perioperative period, serum electrolytes should be maintained at normal levels, with special attention to magnesium and potassium. This is imperative to minimize contributions of dyselectrolytemia to arrhythmias and repolarization abnormalities of neurocardiac aetiology, and detected arrhythmias should be managed appropriately.

Sudden cardiac death:

Tachyarrhythmias such as ventricular fibrillation (VF) and ventricular tachycardia(VT) and bradyarrhythmias such as sinus bradycardia, complete AV block and asystole can lead to sudden cardiac death. Prolonged QTc is a risk factor for torsades de pointes and subsequent VF and sudden cardiac death. The neurologic

condition most classically associated with sudden death in epilepsy. Sudden death in epilepsy(SUDEP) is defined as an unexpected sudden death in a patient with epilepsy who has no evidence of a secondary cause. Acute cardiac arrest and sudden death have also been described in Subarachnoid haemorrhage(SAH) and stroke. (4,5,23)

Cardiac enzyme changes:

Troponin, which is known to be a sensitive marker for cardiac injury, has been found to be elevated in patients with SAH and stroke, though it has not been associated with any underlying cardiac disease. Ay, et al. detected changes on ECG suggestive of cardiac ischemia in only 2 of 10 patients with high troponin levels. (7,46) Patients with troponin elevations have been found to be at greater risk for the development of arrhythmias. Raza et al. found that elevated troponin levels were significantly associated with adverse cardiac events. B-type natriuretic peptide (BNP) is found to be sensitive though not a specific marker in the evaluation of cardiac status in patients with neurovascular pathologies. (47)

Neurogenic stunned myocardium

Neurogenic stunned myocardium, which is a part of the stress-related cardiomyopathy syndrome spectrum, is myocardial dysfunction due to the stress of catecholamine excess, which is triggered by an acute neurological injury. (5,23,48,49)

Takotsubo cardiomyopathy

Takotsubo cardiomyopathy, similar to stunned neurogenic myocardium is a part of stress-related cardiomyopathy syndrome. It mimics an acute coronary event, and echocardiography shows transient left ventricular regional wall motion abnormalities.

There are apical and mid-ventricular hypokinesia and basal hyperkinesia. The regional wall motion abnormalities and electrocardiographic changes extend beyond a single epicardial coronary artery's territory of distribution which helps differentiation from myocardial infarction. (38)

Reversibility of cardiac dysfunction:

Although usually transient and reversible and, thus, requiring only supportive treatment, the clinical course of Neurogenic stress cardiomyopathy (NSC) can be severe, with hypokinesis, akinesis, or dyskinesis of the left ventricle and can be detrimental, especially if occurring in the acute phase of an acute brain injury, when maintenance of systemic homeostasis is mandatory to reduce secondary brain injury. (5,6,9,23)

Haemodynamic instability, arrhythmias, cardiogenic shock, pulmonary oedema, and sudden cardiac death are the main concerns in the management of these patients in the Neuro ICU and in the perioperative setting because these complications occur more frequently than previously suspected. The clinical presentation may be similar to an acute myocardial infarct, and the ejection fraction may decrease significantly. (50) LV dysfunction with impaired haemodynamics and possible embolization from LV mural thrombus formation in those with apical involvement may jeopardize cerebral blood flow and induce ischaemic brain damage. Dynamic LV outflow tract obstruction may be evident when a small LV becomes hypercontractile, especially in the basal segments. (5,6,9,23)

Insights from cardiac transplantation:

The unique setting of brain death, followed by cardiac explantation for the purpose of transplantation allows us to gain insight into the effect of the extra-cardiac milieu upon the heart.

In 2000, Deibert et al. presented a case report in which a patient with subarachnoid haemorrhage and brain death was initially refused as a heart donor for diffuse myocardial dysfunction and elevated cardiac troponin I; however, after a normal cardiac catheterization, the heart was transplanted with good results. They postulated that cardiac dysfunction in such cases is reversible. (51) Potapov et al. evaluated the value of cardiac troponin I and cardiac troponin T for selection of heart donors and as predictors of early graft failure. They found that hearts with more elevated cardiac troponin I and troponin T had subsequently impaired graft function once explanted. (10). Goel et al. reported a case of cardiac transplantation where, despite the presence of ventricular dysfunction, the heart was transplanted to a recipient successfully with complete recovery of ventricular function in the late postoperative course. This gives us insight into the mechanisms of reversible forms of cardiac injury wherein removing the initiating neurological insult can result in the recovery (8)

TRANSTHORACIC ECHOCARDIOGRAPHY

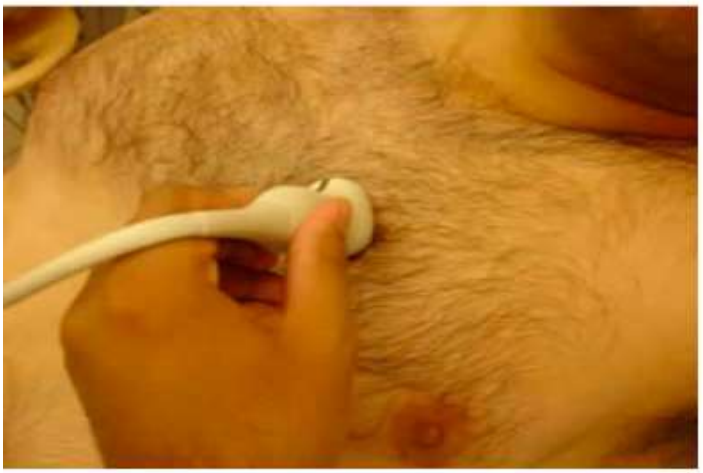
Echocardiography (ECHO) is the basic non-invasive imaging method in cardiology, which is capable of detailed assessment of heart morphology and function, employing a variety of methods (2D (two-dimensional) imaging, M-mode, colour Doppler mapping and measurement of blood flow velocity, tissue Doppler imaging, stress test and contrast examination, three-dimensional imaging). Echocardiography does not

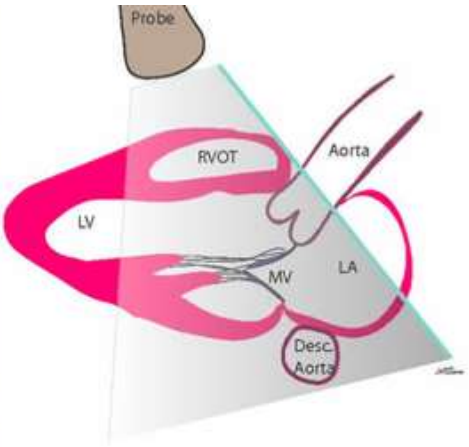
stress the patient, it is repeatable, well reproducible and repeated measurements allow the dynamics of monitored parameters to be compared and assessed. (52,53)

Fundamentals for the measurement of structure and systolic function of the left ventricle(54)

ASE (American Society of Echocardiography) recommendations are used for the imaging respecting the leading-edge to leading-edge principle, i. e. the marker placed at the front of the measurement interface. In 2D imaging, essential are subcostal, apical (four- chamber) and parasternal projections. These projections are used to assess left ventricular morphology, wall kinetics, endocardial state, morphology and the movement of the mitral valve leaflets, chordae and papillary muscles, outflow tract, aortic root and aortic valve. After the basic assessment, the recommended projections are continued by examining the left ventricle in the parasternal long axis [Figure 6], measuring various parameters using the M-mode. (53)

Parasternal Long axis(LAX) view: Figure





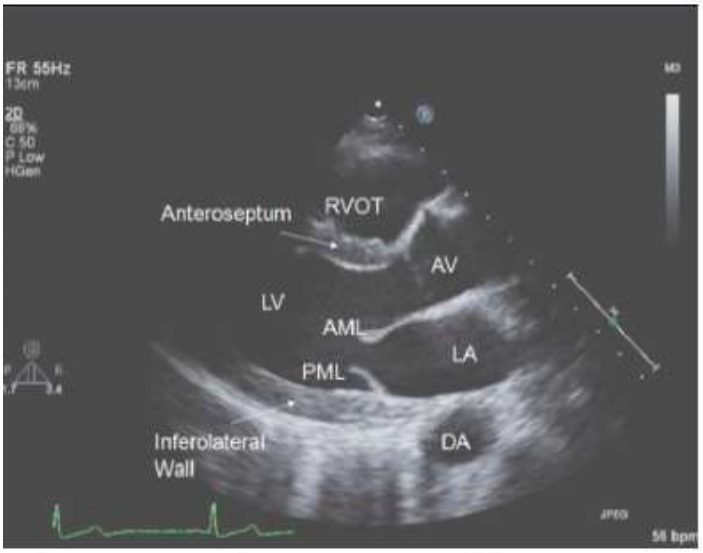


Figure 4,5,6: Parasternal long axis view

The transducer is placed 2-3 inches to the left of the sternum in the 4th or 5th rib interspace. The notch on the transducer should be facing towards the 10 o'clock position toward the right shoulder. From this position, the standard view can be obtained. By manipulating the tip of the transducer, the RV inflow view and PA long axis view can also be obtained

.

RVOT:right ventricular outflow tract, AV: aortic valve, LV: left ventricle, AML: anterior mitral leaflet, PML: Posterior mitral leaflet, DA: descending aorta, LA: left atrium

M-Mode measurement in parasternal long axis (PLAX) view:

The M-mode is the basic method for the assessment of the left ventricle: it is used to measure the thickness of the septum and posterior wall, and left ventricle size, all in cardiac diastole and systole [Figure 7]. The cursor is placed perpendicular to the interventricular septum below the mitral valve leaflets and above the peaks of the papillary muscles The patient is connected to ECG, diastolic measurement is made at the beginning of the QRS complex (onset of the R wave), systolic measurement when backward movement of the ventricular septum is at its maximum.

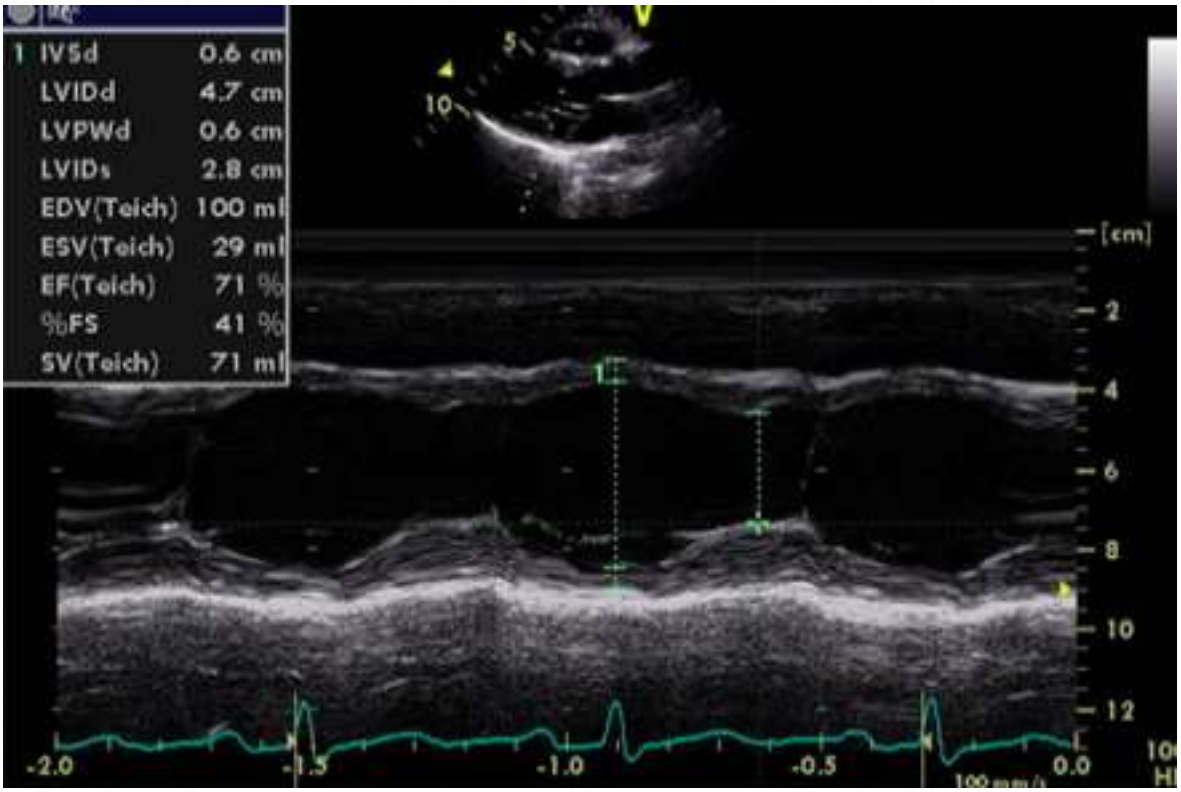


Figure 7: M mode echocardiography showing the structures and the evaluation of LV systolic function.

The measurement also includes the assessment of systolic function. The assessment mainly uses the calculation according Teicholz, resulting in ejection fraction values

(EF, normal values 0. 6–0. 8) and fractional shortening of muscle fibre (FS, normal values 0. 26–0. 45). To assess the left ventricular geometry, the parameter RWT(relative wall thickness) is used. (55)

Parasternal Short Axis view:

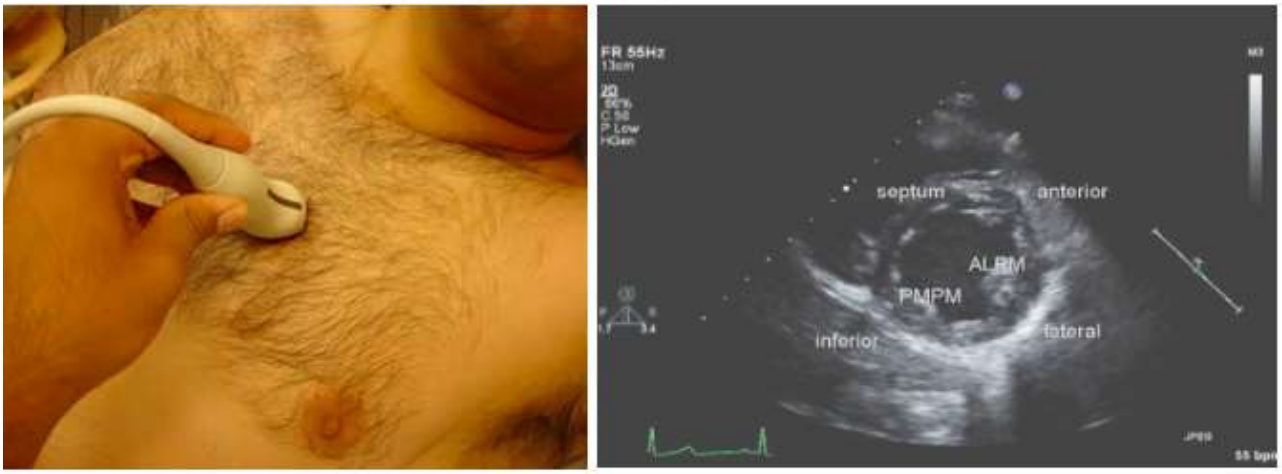
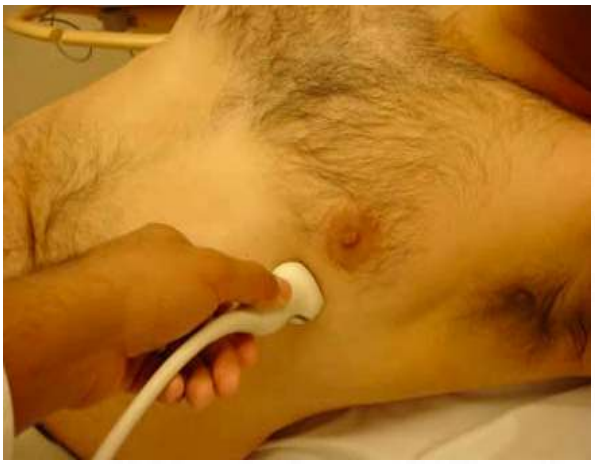


Figure 8: Transducer position to obtain the short axis view; the probe is turned clockwise. Typically the probe marker is now oriented at 2 o'clock (toward the patient's left shoulder). From here, tilting probe handle up and down allows one to scan up and down the ventricle to obtain apical and basal views. The mid ventricle level is identified by the presence of the two papillary muscles, which should not be confused for masses or thrombus. ALPM - anterolateral papillary muscle. PMPM - posteromedial papillary muscle.

Apical View



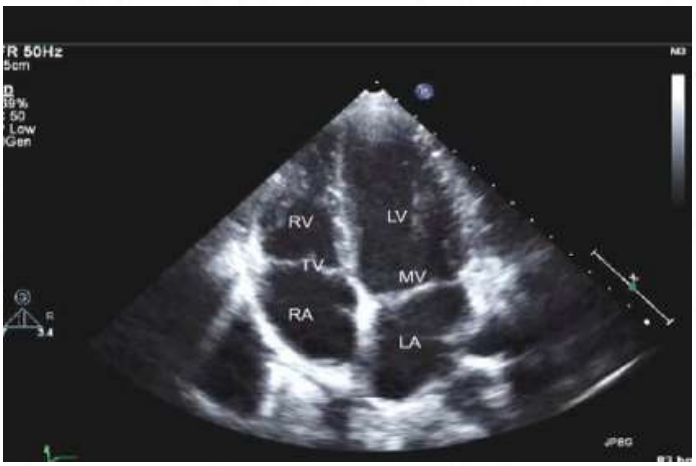


Figure 9: Apical view :are obtained by placing the transducer at the point of maximal impulse. The 4 chamber view is usually obtained first with the probe indicator at 3 o'clock (toward the patients left side).

To assess the volumes and function of the left ventricle, there are many 2D measurement equations, wherein the most commonly used one being the disc summation method (Simpson's rule). The assessment of structure, overall functionality and haemodynamics are detailed below. (52–54,56,57)

Colour Doppler mapping, and pulsed and continuous Doppler measurements are used to analyse the flows through the various valves and to evaluate their possible incompetence or stenosis. Pulsed Doppler measurement may be used to assess

transmitral flow to the left ventricle and the pulmonary veins flow in the examination of diastolic left ventricular function. Tissue Doppler imaging can be used when assessing the state of left ventricular contractility; the method analyses low-speed movement of the myocardium, is able to detect regional differences, assess regional systolic and diastolic dysfunction, and the global left ventricular function. (52,53,56)

ASSESSMENT OF GLOBAL LEFT VENTRICLE SYSTOLIC FUNCTION

Assessment Of Changes In The Left Ventricle Volumes And Dimensions:

The measurements using M-mode and two dimensional echocardiography(2D) are used to measure left ventricular volumes and dimensions(58) The recommended calculations are as follows(59):

- Fractional shortening (FS)
- Fractional area change (FAC)
- Ejection fraction (EF)
- Stroke volume (SV) and CO.

FRACTIONAL SHORTENING (52,58,59)

The measurement of LV diameters are taken just below or at the tip of the mitral valve leaflets in the parasternal long axis(PLAX)view ,during diastole and systole. FS is thereafter calculated by the following equation.

$$\text{Fractional shortening(FS)} = ([\text{LVIDd} - \text{LVIDs}]/\text{LVIDd}) \times 100\%.$$

Where, LVIDd = left ventricular internal diameter at end diastole and LVIDs = LV internal diameter at end systole.

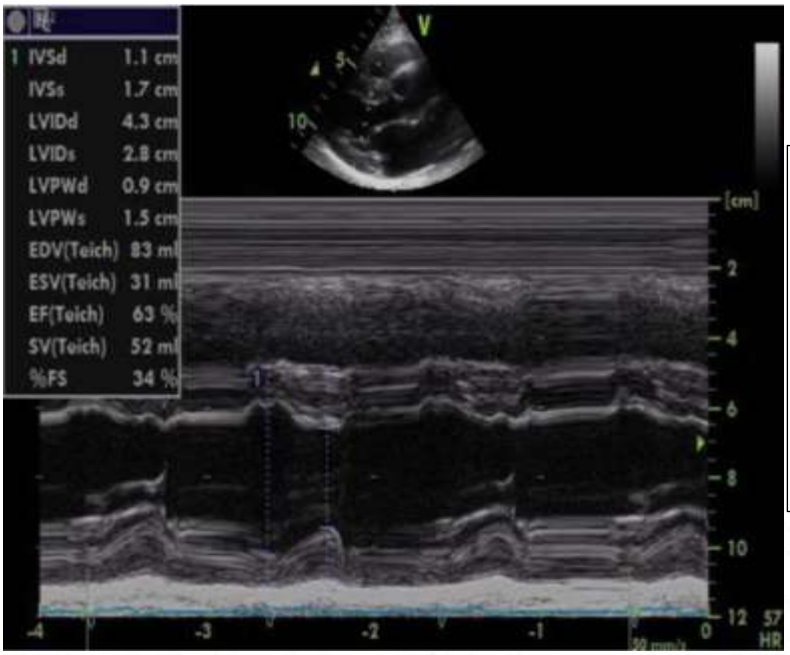


Figure 10: Fractional shortening measurement using M-mode echocardiography and ejection fraction calculated by Teichholz method

LEFT VENTRICULAR EJECTION FRACTION (53,59,60)

Left ventricular ejection fraction (EF) represents stroke volume as a percentage of end-diastolic volume.

$$EF = [SV/LVEDV] \times 100\% = [(LVEDV - LVESV)/ LVEDV] \times 100\%.$$

Where, SV -sytoke volume, LVEDV - left ventricular end-diastolic volume, LVESV - left ventricular end-systolic volume. (61)

BIPLANE SIMPSON'S METHOD OF MULTIPLE DISCS (53,61)

Biplane Simpson's method of multiple discs is the only method currently recommended by American society of echocardiography for the calculation of left ventricular volumes and ejection fraction using 2D echocardiography. This employs the principle of summation of twenty cylindrical discs of equal height, the diameter of which will vary depending on the shape of the left ventricular cavity. In the apical 2D view, the endocardial border is traced and connected at the mitral valve level by a

straight line. In the apical 4 chamber view, left ventricular volumes are measured at end diastole and end systole in both the planes and ejection fraction is calculated as described earlier.

Reference values of ejection fraction as measure of LV systolic function:

- Normal LV function - EF >55%
- Mild LV dysfunction – EF 45%–54%
- Moderate LV dysfunction – EF 30%–44%
- Severe LV dysfunction - EF<30%.

CARDIAC OUTPUT AND CARDIAC INDEX (53,60):

Left ventricular outflow tract is measured at the apical 4 chamber view. Pulsed wave doppler(PWD) is then used just below the aortic valve and velocity time integral(VTI) is calculated from the spectral display of the PWD. Velocity time integral represents the height of the column of blood which has passed through that particular area where the sample volume of the PWD is positioned during systole.

2D and Doppler echocardiography modalities can be used to calculate CO using the following formula:

- SV = (CSA(Cross-sectional area) × VTI (velocity time integral [VTI])
- CO = [stroke volume(SV) × HR (heart rate [HR])
- Cardiac index (CI) = Cardiac output (CO)/BSA (body surface area [BSA].

Systolic dysfunction in neurological conditions :

Systolic dysfunction has not been described previously in patients with supratentorial brain tumours, though there is substantial literature about the same in TBI, AIS, SAH. Neurogenic stress cardiomyopathy(NSC), as detailed above, has been extensively researched in the clinical settings of SAH, TBI, stroke, seizure and other neurological injuries. But isolated systolic function evidenced by depressed EF and FS has not been widely studied. Krishnamoorthy et al. , in their study in adult TBI patients, assessed systolic function and found that 22% of their patients had systolic dysfunction, and all patients with early systolic function recovered after one week. (62,63). Chronic systolic dysfunction has also not ben much described in neurological clinical settings though recent experimental studies indicate the same. (64) Bieber et al. in their study to determine the cardiac dysfunction due to focal cerebral ischemia, subjected mice to a 30-minute transient MCA occlusion and analyzed cardiac function by serial TTE for eight weeks after surgery. They found a reduction in EF and opined that chronic systolic dysfunction was due to increased sympathetic activity

DIASTOLIC DYSFUNCTION: Impaired LV relaxation and increased chamber stiffness leading to increased cardiac filling pressures can lead to LV diastolic dysfunction. (58) While performing TTE evaluation for patients with potential diastolic dysfunction, markers of impaired LV relaxation,increased chamber stiffness and left ventricular filling pressure should be measured.

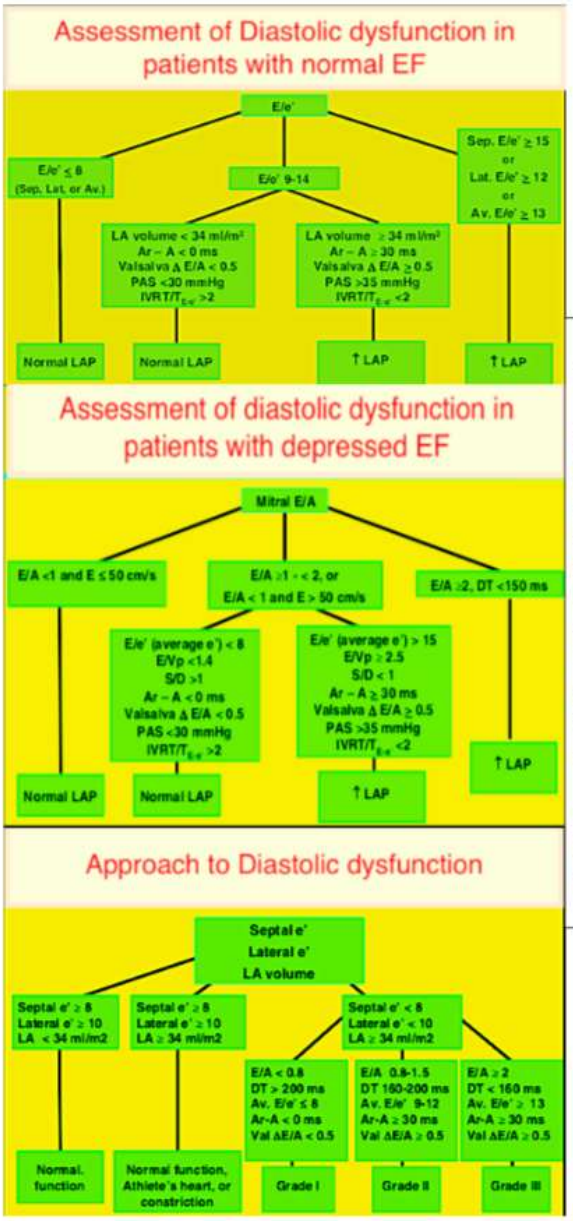


Figure 11:

A.Flowchart showing the assessment of diastolic dysfunction in patients with normal LV EF.

B.Flowchart showing the assessment of diastolic dysfunction in patients with depressed LV EF.

C.Flowchart showing grading of diastolic dysfunction

Diastolic dysfunction in neurosurgical conditions:

Kopelnik et al. studied prospectively 20 SAH patients, and diastolic dysfunction was observed in 71% of patients. (65) In their study, the prevalence of diastolic dysfunction was higher when the duration from onset of SAH increased. This was in contrast to the earlier time course of cardiac enzyme (troponin) release, and they

suggested that this might be because diastolic dysfunction is a more persistent form of neurocardiac injuries. The cause of this persistence of diastolic dysfunction over time is not completely understood. Similarly, in TBI patients, Krishnamoorthy et al. found a lower deceleration time in moderate to severe TBI patients. This suggested a restrictive filling pattern; however, they did not find an increased prevalence of diastolic dysfunction in their patients. Another study in TBI patients was by Cuisinier et al. performed conventional, and speckle tracking echocardiography and found that in severe TBI patients, diastolic dysfunction was slightly impaired. (66) In the TBI cohort, the isovolumic relaxation time was significantly higher compared to the control group. (125 s vs 107 s).

AIMS AND OBJECTIVES

Hypothesis:

In patients presenting with primary brain tumors, with features of gradual increase in ICP, there will be impairment of cardiac function ; which will be reversed once ICP is normalized after the neurosurgical procedure.

Aims And Objectives:

The aim of this study is to evaluate our hypothesis that in patients with gradual raised ICP, there is impairment of cardiac function and following normalization of ICP after neurosurgery, the cardiac changes will revert to normal.

Primary Objectives:

- To evaluate and compare haemodynamics and cardiac function with TTE, before and after neurosurgery; in patients presenting with primary brain tumours with and without features of increased ICP.

Secondary Objectives

- To study and compare the intraoperative hemodynamic parameters in the two group of patients(patients with and without raised ICP)
- To study and compare the intraoperative characteristics such as the requirement of vasopressors, fluid balance, brain relaxation in the two groups of patients (patients with and without raised ICP)
- To study and compare electrocardiographic changes in the two group of patients (patients with and without raised ICP)

Materials

&

Methods

STUDY DESIGN: Prospective Pilot observational study.

SETTING: Patients with primary supratentorial brain tumours admitted to Department of Neurosurgery at Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum (SCTIMST) which is a tertiary referral centre.

DURATION OF STUDY: 18 months from August 2018- January 2020

ENROLLMENT: The patients for the study were enrolled from elective neurosurgical operation list of SCTIMST.

RECRUITMENT: Recruitment was done by the Principal Investigator (PI) and the Guide. Patients presenting with primary supratentorial brain tumours admitted to neurosurgery wards of SCTIMST were screened for eligibility for the study based on the inclusion and exclusion criteria (subsequently described). After explaining study procedure, Patient information sheet (see Annexure) was provided to the patients and written informed consent (see Annexure) was obtained prior to recruitment.

Institute Technical Advisory Committee approval was obtained prior to conduct of the study vide TAC registration number: SCT/S/2018/759 dated 09. 07. 2018. Institutional ethics committee clearance was obtained prior to initiating the study vide approval number SCT/IEC/1242 dated 07/09/2018.

SUBJECT SELECTION:

For this prospective pilot observational study we enrolled sixty patients presenting for neurosurgery and randomised them to two groups.

a) Group 1 consisted of 30 adult male or female patients with supratentorial primary brain tumour and without clinical and radiological features of raised ICP, undergoing neurosurgical procedures.
b) Group 2 consisted of 30 adult male or female patients with supratentorial primary brain tumour and with features of raised ICP, undergoing neurosurgical procedures.

Pregnant women, Paediatric or Geriatric age group patients, Prisoners, Normal/Healthy volunteer, Student, Staff of the institute were not included in the study

Following are the inclusion and exclusion criteria for our study.

Inclusion criteria:

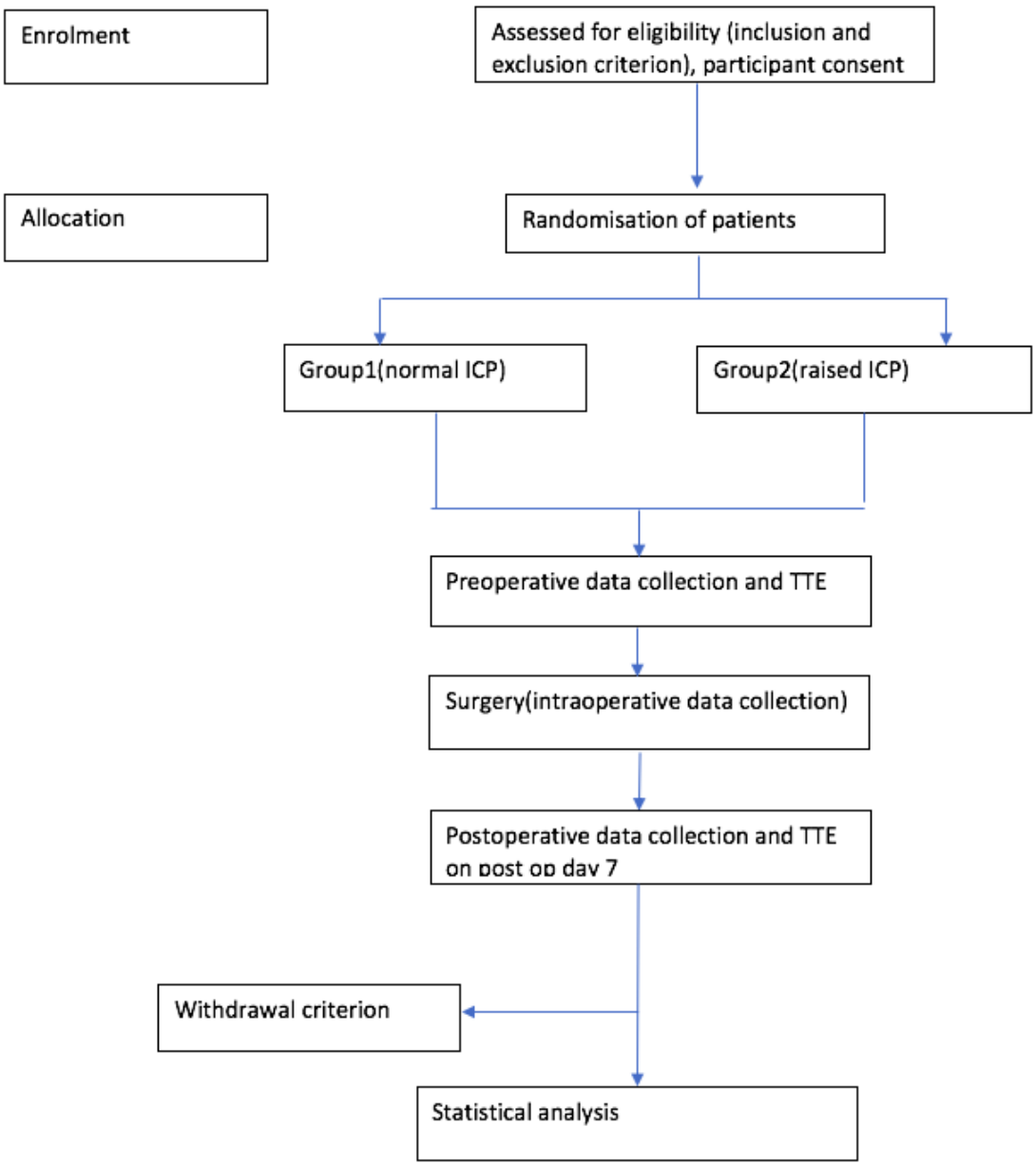
- Consenting adult patients with age more than 18 years undergoing neurosurgical procedures
- ASA (American Society of anaesthesiologists) 1 and 2 patients
- Age 18-60 years
- In group 1
    - Patients with symptoms and signs suggestive of raised ICP (headache, vomiting, papilledema)

  - Evidence of raised ICP in CT/MRI (such as cerebral oedema, midline shift > 5mm, hydrocephalus, grey-white matter effacement)
- In group 2
  - Patients with no symptoms and signs suggestive of raised ICP
  - No evidence of raised ICP in CT/MRI

Exclusion criteria

- Patient refusal.
- Age less than 18 years and more than 60 years.
- Diabetes mellitus Hypertension, Vascular diseases, Chronic obstructive pulmonary disease
- Known case of cardiac illness (coronary heart disease, valvular heart disease, congenital heart disease, congestive heart failure)
- Poor echo window
- Obesity
- American Society of Anaesthesiologists(ASA) 3,4,5 patients
- Patients with a prior history of chemotherapy or radiotherapy
- Pregnant & nursing mothers
- Patients with lesions in the prefrontal cortex, insula, hypothalamus, amygdala, hippocampus

A simplified consort diagram showing study protocol:



DETAILED DISCUSSION OF THE STUDY PROTOCOL:

Anaesthesia protocol was standardized for all the patients included in the study. Once a patient was recruited to the study, the PI/Guide visited the patient 24 hours prior to the scheduled neurosurgical procedure and the following parameters were noted in the proforma at the time of pre-anaesthetic check-up :

- Patient demographic data (age, gender, weight)
- Primary diagnosis and the proposed procedure
- American Society of Anaesthesiologists (ASA grading)
- GCS (Glasgow coma scale) at admission
- Vitals (Heart rate, Systolic blood pressure, Diastolic blood pressure, mean arterial pressure)
- Any symptoms of raised ICP
- Any CT/MRI findings of raised ICP
- Treatment and drug history (use of steroids, diuretics)
- Electrocardiography (ECG)changes

  In all the recruited patients, Transthoracic echocardiography was performed twice ; the first one 24 hours prior to the scheduled neurosurgical procedure, and the other on 7^{th} postoperative day following the tumor removal. Transthoracic echocardiogram (TTE) was done using 2 Mhz (S2 Phased array probe)(Vivid I GE Health Care, Milwaukee, USA)with the patients in supine and in the left lateral position as per guidelines for imaging. As per the recommendations of evaluation of cardiac function by the American Society of Echocardiography (ASE), TTE was done using standard views.

DETAILED DESCRIPTION OF TTE BASED EVALUATION AND MEASUREMENTS:

- The patient was asked to position himself in the supine and left lateral decubitus position and after applying the ultrasound gel onto the probe, the examination was begun.
- **PLAX(parasternal long axis) View :**

  Parasternal long axis view was obtained with patients in supine and the USG probe was kept in 4 or 5th intercostal space in the left parasternal region. Imaging sequences consisted of initially 2D mode followed by M mode and colour doppler. The linear measurement included left ventricular outflow tract(LVOT) and aortic annular diameters. After acquiring this, M mode measurement of LV chamber dimensions were taken for chamber quantification and Fractional shortening (FS)

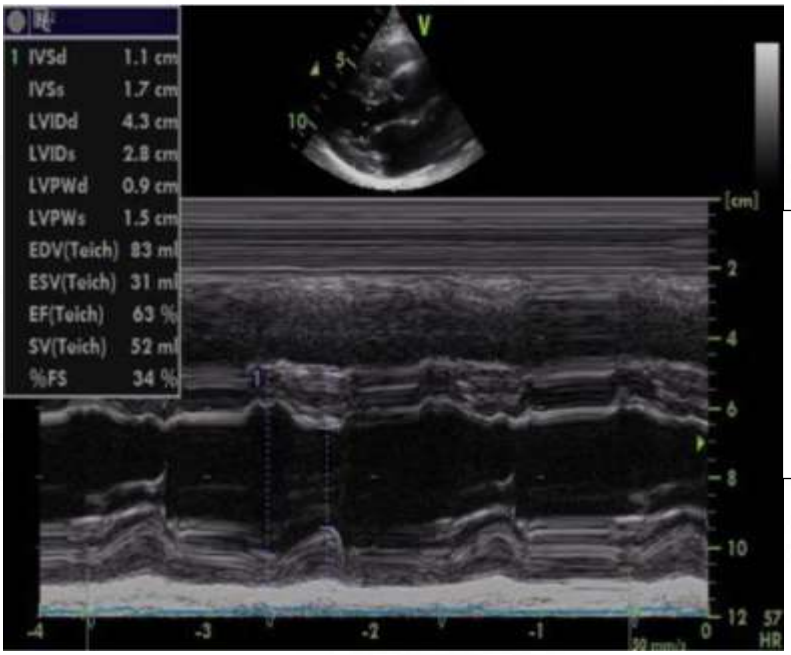


Figure 12: M-mode measurements of left ventricle in PLAX view

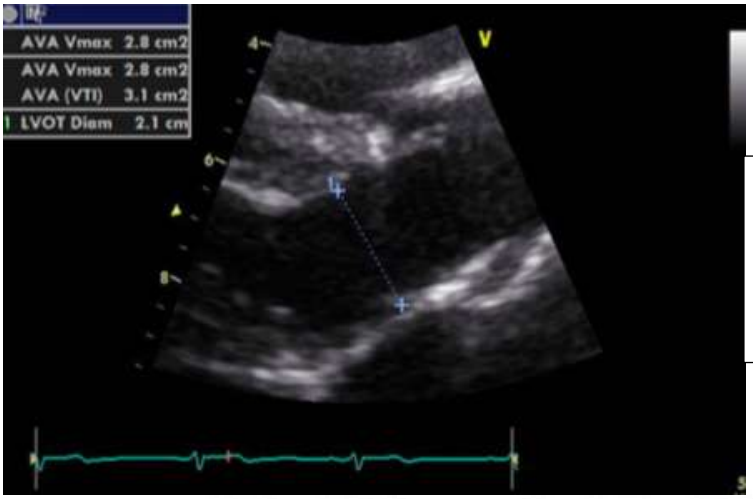


Figure 13:Measurements of left ventricle outflow tract diameter

Parasternal short axis (PSAX) views :

With the same patient position as for PLAX, Parasternal short axis view was obtained after rotating the USG probe 90 degrees and any regional wall motion abnormality if present was noted at basal, mid and apical views.

A4C (apical 4 chamber):

Patients were turned to left lateral position and the apical 4 chamber view was obtained by placing the USG probe at 5 or 6th intercostal space close to apex beat and apical 4 chamber view was obtained. Initially 2D mode and later pulse wave, tissue and color doppler images were obtained. After obtaining Apical 4 chamber view, 2D measurements were taken

1. Left ventricular volume(LV Volume) and Ejection fraction:

Biplane Disk Summation: The biplane summation-of-disks method was used for measuring 2D volume. Measurements for LV volume are made by tracing the LV cavity at end-diastole and end-systole, defined as the largest and smallest visible

areas. Papillary muscles and trabeculae are excluded from tracing and are considered to be part of the chamber.

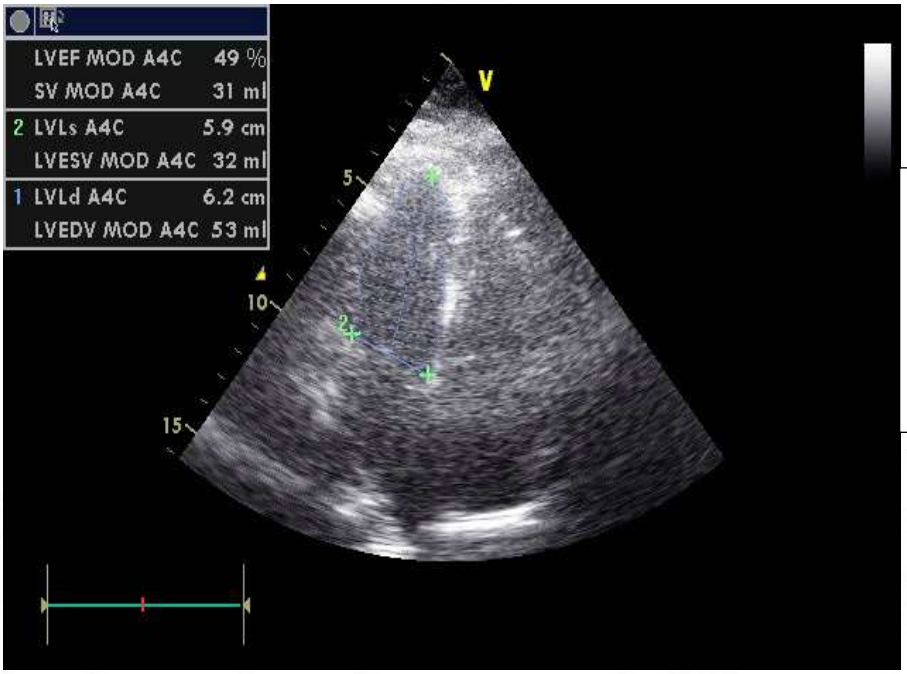


Figure 14: Measurement of Ejection Fraction in apical 4 chamber view

2. Left atrial volume(LA Volume):

Biplane Disk Summation : LA endocardial borders is traced after identifying maximum volume at end systole, by drawing a line from one end of the annulus to the opposite side. The calliper was placed at the center of the mitral annulus and extended to the inner edge of the farthest end of the traced superior left atrial wall.

Spectral Doppler Imaging Measurements:

After obtaining A4C, spectral doppler imaging measurements were taken as follows:

Mitral Valve(MV) :

Spectral Doppler was used to characterize the patterns of forward diastolic flow across the MV and to measure several indices of mitral regurgitation, if present. In the A4C view, the cursor(sample volume) was positioned at the tips of the open MV leaflets and PW Doppler recording of the peak E (early diastolic) and A (atrial contraction) velocities and MV early diastolic deceleration time is recorded. If mitral regurgitation was present, it was noted.

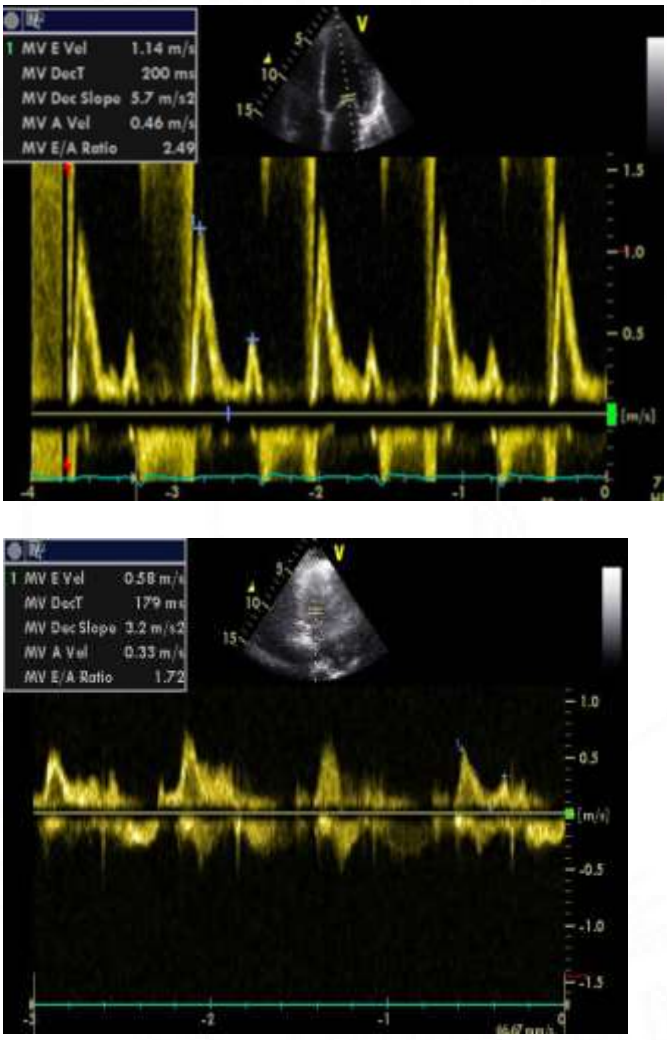


Figure 15: Spectral doppler imaging measurement of Mitral valve

Aortic Valve(AV):

At the level of aortic valve, continuous wave(CW) Doppler was used to trace a peak velocity and velocity time integral(VTI), stroke volume and cardiac output.

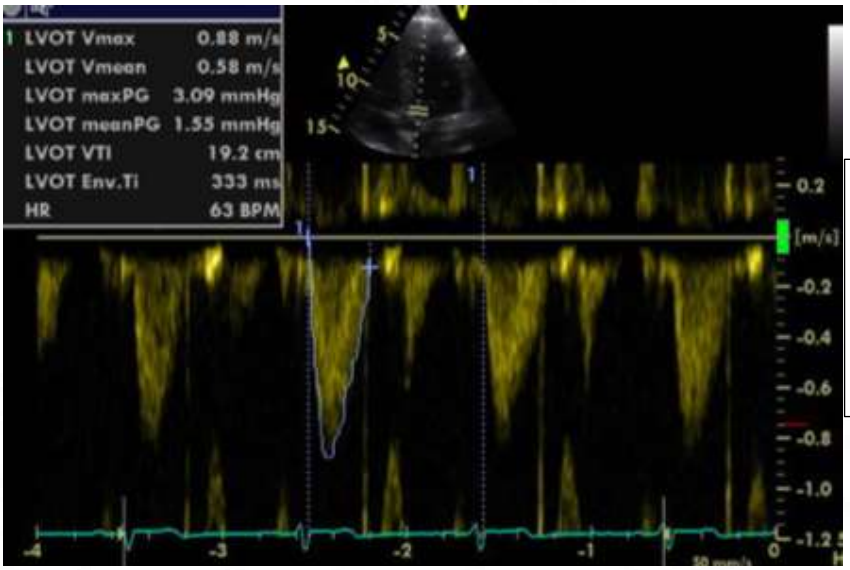


Figure 16: Spectral doppler imaging measurement of aortic valve

Tissue Doppler of Left ventricle

Tissue Doppler is used to record velocities of the longitudinal excursion of the lateral and medial mitral annulus as well as the lateral tricuspid annulus. s' is systolic velocity, e' is early diastolic velocity and a' is velocity during atrial contraction. Average of the peak lateral and medial velocities are used.

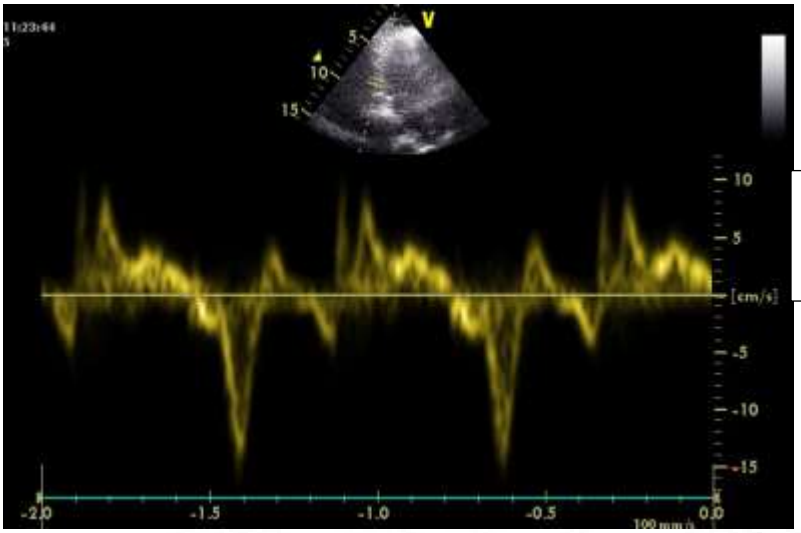


Figure 17: Tissue doppler imaging of mitral valve

M mode measurement at the level of tricuspid valve(TV) annulus:

At level of tricuspid annulus, tricuspid annular plane systolic excursion (TAPSE) and velocity measurements are also done.

Tricuspid annular plane systolic excursion (TAPSE):

The tricuspid valve(TV)annulus is demonstrated as large as possible without eliminating relational anatomic structures. The M-mode cursor is aligned along the RV free wall and measurement is taken.

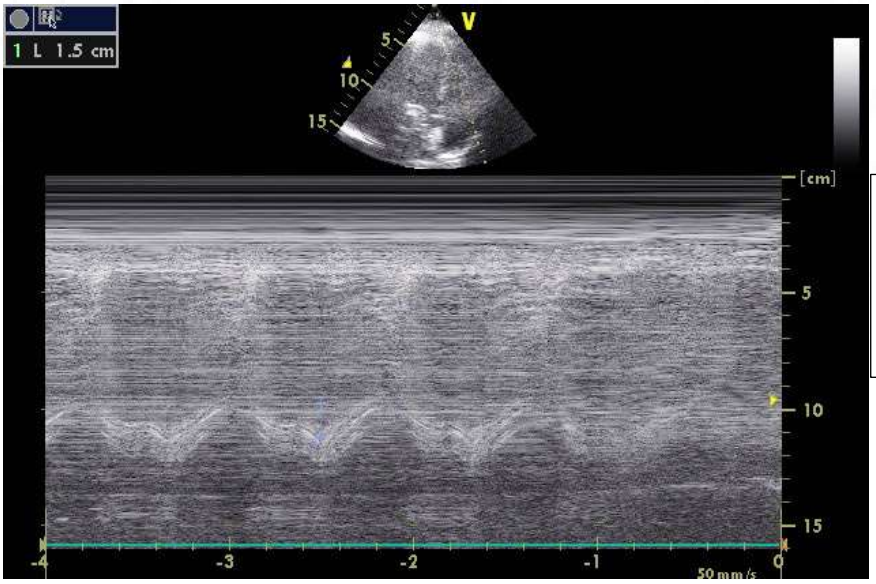


Figure 18: M-mode measurements of left ventricle in PLAX view

Table 3: Echocardiographic variables assessed as per study protocol

All the measurements were taken three times and the average of the three readings were documented in proforma and excel file for analysis.

Chamber Dimensions	**Left Ventricular systolic function**	**Left Ventricular Diastolic function**	**RV systolic function**
• LVIDd (left ventricular internal diameter at end diastole) • LVIDs (left ventricular internal diameter at end-systole) • IWIDd (inferior wall internal diameter at end diastole) • IWIDs (inferior wall internal diameter at end-systole) • IVSd (interventricular septum thickness at end-diastole) • IVSs (interventricular septum thickness systole) • RWT (relative wall thickness) • LVMI (left ventricular mass index) • LVOT diameter (left ventricle outflow tract diameter)	• FS (left ventricular fractional shortening) • EF (left ventricular ejection fraction) • RWMA (regional wall-motion abnormality) • LVOT area (left ventricular outflow tract area) • Aortic VTI (aortic velocity time integral) • SV(stroke volume) • CO(cardiac output)	• E wave velocity • A wave velocity • DecT(deceleration time) • e'(e prime) • E/A • E/e' • LAVI (left atrial volume index)	• TAPSE (tricuspid annular plane systolic excursion) • Other variables noted: - Any valvular stenosis/ regurgitation - Any Pericardial Effusion/ clot

Statistical Analysis

All statistical analyses were done using SPSS software version 17. 0 (Chicago, SPSS inc.)

A)Sample size calculation

There were no prior studies available on evaluation of cardiac function using echocardiogram in patients with chronically raised ICP in primary brain tumors. Hence we could not get data for sample size calculation for the present study and initiated the study proposal as a pilot study.

B) Statistical Analysis of the Data

We performed the following two analysis of the recorded data;

I. Inter group analysis: This was done to evaluate whether the variables pertaining to cardiac function were significantly different between the two groups.
II. Intra group analysis: This was done to evaluate whether the variables pertaining to cardiac function were significantly different before and after neurosurgery.

Observations obtained from the study were expressed in Mean+/- SD. Comparison of categorical variables were done using chi-square test. Comparison of normally distributed continuous variables were evaluated with students t-test. "p" value less than 0. 05 was considered as statistically significant.

Results

&

Observations

For this prospective pilot observational study, we enrolled 84 patients who had a diagnosis of primary brain tumours, who were randomised into two groups based on the presence or absence of raised ICP. Of these eight patients in group 1 and sixteen patients in group 2 had postoperative complications and were excluded.

Finally, sixty patients were included (30 in each group) for analysis(Figure 19)

1. Group 1 consisted of 30 adult male or female patients with a supratentorial primary brain tumour and without clinical and radiological features of raised ICP, undergoing neurosurgical procedures.
2. Group 2 consisted of 30 adult male or female patients with a supratentorial primary brain tumour and with features of raised ICP, undergoing neurosurgical procedures.

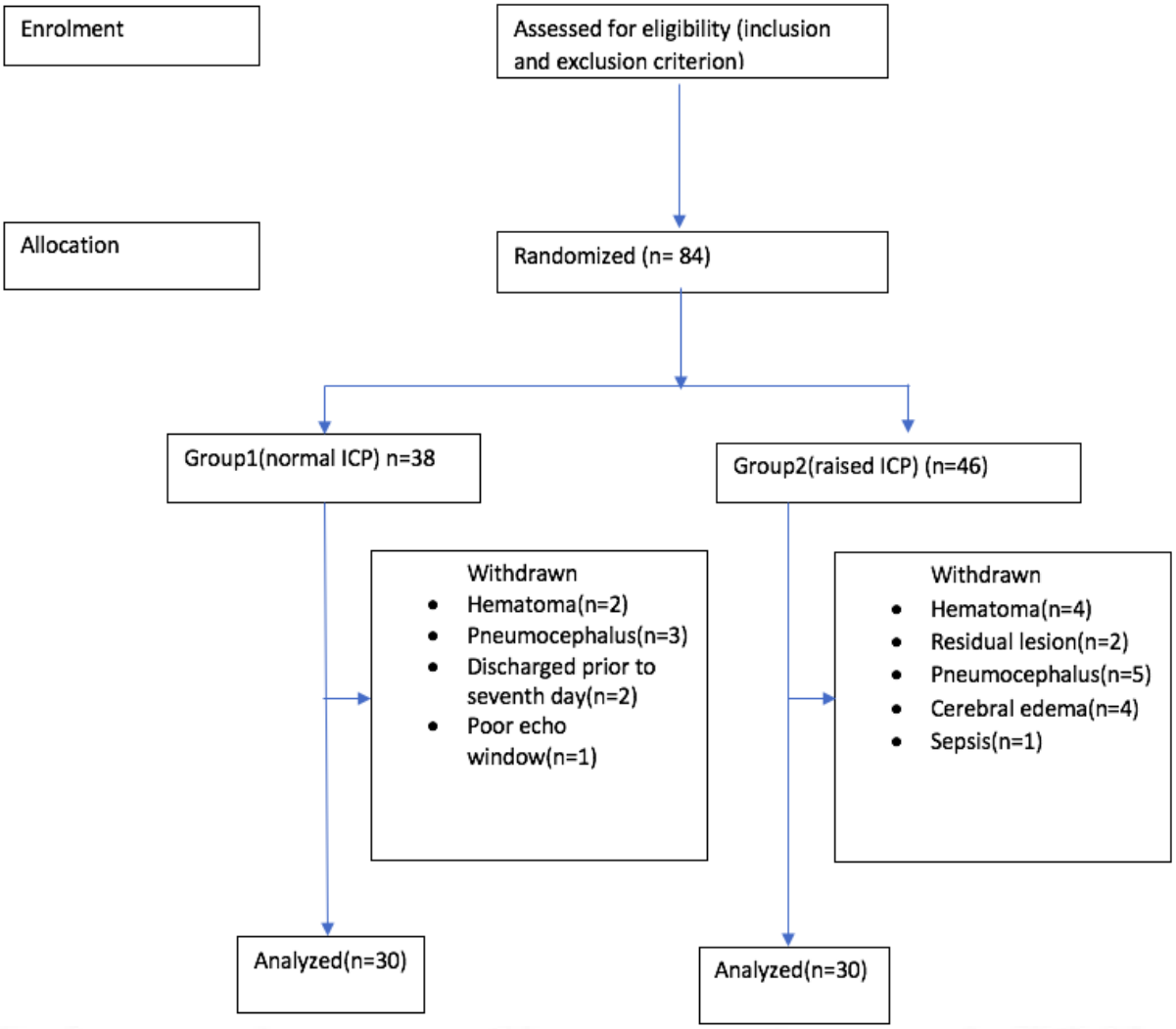
The demographic variables and the neurosurgical diagnosis of the recruited patients in the two groups are depicted in section A in Tables 4, 5 and 6.

Study variables were classified as intraoperative characteristics, hemodynamic, electrocardiographic and echocardiographic variables.

Hemodynamic and electrocardiographic variables, along with intraoperative characteristics, are depicted in section B as Tables 7,8, and 9.

The results of the echocardiographic evaluation are depicted in Section C. The echocardiographic variables were further classified as variables pertaining to chamber dimensions, LV systolic function, LV diastolic function, RV systolic function. The results of the intergroup analysis are shown in Tables 16-13. The results of the intragroup analysis are shown in Tables 17-23.

Figure 19: The consort diagram showing the recruitment of individuals for this study



A. Analysis Of Basic Demographic Data:

Table 4: Comparison of basic demographic data in the two groups

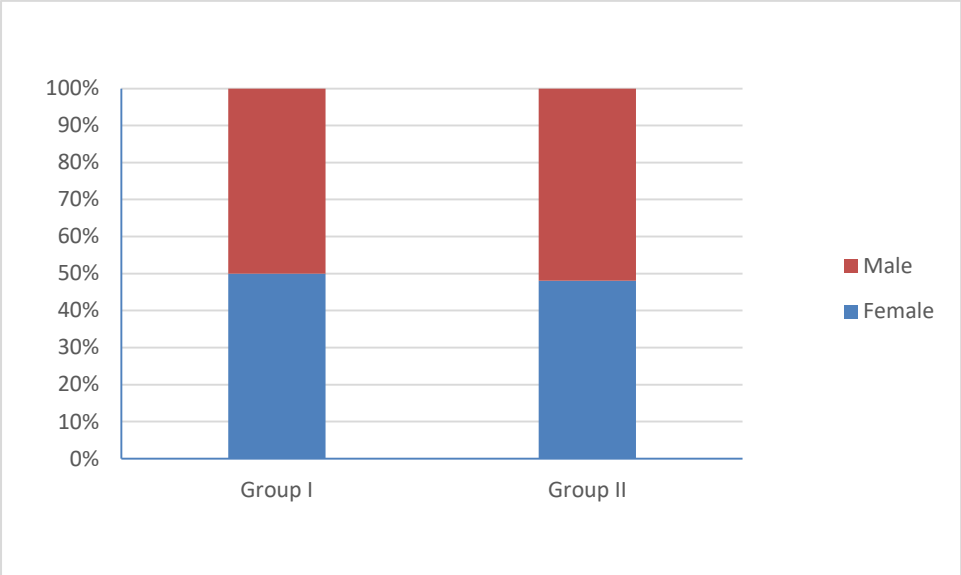
Variables	Group I (n=30)	Group II (n=30)	t	p
	Mean± SD	Mean± SD		
Age(years)	35. 5±9. 6	38. 5±9. 8	-1. 185	0. 241
Weight(kgs)	65. 7±9. 3	62. 5±10. 0	1. 257	0. 214
Height(cms)	164. 3±6. 9	162. 2±9. 8	0. 944	0. 349
Body Surface Area (/metre^2)	1. 7±0. 1	1. 7±0. 2	1. 266	0. 211
Body Mass Index (kg/m^2)	24. 3±2. 9	23. 7±2. 9	0. 79	0. 433
Preoperative GCS	14. 9±0. 5	14. 0±1. 1	3. 85	**0. 000***

There was statistically no significant difference (p > 0. 05) between the two groups in terms of demographic characteristics such as age, weight, height, Body Mass Index(BMI) and Body Surface Area(BSA) [**Table 4**]. The Glasgow coma Scale (GCS) score was different between the two groups. Group 1 had higher score of 15 whereas in Group II the score was 14. It was statistically significant. (p<0. 00).

Table 5: Comparison of the gender distribution in the two groups

Gender	Group I		Group II		Total		p
	n	%	n	%	n	%	
Female	15	50	16	48. 1	28	49. 1	0. 889
Male	15	50	14	51. 9	29	50. 9	

Figure 20: Bar graph showing comparison of gender distribution in the two groups.



There was equal preponderance of male and female patients in both the groups and was not statistically different between the groups. [**Table 5, Figure 20**].

Table 6: shows the neurosurgical diagnosis for which patients in each group underwent surgery

Diagnosis	**Group1 (normal ICP)**	**Group 2 (raised ICP):**
Parasagittal meningioma	2(6. 6%)	2(6. 6%)
Parafalcine meningioma	1(3. 3%)	2(6. 6%)
Occipital meningioma	1(3. 3%)	1(3. 3%)
Frontal epidermoid tumour	1(3. 3%)	-
Parietal ependymoma	2(6. 6%)	-
Frontal glioma	6(20%)	4(13. 3%)
Temporal glioma	5(16. 6%)	-
Parietal glioma	5(16. 6%)	2(6. 6%)
Thalamic glioma	1(3. 3%)	-
Frontal DNET	3(10%)	-
Temporo parietal glioma	-	4(13. 3%)
Parieto occipital glioma	-	3(10%)
Parietal DNET	3(10%)	-
Craniopharyngioma	-	1(3. 3%)
Third ventricular colloid cyst	-	7(23. 3%)
Choroid plexus papilloma	-	2(6. 6%)
Third ventricular ependymoma	-	2(6. 6%)
	Total 30(100%)	Total 30(100%)

Table 6 shows the diagnosis of various primary brain tumours in both the groups. There was no preponderance of any particular tumour and they were of varied types like meningiomas, gliomas, ependymoma, DNET.

B. Hemodynamic And Electrocardiographic Results

Table 7: Comparison of the baseline hemodynamic variables between two groups

	Group I (n=30)	Group II (n=30)	p
	Mean± SD	Mean± SD	
HR	73. 7±8. 5	70. 6±11. 8	0. 098
SBP(mm Hg)	115. 3±10. 9	128±14. 3	**0. 000**
DBP(mm Hg)	73. 5±6. 5	78. 9±7. 9	**0. 007**

(HR- heart rate, SBP-Systolic blood pressure, DBP-Diastolic blood pressure, p< 0. 05 significant)

The baseline heart rate was within normal limits in both groups **[Table 7 and Figure 21**] and we did not find bradycardia in group 2 despite features of raised ICP. However, analysis of baseline hemodynamic parameters SBP and DBP showed a significant difference between the two groups (p<0. 05). The group 2 patients had a statistically significantly(p< 0. 05) higher baseline SBP(128+/-14. 3mm Hg) as compared to the group 1(115. 3+/-10. 9mm Hg). Similarly, the DBP was also higher in the group 2 (78. 9+/-7. 9mm Hg) compared to group 1 (73. 5+/-6. 5mm Hg). [**Table 7,Figure 22]**

Figure 21: Bar graph showing comparison of baseline heart rate of the two groups

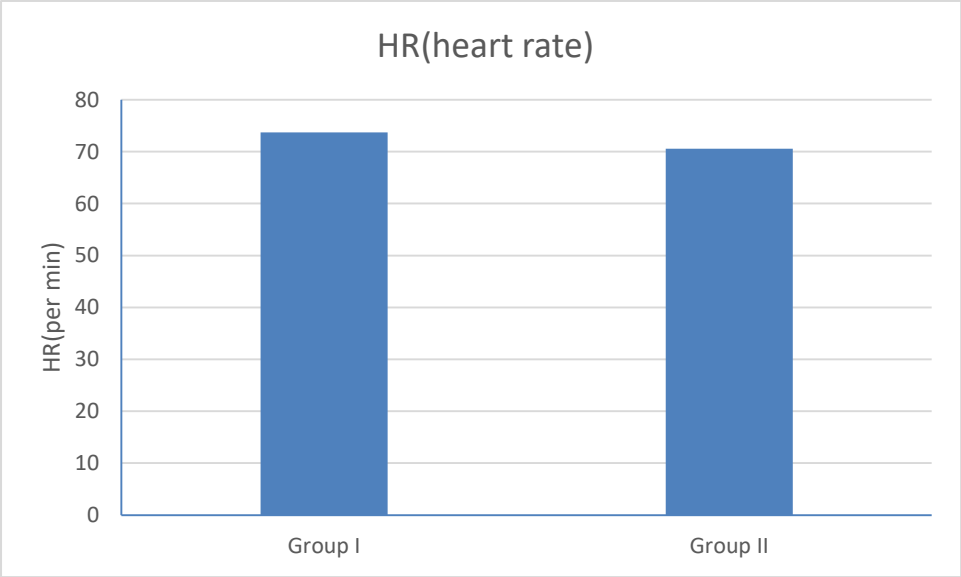
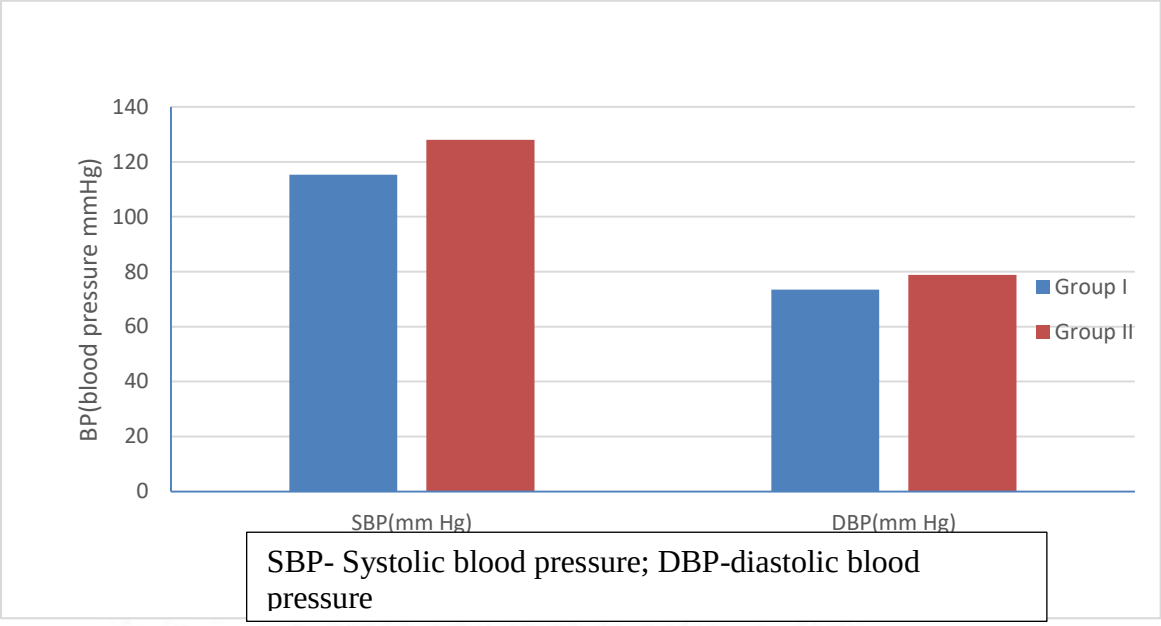


Figure 22: Bar graph showing comparison of SBP and DBP between the two groups

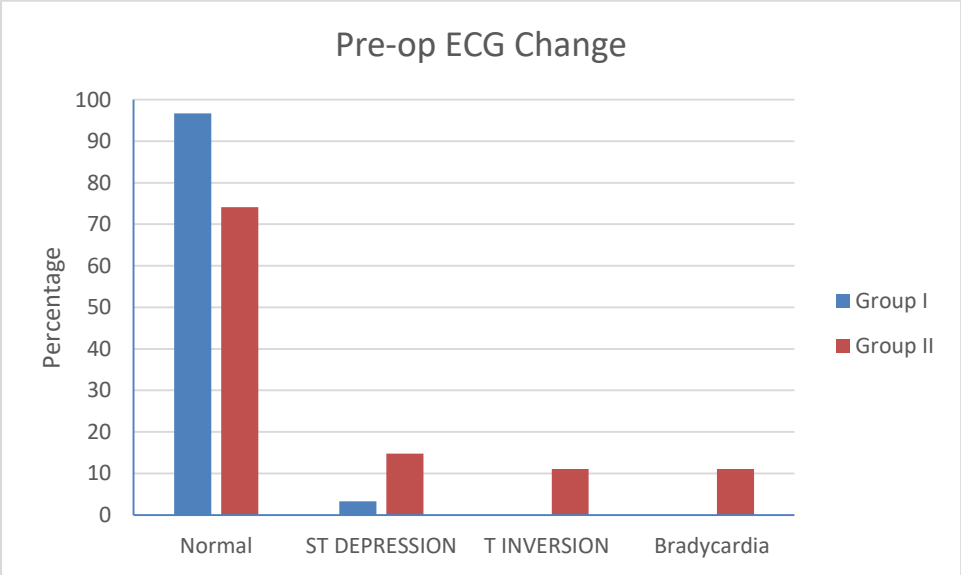


SBP- Systolic blood pressure; DBP-diastolic blood pressure

Table 8: Pre-operative ECG findings in the two groups

Pre-op ECG Change	Group I		Group II		p
	n	%	n	%	
Normal	29	96. 7	20	74. 1	
ST DEPRESSION	1	3. 3	4	14. 8	**0. 043**
T INVERSION	0	0	3	11. 1	
Bradycardia (HR<50/')	0	0	3	11. 1	

Figure 23: Bar graph showing baseline ECG changes in the two groups



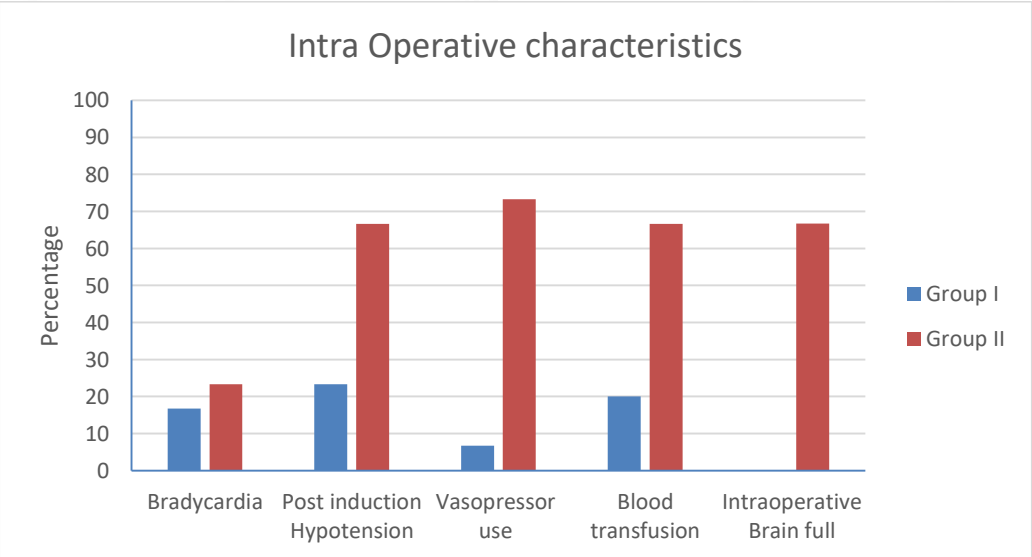
The analysis of baseline electrocardiographic (ECG) parameters showed that all the patients in Group 1 had normal ECG whereas only 20 patients in group 2 had normal ECG. This was significantly different in Group 2 compared to Group 1 (p<0. 05). Ten patients (30%) in group 2 had ECG changes of which 14. 8% of patients had ST

depression, 11% had T inversion and 11% had bradycardia. Only one person in the group 1 had ST depression. [**Table 8, Figure 23**]

Table 9: Table showing comparison of the intraoperative adverse events between the two groups

Intra Operative characteristics	Group I		Group II		p
	n	%	n	%	
Bradycardia	5	16. 7	7	23. 3	0. 392
Post induction Hypotension	7	23. 3	20	66. 6	**0. 000**
Vasopressor use	2	6. 7	22	73. 3	**0. 000**
Blood transfusion	6	20	20	66. 6	**0. 000**
Intraoperative full brain	0	0	20	66. 7	**0. 000**

Figure 24 : Bar graph showing comparison of intraoperative characteristics between the two groups



We have recorded the intraoperative adverse events which can have impact on the postoperative cardiac functions. We found increased incidence of hypotension, vasopressor use, bleeding requiring blood transfusion and impaired brain relaxation occurring in the intraoperative period. There was a highly significant difference between the two groups in terms of the intraoperative adverse events like post induction hypotension, vasopressor use, need for blood transfusion, and full brain. [**Table 9, Figure 24**] Group 2 patients had higher incidence of post induction hypotension (66. 6%), increased vasopressor use (73. 3%) and increased blood transfusion (66. 6%) compared to group 1.

(C) Evaluation of cardiac Function by Transthoracic Echocardiography:

1) **Intergroup analysis: Results of Echocardiographic variables of cardiac function between the two groups**

We have analyzed the echocardiographic variables based on changes in chamber dimensions, left ventricular systolic function, left ventricular diastolic function and right ventricular systolic function.

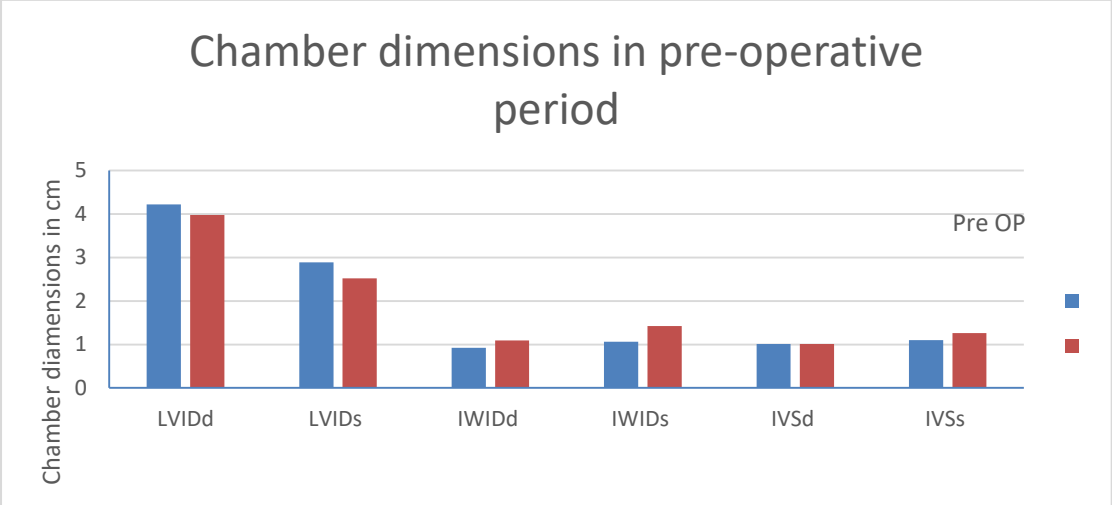
I. Intergroup analysis of cardiac chamber dimensions

Table 10: Comparison of the cardiac chamber dimensions in the two groups in the preoperative and postoperative period.

CHAMBER DIMENSIONS		Group I (n=30)	Group II (n=30)	p
		Mean± SD	Mean± SD	
LVIDd(cm)	Preop	4. 22±0. 43	3. 98±0. 93	0. 218
	Postop	4. 19±0. 26	3. 92±0. 91	0. 128
LVIDs (cm)	Preop	2. 89±0. 36	2. 52±0. 81	**0. 025**
	Postop	2. 90±0. 34	2. 47±0. 85	**0. 013**
IWIDd (cm)	Preop	0. 92±0. 20	1. 09±0. 36	**0. 025**
	Postop	0. 92±0. 19	1. 12±0. 45	**0. 032**
IWIDs (cm)	Preop	1. 06±0. 28	1. 42±0. 34	**0. 000**
	Postop	1. 17±0. 35	1. 41±0. 51	**0. 040**
IVSd (cm)	Preop	1. 01±0. 20	1. 01±0. 37	0. 971
	Postop	1. 05±0. 28	0. 97±0. 28	0. 326
IVSs (cm)	Preop	1. 10±0. 25	1. 26±0. 45	0. 107
	Postop	1. 14±0. 35	1. 19±0. 36	0. 657
RWT	Preop	0. 44±0. 14	0. 63±0. 43	**0. 028**
	Postop	0. 44±0. 08	0. 62±0. 35	**0. 008**
LVMI (gm/m^2)	Preop	77. 4±19. 9	82. 5±30. 5	0. 456
	Postop	79. 3±25. 6	82. 9±41. 2	0. 688

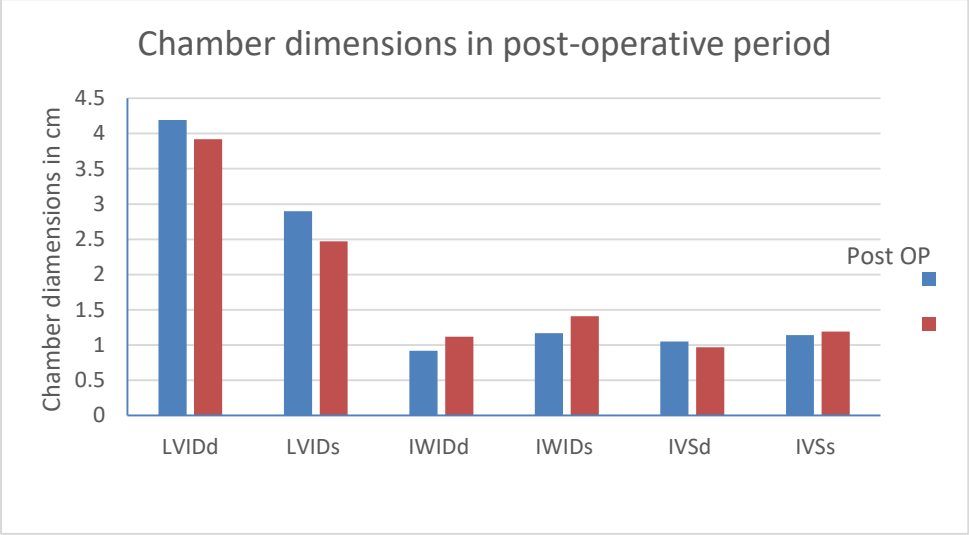
[LVIDd (left ventricular internal diameter end diastole),LVIDs (left ventricular internal diameter end-systole,IWIDd (inferior wall internal diameter end diastole, IWIDs (inferior wall internal diameter end-systole), IVSd interventricular septum thickness end-diastole), IVSs (interventricular septum thickness systole), RWT(relative wall thickness), LVMI(left ventricular mass index)]

Figure 25: Bar graph showing comparison of chamber dimensions between the two groups in pre-operative period



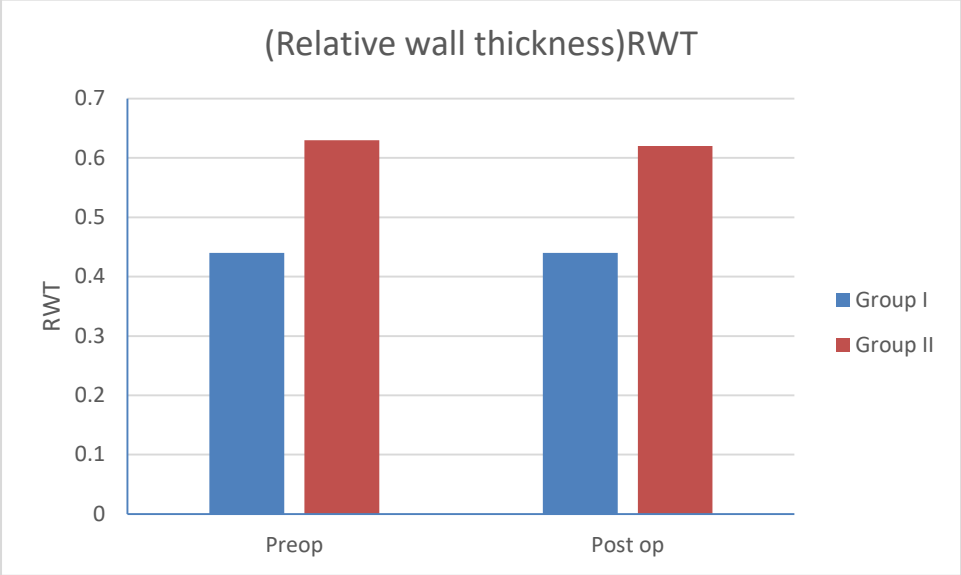
Chamber dimensions and wall thickness were calculated using left parasternal long axis view. Preoperative analysis of chamber dimensions showed differences in the left ventricular cavity size between the groups where the size of LV in both systole and diastole were smaller in group 2 compared to group 1; however the significant difference was seen only in systole. The preoperative LVIDs in the raised ICP group was 2. 52±0. 81 cm compared to 2. 89±0. 36 Cm in the normal ICP group(p=0. 02). When analyzing the thickness of the LV wall we found that patient in group 2 had significantly increased inferior wall thickness in both systole and diastole as well as calculated relative wall thickness. The preoperative IWIDd was increased in the raised ICP group (1. 09±0. 36cm) compared to the normal ICP group (0. 92±0. 20cm). The variables LVIDd, IVSd, IVSs and LVMI did not differ significantly between the two groups. [**Table 10, Figure 25]**

Figure 26: Bar graph showing comparison of chamber dimensions between the two groups in the post-operative period



Comparison of post-operative chamber dimensions revealed that the changes seen in the preoperative period and the significant differences in LVIDs, IWIDs, IWIDd and RWT persisted between the two groups. The post-operative LVIDs in group 2 was 2. 47±0. 85 cm compared to 2. 9±0. 34 Cm in the normal ICP group(p=0. 01). The post-operative IWIDd was increased in the group 2 (1. 12±0. 45cm) compared to group 1 (0. 92±0. 19cm). The post-operative IWIDs in group 2 was higher (1. 41±0. 51 cm) compared to group 1 (1. 17±0. 35). The variables LVIDd, IVSd, IVSs and LVMI did not differ significantly between the two groups in the post-operative period[**Table 10, Figure 26]**

Figure 27: Bar graph showing comparison of relative wall thickness(RWT) between both the groups



The relative wall thickness in both the pre and post-operative period significantly varied between the two groups. During the preoperative period, the relative wall thickness(RWT) in group 2 was 0. 63±0. 43 which was higher than that of group 1(0. 44±0. 14). The difference persisted in the post-operative period where the RWT of group 2 patients was higher (0. 62±0. 35) than in group1(0. 44 ± 0. 08)[**Table 10, Figure 27]**

Analysis of our findings on chamber dimensions shows that there was a relative hypertrophy of the left ventricle preferentially the left ventricular free wall rather than septum, in patients with raised ICP. This increased muscle mass might have caused enhanced systolic contraction and reduced LV end systolic dimensions. This changes may be attributable to overall increased sympathetic activity in raised ICP to maintain the CPP in the face of slowly rising ICP. Concurrently we have observed increased systolic and diastolic blood pressure in group 2 compared to group 1.

II. Intergroup Analysis of Ventricular systolic Functions

Table 11– Comparison of the parameters relevant to left ventricular systolic function between the two groups

Variables		Group I (Normal ICP)(n=30)	Group II(Raised ICP) (n=30)	p
		mean±sd	mean±sd	
LVOTarea(cm^2)	Preop	3. 15±0. 93	3. 18±0. 9	0. 9
	Postop	3. 13±0. 87	3. 15±0. 94	0. 91
Aortic VTI (cm)	Preop	18. 8±1. 3	17. 7±3. 9	0. 169
	Postop	19. 4±2. 0	18. 4±3. 4	0. 166
SV (ml)	Preop	58. 6±16. 0	56. 5±16. 7	0. 127
	Postop	60. 6±17. 0	57. 96±17. 3	0. 107
CO (L)	Preop	4. 40±1. 69	4. 71±1. 97	0. 521
	Postop	4. 82±1. 95	5. 06±1. 99	0. 642
LVFS (%)	Preop	31. 4±5. 7	37. 7±9. 6	**0. 004**
	Postop	30. 6±6. 9	37. 5±13. 2	**0. 016**
LVEF (%)	Preop	70. 0±7. 7	61. 0±12. 3	**0. 001**
	Postop	72. 1±7. 7	68. 5±9. 6	0. 122

LVOT(ventricular outflow tract area), Aortic VTI(aortic velocity time integral), SV(stroke volume), CO(cardiac output), LVFS (left ventricular fractional shortening), LVEF (left ventricular ejection fraction)]

Left ventricular systolic function was analysed between the groups in the preoperative and postoperative period using indices like aortic velocity time integral, stroke volume, cardiac output, left ventricular fractional shortening and left ventricular ejection fraction. We found that fractional shortening (FS)and ejection fraction(EF) was also significantly different between the two groups in the preoperative group. During the pre-operative period, FS was higher in the group 2 (37. 7±9. 6) compared to group1 (31. 4±5. 7). In the post-operative period also, the difference persisted when in group 2, FS was higher (37. 5±13. 2) compared to group 1 (30. 6±6. 9) [**Table11,Figure 28**]. During the pre-operative period, EF was lower in the group2(61±12. 3) compared to group 1(70±7. 7). But in the postoperative period, an increase in EF in group 2 was seen and there was no difference between the groups in postoperative period [**Table 11, Figure 29].** We did not find differences in other variables like SV, CO, LVOT area, and aortic VTI between the two groups in pre and postoperative period.

Figure 28: Bar graph showing comparison of left ventricular fractional shortening between the two groups in the pre and post-operative period

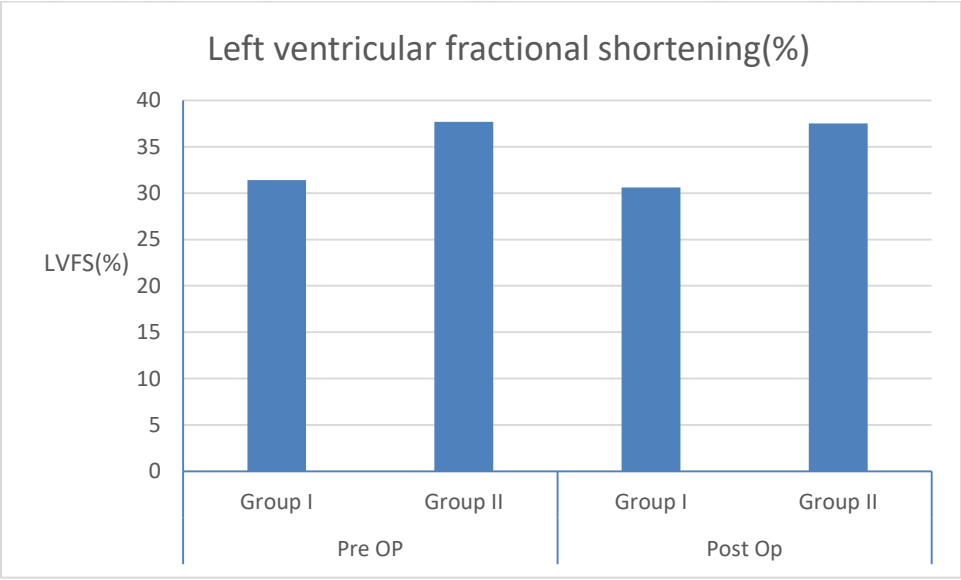


Figure 29: Bar graph showing comparison of left ventricular fractional ejection fraction between the two groups in the pre and post-operative period

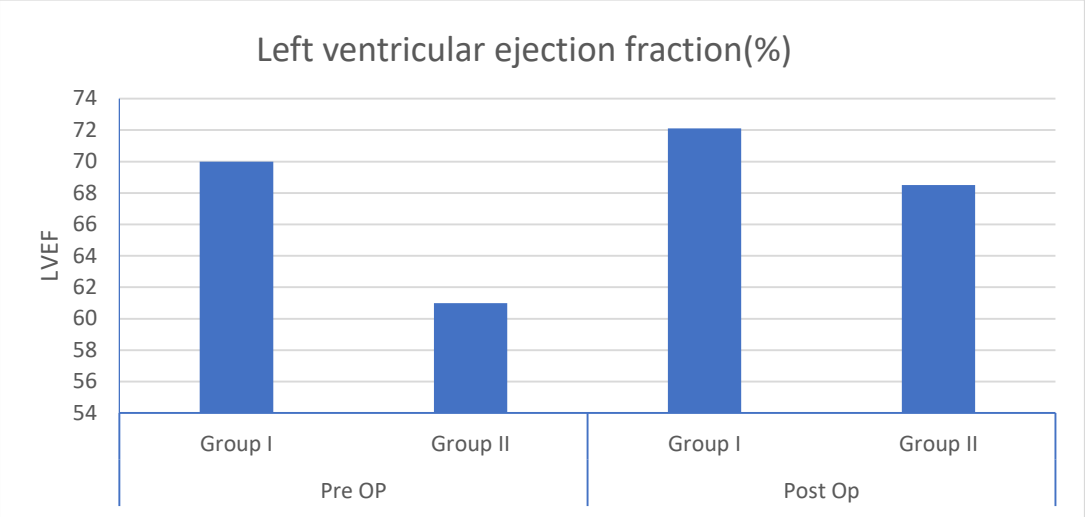
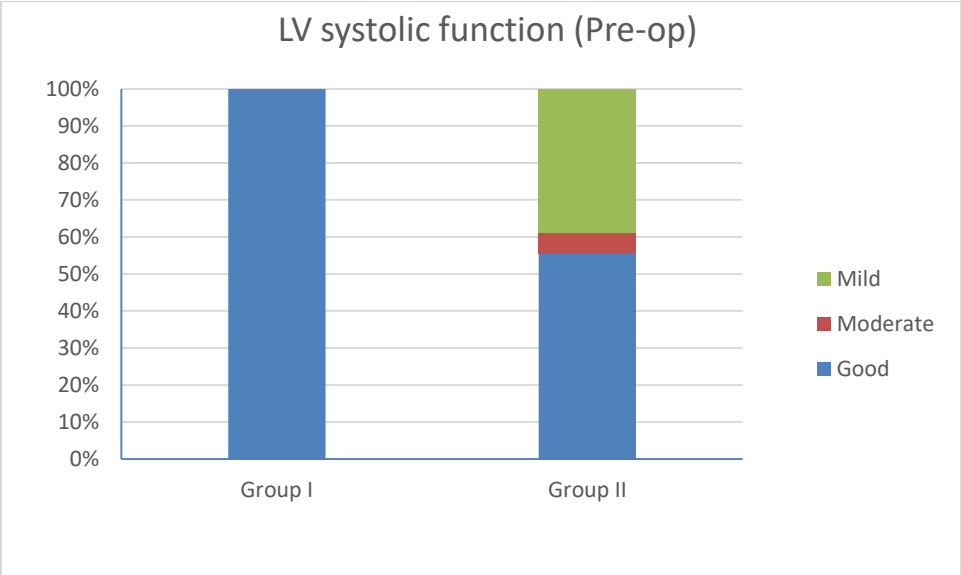


Table 12– Comparison of the LV systolic function as assessed by ejection fraction in the two groups

	LV Systolic function as assessed by EF	Group I		Group II		p
		n	%	n	%	
Pre-Operative period	Good (EF >55%)	30	100	22	33. 3	**0. 024**
	Moderate (EF 30-45%)	0	0	1	3. 3	
	Mild (EF-45-55%)	0	0	7	23. 3	
Post-Operative period	Good	30	100	30	100	1

Figure 30: Bar graph showing comparison of LV Systolic function between the two groups in the pre-operative period.



We further sub-analysed the LV EF and found that, 8 patients (26. 7%) in group 2 had systolic dysfunction whereas none of the patients in group 1 had systolic dysfunction. Among the patients in the group 2, seven patients (23. 3%) had mild LV dysfunction and one patient (3. 3%) had moderate LV dysfunction. In the postoperative period, none of the patients in both the groups had any LV systolic dysfunction.

III. Intergroup Analysis of Ventricular Diastolic Functions

Table 13– Table comparing the parameters relevant to left ventricular diastolic function in the two groups

Variables		Group I (n=30)	Group II (n=30)	p
		Mean ±SD	Mean ±SD	
E Vel (m/sec)	Preop	0. 81±0. 07	0. 73±0. 22	0. 061
	Postop	0. 81±0. 08	0. 78±0. 17	0. 371
E/A	Preop	1. 51±0. 26	1. 49±0. 68	0. 870
	Postop	1. 44±0. 17	1. 48±0. 49	0. 664
E' (m/sec)	Preop	0. 12±0. 02	0. 10±0. 03	**0. 001**
	Postop	0. 23±0. 36	0. 11±0. 03	0. 09
E/E'	Preop	6. 87±1. 32	8. 26±3. 25	**0. 036**
	Postop	5. 99±1. 91	7. 94±2. 52	**0. 002**
DecT (msec)	Preop	214. 2±36. 9	196. 8±81. 7	0. 297
	Postop	225. 6±44. 1	229. 6±65. 8	0. 791
LA vol index(ml/m^2)	Preop	21. 6±2. 3	24. 3±2. 6	**0. 000**
	Postop	21. 8±2. 5	24. 6±2. 4	**0. 000**

The echocardiographic variables relevant to assessment of diastolic dysfunction were analysed. Statistically significant difference was noted in the following variables. The preoperative E' in the raised ICP group (0. 1±0. 03) was lesser than in the normal ICP group(0. 12±0. 02). [**Table 13, Figure 31]**In the preoperative period the E' value in group 2 (0. 1±0. 03) was found to be less than group 1 (0. 12±0. 02). [**Table 13, Fig 32**] Pre-operative E/E' in the group2 was 8. 26±3. 25 which was higher than that of

group 1 patients(6. 87±1. 32). The significant difference between the two groups persisted in the post-operative period. Post-operative E/E' was significantly higher in group2 (7. 94±2. 52) than that of group1 (5. 99±1. 91). [**Table 13, Figure 33]**Pre-operative LA volume index was found to be higher (24. 3±2. 6) in group 2 patients compared to group1 patients(21. 6±2. 3). In the post-operative period also, LA volume index was found to be higher (24. 6±2. 4) in group 2 patients compared to group1 patients(21. 8±2. 5). [**Table 13, Figure 34]**

Figure 31: Bar graph showing comparison of E' between the two groups during pre and post-operative period.

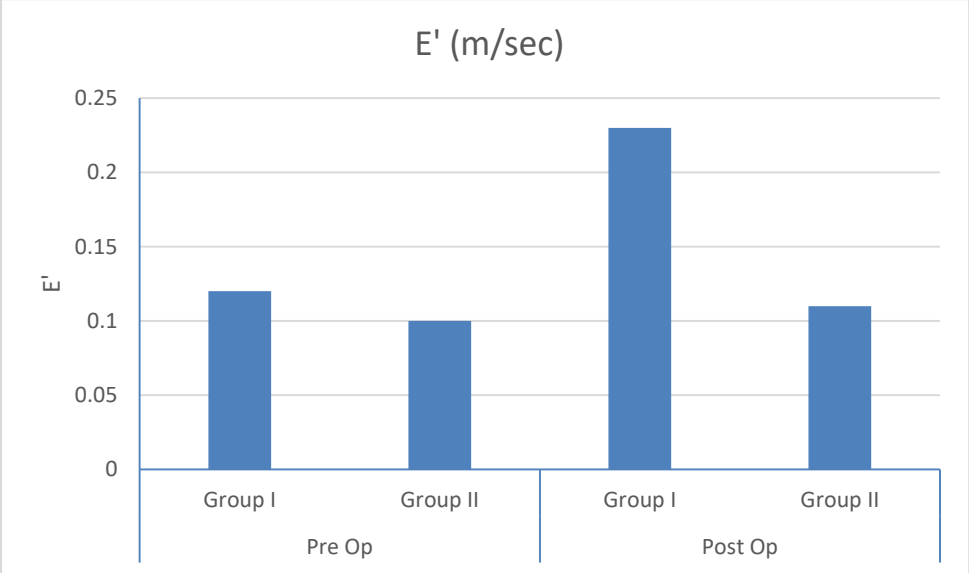


Figure 32: Bar graph showing comparison of E/E' between the two groups during pre and post-operative period.

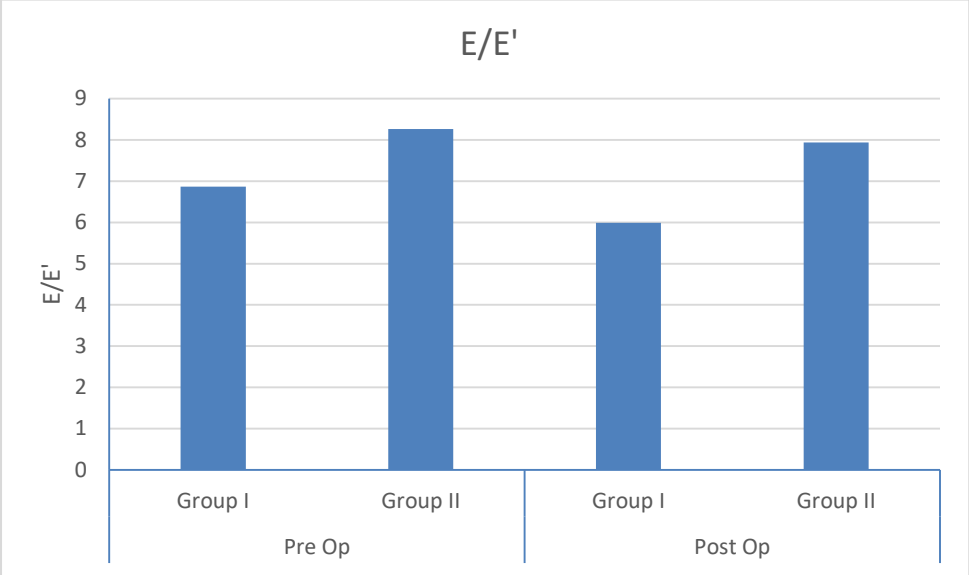


Figure 33: Bar graph showing comparison of LA volume index between the two groups during pre and post-operative period.

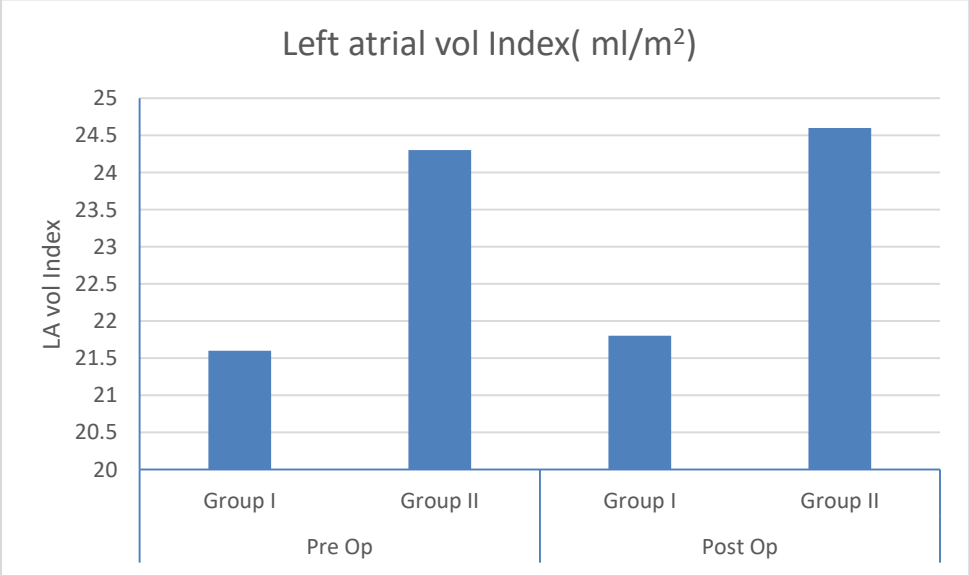


Table 14: Comparison of the diastolic function in the two groups

Diastolic dysfunction	Group I		Group II		p
	Yes(n,%)	No(n,%)	Yes(n,%)	No(%)	
Pre OP	0	30(100%)	10(33. 3%)	20(66. 6%)	<0. 001
Post OP	0	30(!00%)	9(30%)	21(70%)	<0. 001

There was a statistically significant difference in the diastolic function between both the groups during pre-operative and post-operative period. Diastolic dysfunction was present in 33. 3% in the group2 during the preoperative period whereas in the postoperative period 30%of patients had the same. None of the patients in the group1 had diastolic dysfunction. [**Table 14, Figure 34]**

Figure 34: Bar graph showing comparison of diastolic dysfunction between the two groups during pre and post-operative period.

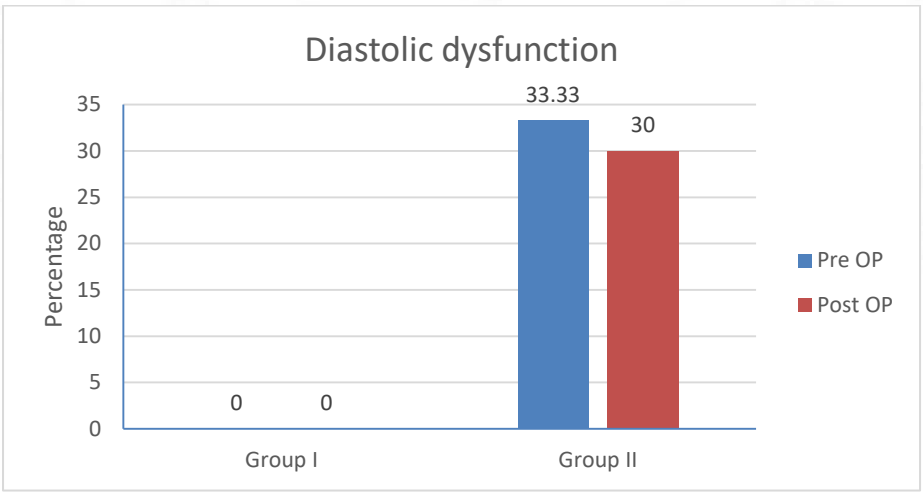


Table 15: Comparison of the preoperative and postoperative echocardiographic variables (for right ventricular systolic function) between the two groups

Variable		Group I (n=30)	Group II (n=30)	t	p
		Mean± SD	Mean± SD		
TAPSE (cm)	Preop	1. 887±0. 264	1. 822±0. 389	0. 739	0. 463
	Postop	1. 986±0. 325	1. 956±0. 299	0. 371	0. 712

[*TAPSE (tricuspid annular plane systolic excursion)]*

There was statistically no significant difference between the two groups in the TAPSE; the echocardiographic variable which was used to analyse the right ventricular function.

Table 16: Comparison of the RV systolic function in the two groups

RV Systolic fn	Group I		Group II		Total		p
	n	%	n	%	n	%	
Good	30	100	30	100	60	100	0. 82

All the patients in both the groups were found to have good RV systolic function.

2) **Intragroup analysis :**

We have hypothesized that the changes in cardiac functions seen in patients with raised ICP can be reversed when the tumour is excised and the ICP returns to normal. We analysed the pre-operative and post-operative cardiac functions to identify the impact of ICP normalisation in these two group of patients.

Table 17: Comparison of the chamber dimensions before and after surgery in the two groups

Chamber dimension	Group I			Group II		
	Pre OP	Post OP	p	Pre OP	Post OP	p
	Mean± SD	Mean± SD		Mean± SD	Mean± SD	
LVIDd (cm)	4. 22±0. 43	4. 19±0. 26	0. 5	3. 98±0. 93	3. 92±0. 91	0. 719
LVIDs (cm)	2. 89±0. 36	2. 90±0. 34	0. 83	2. 52±0. 81	2. 47±0. 85	0. 725
IWIDd (cm)	0. 92±0. 20	0. 92±0. 19	0. 93	1. 09±0. 36	1. 12±0. 45	0. 715
IWIDs (cm)	1. 06±0. 28	1. 08±0. 35	0. 9	1. 42±0. 34	1. 41±0. 51	0. 904
IVSd (cm)	1. 01±0. 20	1. 05±0. 28	0. 37	1. 01±0. 37	0. 97±0. 28	0. 557
IVSs (cm)	1. 10±0. 25	1. 14±0. 35	0. 40	1. 26±0. 45	1. 19±0. 36	0. 407
RWT (cm)	0. 44±0. 14	0. 44±0. 08	0. 89	0. 63±0. 43	0. 62±0. 35	0. 893
LV Mass (gm)	132. 93±31. 60	136. 47±42. 15	0. 56	138. 27±53. 68	139. 25±72. 25	0. 944
LV Mass Index (gm/m^2)	77. 39±19. 94	79. 31±25. 58	0. 61	82. 47±30. 53	82. 93±41. 15	0. 954

[LVIDd (left ventricular internal diameter end diastole),LVIDs (left ventricular internal diameter end-systole,IWIDd (inferior wall internal diameter end diastole, IWIDs (inferior wall internal diameter end-systole), IVSd interventricular septum thickness end-diastole), IVSs (interventricular septum thickness systole), RWT(relative wall thickness), LVMI(left ventricular mass index)]

Analysing the chamber dimensions, we could not find statistically different changes between the preoperative and postoperative period in both the groups.

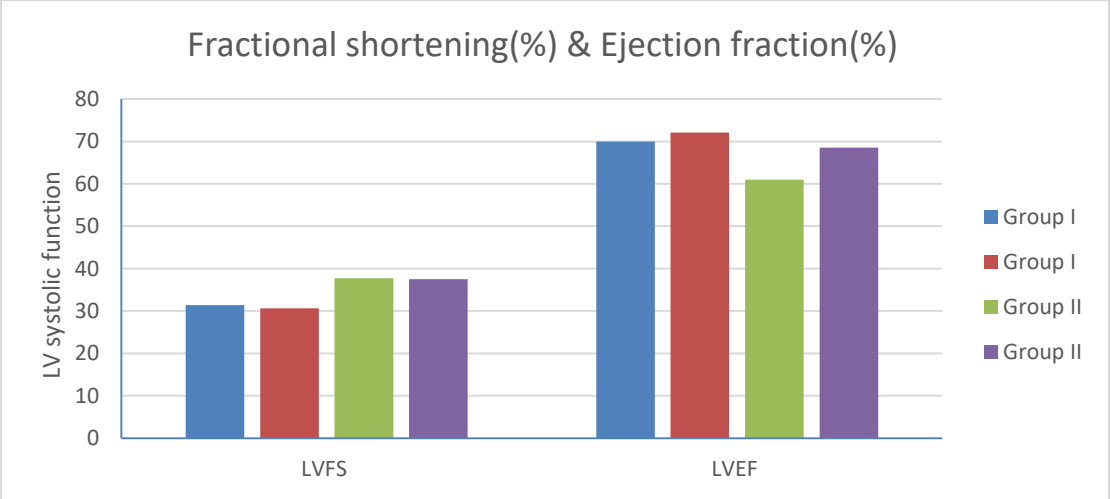
Table 18: Comparison of the parameters relevant to left ventricular systolic function in the two groups before and after neurosurgery

Variables relevant for LV systolic function	Group I(normal ICP)			Group II(raised ICP)		
	Pre OP	Post OP	p	Pre OP	Post OP	p
	Mean± SD	Mean± SD		Mean± SD	Mean± SD	
LVOT area (cm^2)	3. 15 ± 0. 93	3. 13±0. 87	0. 693	3. 82±1. 25	3. 76±1. 19	0. 713
Aortic VTI (cm)	18. 75 ± 1. 31	19. 41±2. 02	0. 074	17. 70±3. 89	18. 37±3. 43	0. 411
HR (bpm)	73. 67 ± 8. 48	76. 07±13. 34	0. 06	70. 63±11. 83	72. 26±11. 11	0. 559
SV (ml)	58. 63±16. 01	60. 59±17. 05	0. 219	67. 55±26. 66	70. 35±27. 29	0. 488
CO (L)	4. 40±1. 69	4. 5±1. 7	0. 06	4. 71±1. 97	5. 06±1. 99	0. 338
LVFS (%)	31. 42±5. 69	30. 64±6. 85	0. 503	37. 68±9. 58	37. 48±13. 19	0. 900
LVEF (%)	70. 00±7. 69	70. 10±7. 7	0. 09	61. 00±12. 25	68. 48±9. 63	**0. 001**
[LVOT area(left ventricular outflow tract area), Aortic VTI(aortic velocity time integral), SV(stroke volume), CO(cardiac output), LVFS (left ventricular fractional shortening), LVEF (left ventricular ejection fraction)]						

The echocardiographic variables relevant for LV systolic function were measured. In group 1 patients, there was no significant difference in the echocardiographic variables measured before and after neurosurgery. In group 2 patients, the ejection fraction(EF) measured after neurosurgery showed an increased value [68. 48+/-9. 63 %]compared to preoperative values, (61+/-12. 25)) which was significant (p<0. 001).

[**Table 18, Figure 35]**Other variables (LVOT area, aortic VTI, SV, CO, FS) did not show any significant variation after neurosurgery.

Figure 35: Bar graph showing comparison of Fractional shortening and Ejection Fraction in the two groups before and after neurosurgery



[Fractional shortening (FS) & Ejection fraction (EF)]

Table 19: Comparison of left ventricular systolic function(by Ejection fraction) in the group 1 before and after neurosurgery

	LV systolic function	Pre Op		Post OP		p
		n	%	n	%	
GroupI (normal ICP)	Good (EF >55%)	30	100	30	100	1. 000
	Moderate (EF 30-45%)	0	0			
	Mild (EF45-54%)	0	0			

All the patients in group 1 had good systolic function before and after neurosurgery.

Table 20: Table showing comparison of left ventricular systolic function in the group 2 before and after neurosurgery

	LV EF	Pre-Op		Post-Op		p
		n	%	n	%	
Group 2 (raised ICP)	Good (EF >55%)	22	73. 3	30	100	**0. 020**
	Moderate (EF 30-45%)	1	3. 7			
	Mild (EF45-54%)	7	18. 5			

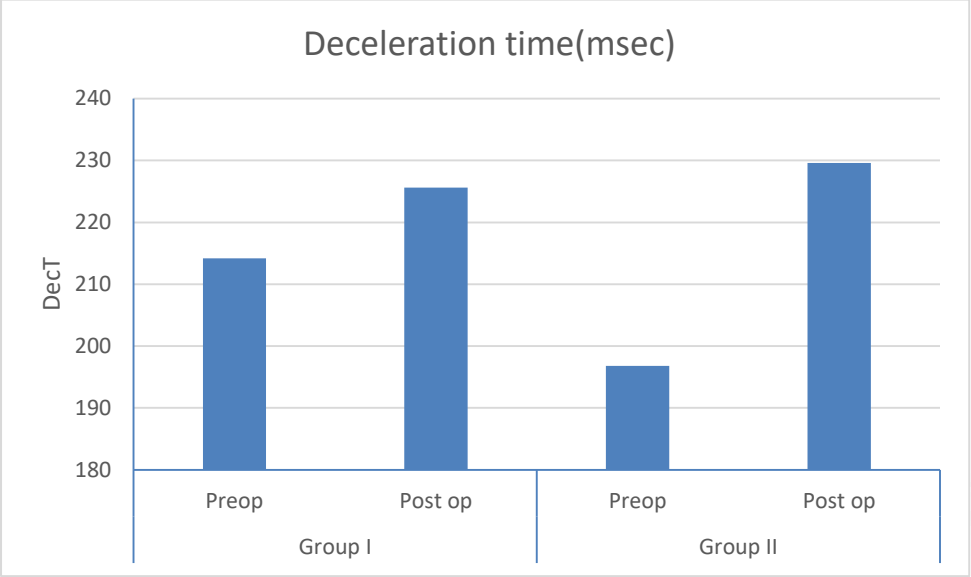
During the pre-operative period, 8 patients (26. 7%) in group 2 had systolic dysfunction of whom seven patients (23. 3%) had mild LV dysfunction and one patient (3. 3%) had moderate LV dysfunction. In the postoperative period, none of the patients had LV systolic dysfunction. This improvement in systolic function was found to be statistically significant($p<0. 02$)

Table 21: Comparison of the parameters relevant to left ventricular diastolic function in the two groups before and after neurosurgery

Variables relevant for LV diastolic function	Group I			Group II		
	Pre-Op	Post-Op	p	Pre OP	Post OP	p
	Mean± SD	Mean± SD		Mean± SD	Mean± SD	
E Vel (m/sec)	0. 81±0. 07	0. 81±0. 08	0. 786	0. 73±0. 22	0. 78±0. 17	0. 203
E/A	1. 51±0. 26	1. 44±0. 17	0. 144	1. 49±0. 68	1. 48±0. 49	0. 917
E' (m/sec)	0. 12±0. 02	0. 23±0. 36	0. 123	0. 10±0. 03	0. 11±0. 03	**0. 007**
E/E'	6. 87±1. 32	6. 99±1. 33	0. 09	8. 26±3. 25	7. 94±2. 52	0. 461
DecT (msec)	214. 20±36. 86	225. 63±44. 07	0. 059	196. 81±81. 71	229. 56±65. 80	**0. 019**
LA vol index (ml/m^2)	21. 59±2. 34	21. 83±2. 45	0. 548	24. 26±2. 55	24. 56±2. 38	0. 512

In group 1, there was no significant difference in the measured echocardiographic variables relevant to diastolic function, before and after surgery. In group 2, E' improved after neurosurgery (0. 11+/-0. 03) compared to before neurosurgery(0. 1+/-0. 03). There was a significant increase in Deceleration time before neurosurgery(196. 8+/-81. 7) compared to after neurosurgery(229. 56+/-65. 8). Other variables (E vel, E/A, E/E',LAVI) did not significantly change after surgery [**Table 22,Figure 36]**

Figure 36: Bar graph showing comparison of deceleration time before and after neurosurgery in the two groups.



[Deceleration time(Dec T)]

Table 22: Comparison of diastolic function before and after surgery

LV Diastolic dysfunction		Pre Op		Post OP		p
		n	%	n	%	
Group I	Yes	0	0	0	0	
Group II	Yes	10	33. 3	9	30	0. 9

None of the patients in group1 had diastolic dysfunction before and after neurosurgery. . However, in group 2, 33. 3% of patients had diastolic dysfunction during preoperative period and 30% of patients had diastolic dysfunction in the post-

operative period. This was not a statistically significant change(p<0. 9) indicating that diastolic dysfunction did not revert in these patients after surgery[**Table 22].**

Table 23: Table showing the comparison of Right Ventricular systolic function using TAPSE in the two groups before and after neurosurgery

TAPSE	TAPSE (cm)		p
	Pre-op	Post-OP	
	Mean± SD	Mean± SD	
Group I	1. 89±0. 26	1. 9±0. 32	0. 09
Group II	1. 82±0. 39	1. 96±0. 3	0. 081

[TAPSE -tricuspid annular plane systolic excursion]

In both the groups, TAPSE did not significantly change before and after neurosurgery. There were no cases of RV systolic dysfunction

Discussion

There is a paucity of literature on the cardiac dysfunction in patients presenting with primary brain tumours, especially with the gradual increase in ICP occurring in most of these patients. In our study we tried to investigate the following;

(i) Evaluation of the cardiac function of patients with supratentorial tumours having intracranial hypertension.

(ii) Evaluation of the reversibility of the cardiac dysfunction(if present in the preoperative period) associated with raised ICP after surgical decompression.

A large volume of data focus on the brain-heart interactions in patients with an acute rise in ICP in the context of neurovascular diseases, traumatic brain injury (TBI), stroke, status epilepticus, brain death and cardiac transplantation. (23,37,46,62,66–68). Even though heart-brain cross talk had garnered much attention in the last decades and that raised intracranial pressure has been implicated as a cause for the neuro-cardiac syndromes, there is a dearth of the scientific data which addressed the cardiac effects of the subacute and chronic rise in intracranial pressure which is encountered in patients with supratentorial tumours.

A. Findings of this study with regard to hemodynamic variables

The systolic and diastolic blood pressure of patients with raised ICP (group 2) was significantly higher than that of patients with normal ICP(group1) ($p<0.05$). Though the heart rate of patients in raised ICP group was lower than that of patients with normal ICP, this was not statistically significant. ($p=0.09$). This could be attributed to a Cushing's response mimicry wherein increased intracranial pressure (ICP) resulted in a reduced CPP and hampered cerebral oxygenation, thereby affecting neuronal function. Cushing's response which is an agonal and terminal event and consists of the triad of hypertension, bradycardia and apnea was thought to be produced by brainstem ischaemia leading to a sympathetic activation response. (13–15) However, it is

debated that this reflex could be a part of a physiological reflex mechanism for arterial blood pressure(ABP) regulation even in scenarios with minimally increased ICP. (13) This debate was further strengthened by studies done by Nakamura et al. , Edvinsson et al. and Donnelly et al. who demonstrated that changes in ABP were parallel to small changes in ICP in dogs, cats, and rabbits(69,70,71). Moreover, Dickinson proved that even a modest and controlled rise in ICP resulted in a concomitant and reversible increase in ABP. (72)(73). Schmidt et al. demonstrated a high incidence of hypertension and HR variance in awake patients having a modest and gradual rise in ICP (15).

Hu and colleagues studied the relationship between ICP and HR variability. They suggested a central neural control, wherein the central nervous system could modulate the set point of the arterial baroreceptor reflex (74) Schmidt et al. demonstrated that a modest seven mmHg ICP rise from 8 to 15 mmHg significantly increased sympathetic activity by 17%. Both in mice and humans, a modest increase in ICP augmented the muscle sympathetic nerve activity (MSNA) which is a quantitative measurement of sympathetic tone. Furthermore, the decrease in ICP was associated with a significant reduction in MSNA, thereby proving the reversibility of the sympathetic activation once the ICP is normalised (18). Hence, animal and clinical studies suggest that even a minimal increase in ICP change can modulate systemic hemodynamics probably via the sympathetic nervous system (SNS) and result in hypertension.

The differences in BP between the two groups in our study signposts towards similar pathophysiology, wherein the patients with raised intracranial pressure had increased blood pressure due to increased sympathetic activity in response to ICP. More studies are warranted as to investigate the temporal course of the changes in blood pressure in chronically raised ICP scenario.

B. Findings of this study with regard to Electrocardiographic changes:

Patients with raised ICP showed ECG changes in the form of ST depression (14. 8%), T inversion (11%) and bradycardia (11%). ECG changes in acute brain injury such as TBI, SAH, stroke has been described in literature wherein common manifestations included arrhythmias and repolarisation abnormalities. In a retrospective analysis of ECG, Koepp et al. have found that 40% of patients with brain tumours had ECG changes, especially QTc prolongation. They also noted that tumours involving the limbic system had a higher percentage of ECG abnormalities compared to the extra limbic system; however, their study excluded patients with raised ICP. (75)We also noted that ECG changes indicate abnormalities of repolarisation and subendocardial ischemia in patients with increased ICP. There is a paucity of literature on similar ECG findings in scenarios with a chronic and subacute rise in ICP. As described earlier, even a minimal increase in ICP can activate the SNS resulting in subclinical effects on myocardium which could be the most likely reason for the changes seen in Group 2.

C. Findings of this study with relevance to the intraoperative adverse events:

Our data analysis showed that patients in the raised ICP group had a significantly higher incidence of post-induction hypotension (66. 6%) and increased vasopressor use (73. 3%) as compared to the normal ICP group. An increased incidence of intraoperative brain bulge, bleeding, and blood transfusion was noticed in the raised ICP group consistent to many other studies. (76) The increased bleeding could be due to the large size of tumour contributing to raised ICP and the higher blood pressure as well as increased vascularity in large tumours. Surgical stress can cause increased

catecholamine levels which can exacerbate hemodynamic stress. Further, the surgical stress and perioperative fluids can increase ventricular pre- and afterload, thus making patients with impaired left ventricular systolic function predisposed to perioperative worsening of cardiac function. (77)

In our study, patients in the raised ICP group had a significantly higher incidence of concentric remodelling and left ventricular diastolic dysfunction (33. 3%) which could have resulted in reduced LV compliance. This causes the left ventricular filling to be dependent on preload. Besides, in patients with LV diastolic dysfunction, the coronary reserve is compromised, thus making them prone to perioperative myocardial damage as well. Thus, any reduction in the preload could result in hypotension and impaired coronary perfusion leading to exacerbation of myocardial injury. (78) Therefore, the higher incidence of post-induction hypotension and the increased need for vasopressor in patients with raised ICP could be due to the LV dysfunction.

D. Echocardiographic evaluation: what was different between the two groups and why ?:

1. Chamber dimensions :

In our study, in the raised ICP group, relative wall thickness(RWT) was increased than in the normal ICP group. The increased RWT was accompanied by a normal left ventricular mass index(LVMI) in the raised ICP group. This could denote a concentric remodelling pattern in this subgroup of patients. Previous studies have shown that concentric remodelling is associated with impaired systolic and diastolic function, adverse cardiovascular events and increased mortality. (58,59,79,80) Our study results of increased wall thickness and decreased LV chamber dimensions are consistent with the study by Ferrera et al. , who evaluated the acute changes in the myocardial

function of Wistar rats with raised ICP. (22). They concluded that the raised ICP and ensuing brain death is associated autonomic storm causing interstitial myocardial oedema leading to myocardial wall hypertrophy.

Burns et al. , in their study to determine the relationship between sympathetic activation and left ventricular mass (LVM) in hypertensive patients found that there was a significant positive correlation between sympathetic activity and left ventricular mass index(LVMI)(79). These findings suggest that central sympathetic activation is associated with the development of left ventricular hypertrophy(LVH) in human hypertension. Therefore, the presence of concentric remodelling and hypertension seen in our study patients with raised ICP could be most likely due to chronic sympathetic activation. Moreover, in our study, the LVIDs in the raised ICP group was significantly lower when compared to that in the normal ICP group. These patients also had a significant increase in fractional shortening (FS). A reduced LVIDs with increased FS is indicative of increased cardiac workload due to sympathetic stimulation (60). This hypercontractile state observed in raised ICP group further strengthens the postulation of chronic sympathetic hyperactivity activity prevalent in this subgroup.

2. Changes in Systolic function:

In our study, 22 % of patients in the raised ICP group had evidence of systolic dysfunction as compared to none in the normal ICP group. The ejection fraction (EF) was significantly lower in the raised ICP group when compared to the normal ICP group. ($p<0.5$)Sympathetic overactivity and higher levels of circulating endogenous catecholamines have been implicated in the pathogenesis of left ventricular dysfunction described in the setting of neurological injury. Majority of patients with raised ICP had mild systolic dysfunction (18. 5%), and only 3. 7% had moderate

dysfunction, none had any evidence of stress-related cardiomyopathies or presence of regional wall motion abnormalities usually seen in acutely raised ICP.

Systolic dysfunction has not been described previously in patients with supratentorial brain tumours, though there is substantial literature about the same in TBI, AIS, SAH. Krishnamoorthy et al. , in their study in adult TBI patients assessed systolic function and found that 22% of their patients had systolic dysfunction, and all patients with early systolic function recovered after one week. (62,63). Bieber et al. in their study to determine the cardiac dysfunction due to focal cerebral ischemia, subjected mice to a 30-minute transient Middle cerebral artery occlusion and analysed cardiac function by serial TTE for eight weeks after surgery. They found a reduction in EF and opined that chronic systolic dysfunction was due to increased sympathetic activity. (64)Osasdchii et al. studied the effects of chronic sympathetic stimulation on cardiac changes in rats, and they found chronic stimulation lead to the increased wall thickness at one month and LV systolic pump dysfunction at six months without intrinsic myocardial failure seen in conditions like myocardial infarction. (81) Our study also shows similar finding in patients with raised ICP, whereas in those without featured of increased ICP, there were no changes in LV structure and LV systolic functions.

3. Changes in Diastolic function:

We have used the 2009 American Society of Echocardiography/ European Association of Echocardiography (ASE/EAE) Guidelines on the evaluation of diastolic dysfunction. (58) Diastolic dysfunction was found in 33. 3% of patients with raised ICP (group 2) in contrast to the absence of the same in patients with normal ICP. The majority were in Grade 1 or 2 diastolic dysfunction as per the guidelines.

The diastolic dysfunction in the patients with raised ICP could be attributed to the increased wall thickness and concentric remodelling contributing to reduced LV compliance as evidenced by higher LA volume index in group2 patients. The LV diastolic dysfunction in the raised ICP population could be due to the effects of chronic sympathetic activity and myocardial norepinephrine discharge encountered in this subset. This subsequently increases the cytosolic calcium in cardiac muscle cells**,** causing an impediment to myocardial relaxation and resulting diastolic dysfunction. This is supported by the study done by De Souza et al. , who found that the presence of asymptomatic left ventricular diastolic dysfunction is associated with increased muscle sympathetic nerve activity(MSNA), independent of blood pressure control(82).

Diastolic dysfunction has been found in other acute neurological diseases such as TBI and SAH. Kopelnik et al. in their study, demonstrated a higher incidence of late-onset diastolic dysfunction in patients with SAH(65). This is in contrast to the peaking of troponins in the initial days' post-SAH, which is an indicator of myocardial injury and they suggested that this might be because that diastolic dysfunction is seen in a persistent form of neurocardiac damages. The cause of this persistence of diastolic dysfunction over time is not entirely understood. Similarly, in patients with TBI, Cuisinier et al. performed conventional, and speckle tracking echocardiography and found that in severe TBI patients, diastolic dysfunction was slightly impaired. (66) In the TBI cohort, the isovolumic relaxation time was significantly higher compared to the control group.

Ferrera et al. evaluated echocardiographic and histological changes in the heart during brain death(22) They postulated that intracranial hypertension induces an autonomic

storm that could result in myocardial injury by causing intracellular calcium overload, free radicals production and interstitial myocardial oedema. This results in increased LV diastolic stiffness and diastolic dysfunction. Myocardial oedema has both short and long term adverse consequences. The development of myocardial interstitial fibrosis could be induced by myocardial oedema as demonstrated by Laine and Allen. (22,83)Interstitial myocardial fibrosis can result in progressive stiffness of the left ventricle leading to impaired relaxation. Hence it can be seen from our study and literature that both acute and chronic increase in ICP causes diastolic dysfunction though by different mechanisms and further experimental studies are needed in future, to validate the same.

Reversibility of cardiac dysfunction:

It is noteworthy that in our study, we observed that the systolic dysfunction reverted post-surgery, whereas the chamber dimensions and diastolic dysfunction persisted. During the preoperative period, 8 patients (26. 7%) in raised ICP group had systolic dysfunction. Among these patients, 7 patients (23. 3%) had mild LV dysfunction, and one patient (3. 3%) had moderate LV dysfunction. In the postoperative period, none of the studied patients had systolic dysfunction. This improvement in systolic function was statistically significant($p<0.02$). In the raised ICP group, 33. 3% of patients had diastolic dysfunction during preoperative period, and in 30% of patients, it persisted in the postoperative period. This was not a statistically significant change($p<0.9$)indicating that the diastolic dysfunction did not revert after normalisation of raised ICP. The reason for this partial reversal of cardiac function is a question to ponder. It could be that stimulus for sympathetic overactivity was abolished post normalisation of intracranial pressure, thus leading to an improvement in the systolic function. Since

the wall thickness did not normalise after the surgery, the concentric remodelling and decreased LV compliance could have persisted in the postoperative period. The resultant increase in the afterload and LV diastolic dysfunction could take a longer time to resolve.

Krishnamoorthy et al. described a case where hypotension occurred in the intraoperative period in a patient with TBI; intraoperative TTE aided in the diagnosis of cardiac dysfunction and guided appropriate management. Patient's cardiac function improved after surgical decompression, demonstrating the reversibility of cardiac dysfunction after surgical decompression in this setting. (84)

The insights from other systemic conditions with raised sympathetic activity could throw light on this issue. Sympathetic nervous activation is at a higher level in end-stage renal disease than in essential hypertension and cardiac failure(85). Even when transplantation restores renal function, the resultant hypertension is not reversed(85) Enhanced sympathetic activation is also seen in liver failure wherein post-transplantation, the cardiac changes are reversed after one year. (80) This indicates that the enhanced sympathetic activity may persist for a much longer time even after the inciting insult is removed. In heart failure, sympathetic activation occurs after the development of the failure which has a profound adverse impact on the clinical outcome(79,80,85) In contrast, in essential hypertension, sympathetic nervous system(SNS) activation has a critical role in the initiation and maintenance of hypertension. Clinical translation of the knowledge in the pathophysiology of these conditions has helped in making the sympathetic nervous system, a therapeutic target in the treatment of these conditions; such as the introduction of beta-adrenergic blockade in the treatment of hypertension.

Further studies are warranted to study the incidence and progress of cardiac dysfunction in the neurosurgical population presenting with intracranial tumours, and we believe our study has set the stage for further research inquiry into this subject.

What are the clinical implications of our study?

In our study population, patients with primary brain tumours with raised ICP had increased incidence of LV systolic and diastolic dysfunction. It is increasingly apparent that LV dysfunction is associated with an increased incidence of perioperative complications. (77) LV diastolic dysfunction is associated with an increased incidence of post-induction hypotension in patients with raised ICP. This could be deleterious as the CPP is already compromised in this subgroup, and any further drop in blood pressure could result in severe neurological injury. Thus a graded induction in this subgroup could help us tide over the crisis. Also, the presence of a diastolic dysfunction will make these patients preload dependent, thereby maintenance of normovolemia and avoidances of any rapid volume shifts is essential in the perioperative period.

Diastolic dysfunction is an independent predictor of postoperative pulmonary oedema and major cardiac events in patients undergoing low- and intermediate-risk surgery. Moreover, it was independently associated with postoperative adverse events and increased hospital length of stay(77) The long term complications of diastolic dysfunction in neurosurgical patients has not been independently studied. Though in routine cardiac evaluation, the systolic ventricular function defined by ejection fraction is readily quantified, and systolic dysfunction is identified, diastolic

dysfunction is less widely appreciated, perhaps because of its complex features which are not readily identified. (77,86)

Patients with initial stages of diastolic dysfunction are usually asymptomatic at rest, but neurosurgery and anaesthesia are scenarios which stresses the cardiovascular system beyond its physiological reserve. The increased use of vasopressors post-induction in the raised ICP group could be attributed to the presence of diastolic dysfunction. These patients may have hemodynamic instability as anaesthetic agents disturb the baseline sympathetic tone. Besides, the frequent use of diuretics, osmotherapy, vomiting in patients with raised ICP can aggravate the reduction of preload, increasing the sensitivity to volume status. The effects of induction drugs on cardiac inotropy and lusitropy as well as vasodilation caused by them can also contribute to hypotension requiring vasopressors.

Hence, patients with diastolic dysfunction have to be identified preoperatively, and they require prudent anaesthetic management to prevent postoperative complications and for ensuring better perioperative outcomes.

How our study differs from existing literature on heart-brain interactions, from the neurosurgical perspective?

Direct stimulation of some regions of the brain, leading to a sympathetic or parasympathetic response or neuroendocrine response of a sympathetic storm has been described in the context of brain-heart cross talk. These heart-brain interactions can manifest as cardiac rhythm disturbances, hemodynamic perturbations and even as cardiac failure and death. This condition has been described to be most commonly encountered in the setting of TBI and SAH where it can manifest from benign ECG changes to NSC or even malignant arrhythmias such as VF. Almost all the cardiac

manifestations that have been described are in the subsetting of TBI and acute neurovascular conditions such as ICH, SAH and AIS. In these settings, the pathophysiology is significantly different from that of brain tumours. There is a paucity of studies on the heart-brain interactions in the subsetting of brain tumours in patients with raised and normal ICP.

Our study has demonstrated that in patients with supratentorial brain tumours having intracranial hypertension, there is an increased prevalence of systolic and diastolic dysfunction. Though the systolic dysfunction improves post normalisation of intracranial pressure, the diastolic dysfunction persisted. This is the first study of its kind, which has addressed the neurocardiac consequences of raised ICP in patients with brain tumours.

Limitations of this study:

1. This pilot prospective observational study was done in 60 patients of a single institute. A larger multicentre trial may be required to confirm our findings, understand the cardiac profile and clinical implications of the same in patients with intracranial hypertension.
2. We have analysed the postoperative echocardiogram on the seventh day after the surgery. And our results have shown that the preoperative cardiac dysfunction is not fully reversed on the seventh day. Though stunned neurogenic myocardium and takotsubo cardiomyopathy are transient and reversible mostly after a week, this may not be similar to the changes encountered in the tumour population of our study. This could be due to the difference in the pathophysiology of cardiac dysfunction. The myocardial dysfunction due to acute rise in ICP could be due to the sudden sympathetic storm. In the scenario of slow increase in ICP, chronically increased sympathetic activity induces not only changes in structure but also the functional changes of chronic increase in myocardial workload. Cardiac dysfunction caused by sympathetic overactivity in other scenarios such as cirrhotic cardiomyopathy which has been assessed 6 months and 1 year after liver transplantation has shown improvement of cardiac function. Whether the cardiac dysfunction in patients with raised ICP is reversible after 6 months or 1 year should be a question for further neuro cardiac studies.
3. We have used 2009 ASE guidelines for assessment of diastolic dysfunction in our study and not the recent 2016 guidelines, as the latter cannot be used in the perioperative setting. In a study comparing evaluation of diastolic dysfunction based on these two guidelines in a general population of over 1000 persons, Almeida et al found that the prevalence of diastolic dysfunction was only 1. 6%

as per recent guidelines whereas it was 38% as per old guidelines. (87)The authors have questioned the value of recent guidelines as it is focused on advanced cases and miss the mild to moderate dysfunction. The implications of these guidelines in our study is unknown as the patients were having mild to moderate dysfunction and not on heart failure.

4. We had excluded patients with lesions in the prefrontal cortex, insula, hippocampus, amygdala and hypothalamus as these regions being part of a central autonomic network can produce cardiac changes, independent of whether they cause raised ICP. But we cannot completely rule out the influence of the same in the study, e. g. hydrocephalus of the third ventricle could cause compression of the hypothalamus. It is clinically near impossible to rule out the complete influence of the central autonomic network on the effects on cardiac function in patients with raised ICP.
5. Though the results of our study indicate sympathetic overactivity, we did not quantitatively measure the same. Further studies measuring the sympathetic activity quantitatively could throw light on the plausible pathophysiologic mechanisms behind the cardiac dysfunction observed.
6. We did not take a postoperative ECG to identify whether the changes seen were reversed following tumour resection. Similarly,we did not measure any markers of cardiac dysfunction such as troponin, pro-brain natriuretic peptide (BNP) in this study. Future studies evaluating the same are required for correlation with the severity of cardiac dysfunction and prognostication.

Conclusion

In conclusion, we demonstrated that patients with primary brain tumours and features of the gradual rise of ICP, there were hemodynamic changes like the significant elevation of systolic and diastolic blood pressure, ECG changes, changes in cardiac structure in the form of increased left ventricular relative wall thickness and features of altered cardiac functions like LV systolic and diastolic dysfunction. Patients without evidence of raised ICP did not have abnormalities in echocardiography. Patients with increased intracranial pressure had more intraoperative adverse events.

Though systolic function improved in postoperative period at follow up echocardiography on 7th postoperative day, changes in LV chamber dimensions and diastolic dysfunction did not revert. Based on the available literature, we believe that the changes noted in our study are due to increased sympathetic activity in response to rising ICP and impaired cerebral perfusion. These changes are different from the cardiac abnormalities usually seen with an acute rise of ICP and sympathetic storm.

Future studies with a larger population are required to understand the pathogenesis, implications of cardiac abnormalities as well as the long term reversibility of the cardiac functions, in this subset of patients.

Bibliography

1. Osteraas ND, Lee VH. Neurocardiology. Handbook of Clinical Neurology. Edited by Eelco F. M. Wijdicks, Andreas H. Kramer Elsevier; 2017: p. 49–65.

2. Mazzeo AT, Micalizzi A, Mascia L, Scicolone A, Siracusano L. Brain–heart crosstalk: the many faces of stress-related cardiomyopathy syndromes in anaesthesia and intensive care. Br J Anaesth. 2014; 112:803–15.

3. Zou R, Shi W, Tao J, Li H, Lin X, Yang S, et al. Neurocardiology: Cardiovascular Changes and Specific Brain Region Infarcts. BioMed Res Int. 2017; 5:1–7.

4. Manikandan S. Heart in the brain injured. J Neuroanaesth Crit Care. 2016 ; 03:S12–5.

5. Hrishi A, Lionel KR, Prathapadas U. Head Rules Over the Heart: Cardiac Manifestations of Cerebral Disorders. Indian J Crit Care Med. 2019 ; 23:329–35.

6. Shivalkar B, Van Loon J, Wieland W, Tjandra-Maga TB, Borgers M, Plets C, et al. Variable effects of explosive or gradual increase of intracranial pressure on myocardial structure and function. Circulation. 1993; 87:230–9.

7. Dixit S, Castle M, Velu RP, Swisher L, Hodge C, Jaffe AS. Cardiac Involvement in Patients With Acute Neurologic Disease: Confirmation With Cardiac Troponin I. Arch Intern Med. 2000; 160:3153.

8. Goel R, Johnson F, Mehra MR. **Brain injury and ventricular dysfunction:Insights** into reversible heart failure Congest Heart Fail. 2005; 11:99-101.

9. Venkateswaran R, Bonser R, Steeds R. The echocardiographic assessment of donor heart function prior to cardiac transplantation. Eur J Echocardiogr. 2005; 6:260–3.

10. Potapov EV, Ivanitskaia EA, Loebe M,Muckel M,Muller C,Sodian R et al. Value of cardiac troponin I and T for selection of heart donors and as predictors of early graft failure. Transplantation. 2001; 71:1394– 1400.

11. Abraham M, Singhal V. Intracranial pressure monitoring. J Neuroanaesthesiol Crit Care. 2015; 2:193–203.

12. Wan WH, Ang BT, Wang E. The Cushing Response: A case for a review of its role as a physiological reflex. J Clin Neurosci. 2008; 15:223–8.

13. Paton JFR, Dickinson CJ, Mitchell G. Harvey Cushing and the regulation of blood pressure in giraffe, rat and man: introducing 'Cushing's mechanism': Blood pressure regulation in giraffe, man and rat. Exp Physiol. 2009; 94:11–7.

14. Fitch W, McDowall DG, Keaney NP, Pickerodt VWA. Systemic vascular responses to increased intracranial pressure: 2 The `Cushing' response in the presence of intracranial space-occupying lesions: systemic and cerebral haemodynamic studies in the dog and the baboon. J Neurol Neurosurg Psychiatry. 1977; 40:843–52.

15. E. A. Schmidt, Z. Czosnyka, S. Momjian. Intracranial baroreflex yielding an early Cushing response in human. Acta Neurochir. 2005; 95:253-256.

16. Fitch W, McDowall DG. Systemic vascular responses to increased intracranial pressure: Effects of progressive epidural ballon expansion on intracranial pressure and systemic circulation. J Neurol Neurosurg Psychiatry. 1977; 40:833–42.

17. Plets C. Arterial hypertension in neurosurgical emergencies. Am J Cardiol 1989; 63:40.

18. Schmidt EA, Despas F, Pavy-Le Traon A, Czosnyka Z, Pickard JD, Rahmouni K, et al. Intracranial Pressure Is a Determinant of Sympathetic Activity. Front Physiol. 2018; 9:11.

19. Fodstad F, Kelley PJ, Buchfelder M. History of the Cushing reflex. Neurosurgery. 2006; 59 :1132-1137

20. Koszewicz M, Michalak S, Bilinska M, Budrewicz S, Zaborowski M, Slotwinski K, et al. Profile of autonomic dysfunctions in patients with primary brain tumor and possible autoimmunity. Clin Neurol Neurosurg. 2016; 151:51–4.

21. Novitzky D, Wicomb WN, Cooper DKC, Rose AG, Reichart B. Prevention of Myocardial Injury During Brain Death by Total Cardiac Sympathectomy in the Chacma Baboon. Ann Thorac Surg. 1986; 41:520–4.

22. Ferrera R, Hadour G, Tamion F, Henry J-P, Mulder P, Richard V, et al. Brain death provokes very acute alteration in myocardial morphology detected by echocardiography: preventive effect of beta-blockers: Acute myocardial alteration during brain death. Transpl Int. 2011; 24:300–6.

23. Mazzeo AT, Micalizzi A, Mascia L, Scicolone A, Siracusano L. Brain–heart crosstalk: the many faces of stress-related cardiomyopathy syndromes in anaesthesia and intensive care. Br J Anaesth. 2014; 112:803–15.

24. Samuels MA. The Brain–Heart Connection. Circulation. 2007; 116(1):77–84.

25. Gregory T, Smith M. Cardiovascular complications of brain injury. Contin Educ Anaesth Crit Care Pain. 2012; 12:67–71.

26. Richter CP. On the Phenomenon of Sudden Death in Animals and Man. Psychosom Med. 1957;3:8.

27. Byer E, Ashman R, Toth LA. Electrocardiograms with large, upright T waves and long Q-T intervals. Am Heart J. 1947; 33:796–806.

28. Burch GE, Meyers R, Abildskov JA. A new electrocardiographic pattern observed in cerebrovascular accidents. Circulation. 1954; 9:719–723.

29. Cropp GJ, Manning GW. Electrocardiographic Changes Simulating Myocardial Ischemia and Infarction Associated with Spontaneous Intracranial Hemorrhage. Circulation. 1960 ; 22:25–38.

30. Raab W, Stark E, Macmillan WH, Gigee WR. Sympathogenic origin and antiadrenergic prevention of stress-induced myocardial lesions. Am J Cardiol. 1961; 8:203–211.

31. Barger AC, Herd JA, Liebowitz MR. Chronic catheterization of coronary artery induction of ECG pattern of myocardial ischemia by intracoronary epinephrine. Proc Soc Exp Biol **Med**. 1961; 107: 474–477

32. Melville KI, Blum B, Shister HE, Silver MD. Cardiac ischemic changes and arrhythmias induced by hypothalamic stimulation. Am J Cardiol. 1963; 12:781–91.

33. Koskelo P, Punsar SO, Sipila W. Subendocardial haemorrhage and ECG changes in intracranial bleeding. BMJ. 1964; 1:1479–1483.

34. Connor RCR. Myocardial damage secondary to brain lesions. Am Heart J**.** 1969; 78: 145–148.

35. Greenshoot JH, Reichenbach DD. Cardiac injury and subarachnoid haemorrhage. J Neurosurg. 1969; 30:521–531.

36. Hunt D, Gore I. Myocardial lesions following experimental intracranial hemorrhage: Prevention with propranolol. Am Heart J. 1972; 83(2):232–6.

37. Tung P, Kopelnik A, Banki N, Ong K, Ko N, Lawton MT, et al. Predictors of Neurocardiogenic Injury After Subarachnoid Hemorrhage. Stroke. 2004; 35(2):548–51.

38. Van der Wall EE, van Gilst WH. Neurocardiology: close interaction between heart and brain. Neth Heart J. 2013; 21:51-52.

39. Nagai M, Hoshide S, Kario K. The insular cortex and cardiovascular system: a new insight into the brain-heart axis. J Am Soc Hypertens 2010; 4:174 – 82.

40. Fink JN, Selim MH, Kumar S, Voetsch B, Fong WC, Caplan LR. Insular cortex infarction in acute middle cerebral artery territory stroke: predictor of stroke severity and vascular lesion. Arch Neurol 2005; 62:1081 – 5.

41. Oppenheimer SM, Gelb A, Girvin JP, Hachinski VC. Cardiovascular effects of human insular cortex stimulation. Neurology. 1992; 42:1727–1732.

42. Lavy SL, Yaar I, Melamed E. The effect of acute stroke on cardiac functions as observed in an intensive stroke care unit. Stroke. 1974; 5:775–780.

43. Goldstein DS. The electrocardiogram in stroke: relationship to pathophysiological type and comparison with prior tracings. Stroke. 1979; 10:253–259.

44. Kallmuenzer B,Breuer L,Kahl N. Serious cardiac arrhythmias after stroke: incidence, time course, and predictors – a systematic, prospective analysis. Stroke. 2012; 43:2892–2897.

45. Wang TD, Wu CC, Lee YT. Myocardial stunning after cerebral infarction. Int J Cardiol. 1997; 58:308–311.

46. Ay H, Koroshetz WJ, Benner T,Vangel MG,Melinosky C, Arsava EM et al. Neuroanatomic correlates of stroke-related myocardial injury. Neurology. 2006; 66:1325–1329.

47. Garcıa-Berrocoso T, Giralt D, Bustamante A, Etgen T, Jensen J, Sharma JC,et al. B-type natriuretic peptides and mortality after stroke: a systematic review and meta-analysis. Neurology. 2013; 81:1976–1985.

48. Bybee KA, Prasad A. Stress-related cardiomyopathy syndromes. Circulation. 2008; 118: 397–409.

49. Wittstein IS, Thiemann DR, Lima JA,Baughman KL,Schulman SP, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med. 2005; 352: 539–48.

50. Lechowicz-Glogowska E, Rojek A, Duszynska W. The Irreversible Neurogenic Stress Cardiomyopathy During Large Supratentorial Brain Tumor Resection. Neurocrit Care. 2019; 31:587–91.

51. Deibert E, Aiyagari V, Diringer MN. Reversible left ventricular dysfunction associated with raised troponin I after subarachnoid haemorrhage does not preclude successful heart transplantation. Heart. 2000; 84:205– 207.

52. Porter TR, Shillcutt SK, Adams MS, Desjardins G, Glas KE, Olson JJ, et al. Guidelines for the Use of Echocardiography as a Monitor for Therapeutic Intervention in Adults: A Report from the American Society of Echocardiography. J Am Soc Echocardiogr. 2015; 28(:40–56.

53. Mitchell C, Rahko PS, Blauwet LA, Canaday B, Finstuen JA, Foster MC, et al. Guidelines for Performing a Comprehensive Transthoracic Echocardiographic Examination in Adults: Recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr. 2019; 32:1–64.

54. Hillis GS, Bloomfield P. Basic transthoracic echocardiography BMJ. 2005; 330:1432-1436.

55. Chopra S, Peter S. Screening for coronary artery disease in patients with type 2 diabetes mellitus: An evidence-based review. Indian J Endocrinol Metab. 2012; 16:94-101.

56. Rosen BD, Edvardsen T, Lai S, Castillo E, Pan L, Jerosch-Herold M, et al. Left Ventricular Concentric Remodeling Is Associated With Decreased Global and Regional Systolic Function: The Multi-Ethnic Study of Atherosclerosis. Circulation. 2005; 112:984–91.

57. Caballero L, Kou S, Dulgheru R, Gonjilashvili N, Athanassopoulos GD, Barone D, et al. Echocardiographic reference ranges for normal cardiac Doppler data: results from the NORRE Study. Eur Heart J Cardiovasc Imaging. 2015; 20:83.

58. Nagueh SF, Appleton CP, Gillebert TC, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr. 2009; 22:107-133.

59. Hahn RT, Abraham T, Adams MS, Bruce CJ, Glas KE, Lang RM, et al. Guidelines for performing a comprehensive transesophageal echocardiographic examination: Recommendations from the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. J Am Soc Echocardiogr 2013; 26:921-64.

60. Chengode S. Left ventricular global systolic function assessment by echocardiography. Ann Card Anaesth. 2016; 19:26.

61. Otterstad JE. Measuring left ventricular volume and ejection fraction with the biplane Simpson's method. Heart. 2002; 88:559-560.

62. Krishnamoorthy V, Prathep S, Sharma D, Gibbons E, Vavilala MS. Association between electrocardiographic findings and cardiac dysfunction in adult isolated traumatic brain injury. Indian J Crit Care Med. 2014; 18:570–4.

63. Krishnamoorthy V, Rowhani-Rahbar A, Gibbons EF, Rivara FP, Temkin NR, Pontius C, et al. Early Systolic Dysfunction Following Traumatic Brain Injury: A Cohort Study. Crit Care Med. 2017; 45:1028–36.

64. Bieber M, Werner RA, Tanai E, Hofmann U, Higuchi T, Schuh K, et al. Stroke-induced chronic systolic dysfunction driven by sympathetic overactivity: Stroke and Systolic Dysfunction. Ann Neurol. 2017; 82:729–43.

65. Kopelnik A, Fisher L, Miss JC, Banki N, Tung P, Lawton MT, et al. Prevalence and Implications of Diastolic Dysfunction After Subarachnoid Hemorrhage. Neurocrit Care. 2005; 3:132–8.

66. Cuisinier A, Maufrais C, Payen J-F, Nottin S, Walther G, Bouzat P. Myocardial function at the early phase of traumatic brain injury: a prospective controlled study. Scand J Trauma Resusc Emerg Med. 2016; 24:129.

67. Akashi YJ, Nef HM, Mollmann H, Ueyama T. Stress cardiomyopathy. Annu Rev Med 2010; 61:271–86.

68. M Krishnamoorthy V, Mackensen GB, Gibbons EF, Vavilala MS. Cardiac Dysfunction After Neurologic Injury: What Do We Know and Where Are We Going? Chest. 2016; 149:1325–31.

69. Nakamura K, Osborn Jr JW, Cowley Jr AW. Pressor response to small elevations of cerebroventricular pressure in conscious rats. Hypertension. 1987; 10:635–641.

70. Edvinsson L, Owman C, West KA. Modification of kaolin- induced intracranial hypertension at various time-periods after superior cervical sympathectomy in rabbits. Acta Physiol. Scand. 1971; 83: 51–59.

71. Donnelly J, Czosnyka M, Harland S, Varsos GV, Cardim D, Robba C, et al. Cerebral haemodynamics during experimental intracranial hypertension. J. Cereb. Blood Flow Metab. 2017; 37:694–705.

72. Dickinson CJ. Neurogenic Hypertension Revisited. Clin Sci. 1981; 60:471–7.

73. Dickinson CJ, McCubbi JW. Pressor effect of increased cerebrospinal fluid pressure and vertebral artery occlusion with and without anesthesia. Circ Res. 1963; 12:190–202.

74. Xiao Hu, Nenov V, Vespa P, Bergsneider M. Characterization of Interdependency Between Intracranial Pressure and Heart Variability Signals: A Causal Spectral Measure and a Generalized Synchronization Measure. IEEE Trans Biomed Eng. 2007; 54:1407–17.

75. Koepp M, Kern A, Schmidt D. Electrocardiographic changes in patients with brain tumors. Arch Neurol. 1995; 52:152-155.

76. Rajagopalan V, Chouhan RS, Pandia MP, Lamsal R, Rath GP. Effect of Intraoperative Blood Loss on Perioperative Complications and Neurological Outcome in Adult Patients Undergoing Elective Brain Tumor Surgery. J Neurosci Rural Pract. 2019; 10:631-640.

77. Godfrey GE, Peck MJ. Diastolic dysfunction in anaesthesia and critical care. BJA Educ. 2016; 16:287–91.

78. Flu W-J, van Kuijk J-P, Hoeks SE, Kuiper R, Schouten O, Goei D, et al. Prognostic Implications of Asymptomatic Left Ventricular Dysfunction in Patients Undergoing Vascular Surgery: Anesthesiology. 2010; 112:1316–24.

79. Burns J, Sivananthan MU, Greenwood JP, ChB M. The Relationship Between Central Sympathetic Drive and MRI Determined Left Ventricular Mass In Essential Hypertension. Circulation. 2007; 115:1999–2005.

80. Schlaich MP, Kaye DM, Lambert E, Sommerville M, Socratous F, Esler MD. Relation Between Cardiac Sympathetic Activity and Hypertensive Left Ventricular Hypertrophy. Circulation. 2003; 108:560–5.

81. Osadchii OE, Woodiwiss AJ, Deftereos D, Norton GR. Temporal changes in myocardial adrenergic regulation with the progression to pump dysfunction after chronic beta-adrenoreceptor activation in rats. Pflugers Arch. 2007; 455 :251-260.

82. de Souza SBC, Rocha JA, Cuoco MAR, Guerra GM, Ferreira-Filho JC, Borile S, et al. High Muscle Sympathetic Nerve Activity Is Associated With Left Ventricular Dysfunction in Treated Hypertensive Patients. Am J Hypertens. 2013; 26:912–7.

83. Laine GA, Allen SJ. Left ventricular myocardial edema. Lymph flow, interstitial fibrosis, and cardiac function. Circ Res. 1991; 68:1713–21.

84. Krishnamoorthy V, Sharma D, Prathep S, Vavilala MS. Myocardial Dysfunction in Acute Traumatic Brain Injury Relieved by Surgical Decompression. Case Rep Anesthesiol. 2013; 2013:1–4.

85. Antoine S, Vaidya G, Imam H, Villarreal D. Pathophysiologic Mechanisms in Heart Failure: Role of the Sympathetic Nervous System. Am J Med Sci. 2017; 353:27–30.

86. Lester SJ, Tajik AJ, Nishimura RA, Oh JK, Khandheria BK, Seward JB. Unlocking the Mysteries of Diastolic Function. J Am Coll Cardiol. 2008; 51:679–89.

87. Almeida JG, Fontes-Carvalho R, Sampaio F, et al. Impact of the 2016 ASE/EACVI recommendations on the prevalence of diastolic dysfunction in the general population. Eur Heart J Cardiovasc Imaging 2018; 19:380–6.

Appendix

Appendix1

PROFORMA

Title: Comparison of hemodynamics and cardiac function before and after neurosurgery in patients with and without raised intracranial pressure: A pilot observational study with Transthoracic Echocardiography

GROUP	I / II		Age (Years)		Sl. No		Gender	M/F
Weight (kg)		Height (cm)		BSA (kg/m^2)				
Diagnosis					Surgery			

PREOP DATA

- Symptoms of raised ICP (IntraCranial Pressure): Yes / No
- GCS (Glasgow coma scale) score: E_____V_____M_____
- CT/MRI findings of raised ICP: Yes / No
- Preop neurological deficits:
- Seizures: Yes / No
- Drug history: Steroids / Diuretics/ 3%saline/ other drugs
- Comorbid illness:
- ASA (American Society of Anaesthesiologists) grading:
- Any ECG (Electrocardiography) changes:
- Preop Vitals
  - HR(heart rate)
  - BP(blood pressure)

INTRAOP DATA

- Any episode of haemodynamic instability:
  - Bradycardia: Yes / No Duration:
  - Tachycardia: Yes / No Duration:
  - Hypotension: Yes / No Duration:
  - Hypertension: Yes / No Duration:
- Any use of vasopressors/vasodilators:

    - What drug:
    - Time of starting:
    - Dose:
    - Time of stopping:
- Blood transfusion:
    - Volume:
    - Type:
- Fluid balance:
    - Crystalloids:
    - Colloids:
    - Blood products:
    - Urine output:
    - Blood loss:

POSTOP DATA

- GCS(Glasgow coma scale):
- Any episode of haemodynamic instability:
    - Bradycardia: Yes / No Duration:
    - Tachycardia: Yes / No Duration:
    - Hypotension: Yes / No Duration:
    - Hypertension: Yes / No Duration:
- Any use of vasopressors/vasodilators:
    - What drug:
    - Time of starting:
    - Dose:
    - Time of stopping:
- Blood transfusion:
    - Volume:
    - Type:
- Symptoms of raised ICP: Yes / No
- Seizures: Yes / No
- Any new focal neurological deficit: Yes / No
- Any drugs affecting cardiovascular system : yes / no
    - What drug:
    - Time of starting:
    - Dose:
    - Time of stopping:
        - Any Pain :
        - Visual analogue scale :

PERIOP ECHO

	PreOp	PostOp 7th day/ time of discharge
Chamber Dimensions		
LVIDd(left ventricular internal diameter end diastole) cm		
LVIDs (left ventricular internal diameter end systole) cm		
IWIDd(Inferior wall internal diameter end diastole) cm		
IWIDs (inferior wall internal diameter end systole) cm		
IVSd (Interventricular septum thickness end diastole) cm		
IVSs (interventricular septum thickness end systole) cm		
LVOT (left ventricle outflow tract) cm		
RWT (relative wall thickness)		
LV Mass Index		
LA area (left atrium area) cm2		
LA volume index (cm^3)		
Ventricular function		
LVFS (left ventricle Fraction Shortening)		
LVEF (ejection fraction) %		
RWMA (regional wall motion abnormalty) : Yes/No If Yes (RWMA score)		
LVOT(Left ventricular outflow tract area)		
Aortic VTI(velocity time integral)		
SV(stroke volume)		
CO(cardiac output)		
LV Systolic: Good/Mild/Mod/Severe		
E/A		

E’			
E/E’			
Deceleration time			
LA volume index			
LV Diastolic: Normal/Impaired Relaxation/ Pseudo-normal/Restrictive			
TAPSE (tricuspid annular plane systolic excursion)			
RV Systolic: Good/Mild/Mod/Severe			
Valve			
Mitral: Area Normal/Stenosis/Regurgitation			
Tricuspid: Area Normal/Stenosis/Regurgitation			
Aortic: Area Normal/Stenosis/Regurgitation			
Pulmonary: Area Normal/Stenosis/Regurgitation			
Pericardium/Clot			
Pericardial Effusion: Yes/No			
Clot	Yes/No		
	Location		

APPENDIX2

PATIENT CONSENT AND INFORMATION SHEET

Title of the study:

Comparison of hemodynamics and cardiac function before and after neurosurgery in patients with and without raised intracranial pressure : A pilot observational study with Transthoracic Echocardiography, by Dr Neeraja Ajayan, Senior resident, Neuroanaesthesia divison, Dept of Anaesthesiology, SCTIMST.

Name of the Investigators:

Dr Neeraja Ajayan, Dr. Manikandan. S, Dr Unnikrishnan. P, Dr Prakash Nair

Hemodynamic disturbances (heart rate, rhythm, blood pressure) and changes in cardiac function changes can occur in patients with various neurosurgical conditions especially when the intracranial pressure is high. You are being requested to participate in this study which is done to detect changes in hemodynamics and cardiac function before and after your proposed neurosurgical procedure. This study will require use of transthoracic echocardiography. This is used to monitor cardiac function in this institute and worldwide. We have planned to include about 60 people from this hospital in this study.

What is TTE(trans thoracic echocardiography)?

TTE is a noninvasive method which uses ultrasound to image of your heart structure ans functions. During TTE, a probe is placed on the chest to get various views of the heart.

The ultrasound shows the structure and functions of the heart muscles and valves from different angles. This method is routinely being used all over the world in neurosurgical patients undergoing major surgeries and is painless procedure and is found to be safe.

What happens before the test?

There is no special preparation for the TTE.

What happens during a TTE?

- During a TTE, you will lie on your back or on your left side on a bed or table.
- A small amount of gel will be rubbed on the left side of your chest to help pick up the sound waves.
- The probe is placed over your chest and moved slowly back and forth.
- The echos from the probe are sent to a video monitor that records pictures of your heart for later viewing and evaluation.

If you take part what will you have to do?

TTE is done routinely during preoperative period for all neurosurgical cases.

On the day before surgery, a TTE probe will be placed on your chest to monitor your cardiac function and cardiac functions will be recorded. This procedure is routinely done in our institute prior to neurosurgical procedure.

On the day of surgery you will be taken inside the Operation Theatre. Monitors to check your heart beat, blood pressure and oxygen saturation level will be attached. A small venous cannula will be inserted under local anesthesia in the hand for fluid and

drug administration. Arterial cannula also will be inserted under local anesthesia for monitoring the blood pressure. General Anaesthesia will be induced as per the routine anesthesia practice in the hospital. Hemodynamics (heart rate, blood pressure) will be monitored throughout the surgery as per routine. At the end of surgery, after giving medicines to reverse anaesthesia you will be shifted to intensive care unit for further monitoring and care. TTE will be again performed to assess your cardiac function on seventh postoperative day.

Does TTE use have any side effects?

There are no known risks or side effects to transthoracic echocardiogram

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

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

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

TTE is used in our institute prior to all neurosurgical cases and no additional cost will be incurred.

What happens after the study is over?

After the study is over, the results will be analysed and report will be submitted to this institute as part of thesis

Will your personal details be kept confidential?

You will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr Neeraja Ajayan (Principal investigator) mobile number 9446219309. email: drneerajaajayan@sctimst. ac. in

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

കാര്യബോധത്തോടെയുള്ള സമ്മതപത്രം

പ്രഖ്യാപനം

പങ്കെടുക്കുന്നയാളുടെ പേര് ജനനതിയതി, വയസ്സ് (വർഷത്തിൽ)

ഞാൻ, _____,മകൻ/മകൾ പഠനസംബന്ധമായി എനിക്ക് നൽകിയ വിവരങ്ങൾ വായിച്ചു എന്ന് പ്രസ്താവിക്കുന്നു. (ദയവായി കോളങ്ങളിൽ ടിക് ചെയ്യുക)

തലയോട്ടിക്കുള്ളിൽ വർദ്ധിച്ച സമ്മർദ്ദമുള്ളവരും, ഇല്ലാത്തവരുമായ രോഗികളിൽ ശസ്ത്രക്രിയക്കു മുൻപും ശേഷവും രക്തചംക്രമണ സംവിധാനത്തിന്റെയും ഹൃദയത്തിന്റെ പ്രവർത്തനത്തിന്റെയും താരതമ്യം. ട്രാൻസ് തൊറാസിക് എക്കോകാർഡിയോഗ്രഫിയുപയോഗിച്ചുള്ള ഒരു നിരീക്ഷണാത്മക ലഘു പഠനം.

- എനിക്കുണ്ടായ സംശയങ്ങൾ പരിഹരിച്ചു [ ]
- എന്റെ ഈ പഠനത്തിലുള്ള പങ്കാളിത്തം സ്വമേധയായുള്ളതാണെന്നും, എനിക്ക് ഒരു കാരണവും കൂടാതെ ഏതുസമയത്തും, എനിക്കുള്ള വൈദ്യശുശ്രൂഷയെയോ നിയമപരമായ അവകാശങ്ങളെയോ ബാധിക്കാതെ പിൻവാങ്ങാമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- ഈ പഠനത്തിന്റെ ഗവേഷകർ, നൈതീക കമ്മിറ്റി, നിയന്ത്രണാധികാരികൾ എന്നിവർക്ക് എന്റെ ആരോഗ്യവിവരങ്ങൾ ഞാൻ പഠനത്തിൽനിന്നും പിൻവാങ്ങിയാലും പരിശോധിക്കാൻ എന്റെ സമ്മതം അവശ്യമില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. ഇതിനു ഞാൻ സമ്മതിക്കുന്നു, [ ]
- എനിക്ക് പഠനത്തെപ്പറ്റി കൂടുതലറിയാനോ, പങ്കെടുക്കുന്നയാളുടെ അവകാശങ്ങളെപ്പറ്റി അറിയേണ്ടതായോ വന്നാൽ പ്രധാന ഗവേഷകയുടെ ബന്ധപ്പെടാനുള്ള നമ്പർ എനിക്ക് നൽകിയിട്ടുണ്ട് [ ]
- ഭാവിയിൽ മൂന്നാം കക്ഷികൾക്കോ പ്രസിദ്ധീകരണത്തിനോ നൽകുമ്പോൾ എന്റെ വ്യക്തിവിവരങ്ങൾ വെളിപ്പെടുത്തുകയില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]

- സ്വമേധയാ പഠനത്തിൽ പങ്കെടുക്കാൻ ഞാൻ സമ്മതിക്കുന്നു. [ ]
- സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു പ്രതി എനിക്ക് കിട്ടി. [ ]

പേര്	സാക്ഷിയുടെ പേര്
ഒപ്പ്/ രോഗിയുടെ വിരലടയാളം/	ഒപ്പ്
നിയമപരമായ പ്രതിനിധി	തീയതി
തീയതി	

രോഗിക്കുള്ള കാര്യവിവരണ പത്രം

പഠനശീർഷകം: തലയോട്ടിക്കുള്ളിൽ വർദ്ധിച്ച സമ്മർദ്ദമുള്ളവരും, ഇല്ലാത്തവരുമായ രോഗികളിൽ ശസ്ത്രക്രിയക്കു മുൻപും ശേഷവും രക്തചംക്രമണ സംവിധാനത്തിന്റെയും ഹൃദയത്തിന്റെ പ്രവർത്തനത്തിന്റെയും താരതമ്യം. ട്രാൻസ് തൊറാസിക് എക്കോകാർഡിയോഗ്രഫി യുപയോഗിച്ചുള്ള ഒരു നിരീക്ഷണാത്മക ലഘു പഠനം.

ഗവേഷകരുടെ പേര്.

ഡോ. നീരജ അജയൻ, ഡോ. മണികണ്ഠൻ എസ്, ഡോ. ഉണ്ണികൃഷ്ണൻ പി, ഡോ പ്രകാശ് നായർ

രക്തചംക്രമണ സംവിധാനത്തിലുള്ള (ഹൃദയമിടിപ്പ്, താളം, രക്തസമ്മർദ്ദം) മാറ്റങ്ങൾ, ഹൃദയത്തിന്റെ പ്രവർത്തനത്തിലുള്ള മാറ്റങ്ങൾ എന്നിവ ന്യൂറോളജിക്കൽ സാഹചര്യങ്ങളിലുണ്ടാകാം, പ്രത്യേകിച്ചും തലയോട്ടിക്കുള്ളിലെ സമ്മർദ്ദം ഉയർന്നിരിക്കുമ്പോൾ. താങ്കളുടെ ശസ്ത്രക്രിയക്കു മുൻപും ശേഷവും രക്തചംക്രമണ സംവിധാനത്തിലും ഹൃദയത്തിന്റെ പ്രവർത്തനത്തിലുമുള്ള മാറ്റങ്ങൾ കണ്ടെത്താൻ നടത്തുന്ന ഈ പഠനത്തിൽ പങ്കെടുക്കാൻ താങ്കളോടഭ്യർത്ഥിക്കുന്നു. ഈ പഠനത്തിന് ട്രാൻസ് തൊറാസിക് എക്കോകാർഡിയോഗ്രഫി ഉപയോഗിക്കേണ്ടതുണ്ട്. ഇത് ഹൃദയപ്രവർത്തനം നിരീക്ഷിക്കാൻ ഈ സ്ഥപനത്തിലും ലോകമെമ്പാടും ഉപയോഗിക്കുന്നു. ഈ ആശുപത്രിയിൽനിന്നുള്ള 60 ആളുകളെ ഈ പഠനത്തിൽ ഉൾപ്പെടുത്താൻ ഞങ്ങൾ ആസൂത്രണം ചെയ്യുന്നു.

എന്താണ് റ്റിറ്റിഇ

താങ്കളുടെ ഹൃദയത്തിന്റെ വ്യത്യസ്ത വീക്ഷണങ്ങൾ ലഭിക്കാൻ ഒരു പ്രോബ് നെഞ്ചിൽ വച്ചുള്ള ഹൃദയത്തിന്റെ അൾട്രാസൗണ്ട് ചിത്രീകരണമാണ് റ്റിറ്റിഇ. വ്യത്യസ്ത കോണുകളിൽനിന്നും ഹൃദയപേശികളുടെയും വാൽവുകളുടെയും ഘടനയും പ്രവർത്തനവും അൾട്രാസൗണ്ട് ദൃശ്യമാക്കും. ലോകമെമ്പാടും പ്രധാന ശസ്ത്രക്രിയകൾക്ക് വിധേയരാകുന്ന ന്യൂറോ ശസ്ത്രക്രിയാ രോഗികളിൽ ഈ ഉപകരണം ഉപയോഗിക്കുകയും സുരക്ഷിതമെന്ന് കണ്ടെത്തുകയും ചെയ്തിട്ടുണ്ട്.

പരിശോധനക്കു മുൻപ് എന്ത് സംഭവിക്കും?

പരിശോധനക്ക് പ്രത്യേക തയാറെടുപ്പുകളൊന്നും ഇല്ല.

റ്റിറ്റിഇ ചെയ്യുമ്പോൾ എന്ത് സംഭവിക്കും ?

റ്റിറ്റിഇ ചെയ്യുമ്പോൾ, താങ്കൾ ഒരു ബെഡിലോ മേശയിലോ മലർന്നോ ഇടതുവശം ചരിഞ്ഞോ കിടക്കും

ശബ്ദതരംഗങ്ങൾ ലഭിക്കുന്നതിനായി ചെറിയ ഒരളവ് ജൽ താങ്കളുടെ നെഞ്ചിന്റെ ഇടതുവശത്ത് പുരട്ടും

പ്രോബ് താങ്കളുടെ നെഞ്ചിൽ അമർത്തിവച്ച് പതുക്കെ മുന്നോട്ടും പുറകോട്ടും ചലിപ്പിക്കും.

പ്രോബിൽനിന്നുള്ള പ്രതിധ്വനികൾ, ചിത്രങ്ങൾ രേഖപ്പെടുത്തുന്ന ഒരു വീഡിയോ മോണിറ്ററിലേക്ക് പിന്നീട് പരിശോധിക്കാനും വിലയിരുത്തുവാനുമായി അയക്കും

താങ്കൾ പങ്കെടുക്കുന്നു എങ്കിൽ എന്തുചെയ്യണം?

ശസ്ത്രക്രിയക്കു മുൻപുള്ള ദിവസം താങ്കളുടെ ഹൃദയത്തിന്റെ പ്രവർത്തനം നിരീക്ഷിക്കാൻ റ്റിഇഇയുടെ ഒരു പ്രോബ് താങ്കളുടെ നെഞ്ചിൽ വയ്ക്കും.

ശസ്ത്രക്രിയാ ദിവസം താങ്കളെ ശസ്ത്രക്രിയാമുറിയിൽ പ്രവേശിപ്പിക്കും. താങ്കളുടെ ഹൃദയമിടിപ്പ്, രക്തസമ്മർദ്ദം,പ്രാണവായുവിന്റെ നിലവാരം എന്നിവ പരിശോധിക്കാനുള്ള ഉപകരണങ്ങൾ ഘടിപ്പിക്കും. പ്രാദേശീകമായ മയക്കലിന് വിധേയമാക്കി ദ്രാവകങ്ങളും മരുന്നും നൽകാനായുള്ള ഒരു കുഴൽ കൈയിലെ രക്തക്കുഴലിൽ കടത്തും. പ്രാദേശികമായ മയക്കലിന് വിധേയമായി ആർട്ടിരിയൽ കുഴലും രക്തസമ്മർദ്ദം അളക്കാനായി ഘടിപ്പിക്കും. ആശുപത്രിയിലെ പതിവ് നടപടിക്രമമനുസരിച്ച് പൊതുവായ മയക്കലിനുള്ള മരുന്ന് നൽകും. രക്തചംക്രമണ സംവിധാനം((ഹൃദയമിടിപ്പ്, താളം, രക്തസമ്മർദ്ദം) പതിവ് രീതിയിൽ ശസ്ത്രക്രിയയിലുടനീളം നിരീക്ഷിക്കും.

ശസ്ത്രക്രിയക്കവസാനം മയക്കൽ മാറ്റാനുള്ള മരുന്നുകൾ നൽകി താങ്കളെ നിരീക്ഷണത്തിനായി തീവ്രപരിചരണവിഭാഗത്തിലേക്ക് മാറ്റും. താങ്കളുടെ ഹൃദയത്തിന്റെ പ്രവർത്തനം വിലയിരുത്താൻ ശസ്ത്രക്രിയകഴിഞ്ഞ് 24 മണിക്കൂറിന് ശേഷവും, മൂന്നാം ദിവസവും റ്റിഇഇ ചെയ്യും.

റ്റിഇഇയുടെ ഉപയോഗത്തിൽ പാർശ്വഫലങ്ങളെന്തെങ്കിലുമുണ്ടോ?

ട്രാൻസ് തൊറാസിക് എക്കോകാർഡിയോഗ്രാമിന് അറിയപ്പെടുന്ന അപകടങ്ങളോ പാർശ്വഫലങ്ങളോ ഇല്ല.

പഠനമാരംഭിച്ചശേഷം താങ്കൾക്ക് പിൻമാറാമോ?

താങ്കളുടെ പഠനത്തിലുള്ള പങ്കാളിത്തം തികച്ചും സ്വമേധയായാണ്, പഠനത്തിലെ പങ്കാളിത്തത്തിൽ നിന്നും പിൻമാറാൻ തീരുമാനമെടുക്കാൻ താങ്കൾക്ക് സ്വാതന്ത്ര്യമുണ്ട്. താങ്കളങ്ങിനെ ചെയ്താലും താങ്കളുടെ ഈ ആശുപത്രിയിലെ പതിവ് ചികിത്സയെ ഒരുവിധത്തിലും ബാധിക്കില്ല.

പഠനവുമായി ബന്ധപ്പെട്ട് താങ്കൾക്ക് എന്തെങ്കിലും പരുക്കുണ്ടായാലെന്ത് സംഭവിക്കും?

താങ്കൾ പഠനത്തിൽ പങ്കെടുത്തില്ലെങ്കിലും ഉപയോഗിക്കുന്ന മയക്കൽ സങ്കേതങ്ങളും നിരീക്ഷണ ഉപകരണങ്ങളും ഒന്നുതന്നെയാകയാൽ ഞങ്ങളുടെ പഠനത്തിൽ പങ്കെടുക്കുന്നതുകൊണ്ട് താങ്കൾക്ക് പരുക്കുണ്ടാകുമെന്ന് ഞങ്ങൾ പ്രതീക്ഷിക്കുന്നില്ല. പക്ഷേ പഠനവുമായി ബന്ധപ്പെട്ട് താങ്കൾക്കെന്തെങ്കിലും പാർശ്വഫലങ്ങളോ പ്രശ്നങ്ങളോ ഉണ്ടായാൽ താങ്കൾക്ക് ചിലവുണ്ടാകാതെ ചികിത്സിക്കും. എന്നിരുന്നാലും സാമ്പത്തികമായ നഷ്ടപരിഹാരം നൽകാനാവില്ല.

ഉപകരണങ്ങൾ ഉപോയോഗിക്കുന്നതിന് താങ്കൾ പണം ചിലവാക്കണോ?
റ്റിഇഇ പതിവ് ശസ്ത്രക്രിയാപൂർവ്വ പരിശോധനയുടെ ഭാഗമാണ് താങ്കൾക്ക് അധികച്ചിലവ് ഉണ്ടാകില്ല.

പഠനം കഴിഞ്ഞശേഷം എന്തു സംഭവിക്കും?
പഠനം കഴിഞ്ഞശേഷം ഫലങ്ങൾ വിലയിരുത്തുകയും ഗവേഷണപ്രബന്ധത്തിന്റെ ഭാഗമായുള്ള റിപ്പോർട്ട് സ്ഥാപനത്തിന് സമർപ്പിക്കുകയും ചെയ്യും.

താങ്കളുടെ വ്യക്തിവിവരങ്ങൾ രഹസ്യമായിരിക്കുമോ?
പഠനഫലങ്ങൾ പഠനഗവേഷണത്തിന്റെ ഭാഗമായുള്ള തീസിസിൽ ഉപയോഗിക്കുകയും ഒരു വൈദ്യശാസ്ത്ര ജേർണലിൽ പ്രസിദ്ധീകരണത്തിന് നൽകുകയും ചെയ്യുമെങ്കിലും താങ്കളെ വ്യക്തിപരമായി തിരിച്ചറിയാനിടയാക്കുന്നതൊന്നും പ്രസിദ്ധീകരണത്തിലോ, പഠനഫലങ്ങളുടെ പ്രദർശനത്തിലോ ഉണ്ടാവില്ല. എന്നിരുന്നാലും താങ്കൾ പങ്കെടുക്കുകയാണെങ്കിൽ താങ്കളുടെ ചികിത്സാ വിവരങ്ങൾ പഠനവുമായി ബന്ധപ്പെട്ടവർ താങ്കളുടെ അധികമായ സമ്മതമില്ലാതെ പരിശോധിച്ചേക്കാം.

താങ്കൾക്ക് കൂടുതൽ എന്തെങ്കിലും ചോദ്യങ്ങൾ ഉണ്ടെങ്കിൽ ദയവായി ഡോ. നീരജ അജയൻ (പ്രധാന ഗവേഷക) സീനിയർ റസിഡന്റിനോട് ചോദിക്കുക (ഫോൺ: 9446219309). ഇമെയിൽ. drneerajaajayan@sctimst.ac.in

പഠനവുമായി ബന്ധമില്ലാത്ത വ്യക്തിയെ ബന്ധപ്പെടുന്നതിന് ദയവായി സ്ഥാപനത്തിലെ നൈതീക കമ്മിറ്റി മെംബർ സെക്രട്ടറി ഡോ. മാല രാമനാഥനെ ബന്ധപ്പെടാം. ഫോൺ 0471 2524234, email: iec.mem.sec@sctimst.ac.in

Technical Advisory Committee (Clinical Studies)

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

TAC Registration No: SCT-/S/2018/759

Date:09.07.2018

Project title: COMPARISON OF HEMODYNAMICS AND CARDIAC FUNCTION BEFORE AND AFTER NEUROSURGERY IN PATIENTS WITH AND WITHOUT RAISED INTRACRANIAL PRESSURE: A PILOT OBSERVATIONAL STUDY WITH TRANSTHORACIC ECHOCARDIOGRAPHY

Principal Investigator:	
Dr Neeraja Ajayan, Senior Resident, Neuro Anaesthesiology SCTIMST	Degree: MBBS, MD
Co-Principal Investigator(s)	
Dr S Manikandan, Professor, Neuro Anaesthesiology, SCTIMST	Degree: MBBS, MD, PDCC
Dr Unnikrishnan P, Assistant Professor, Neuro Anaesthesiology, SCTIMST	Degree: MBBS, MD, PDCC
Co- Investigator(s)	
Dr Prakash Nair, Assistant Professor, Department of Neurosurgery, SCTIMST	Degree: MBBS,MS,Mch

Members who participated in the TAC meeting on 16/06/2018
Dr. Rupa Sreedhar (Chairperson)
Dr. Prasantakumar Dash
Dr. Krishna Kumar K
Dr. Sankara Sarma P
Dr. Bijulal S
Dr. Jayadevan ER
Dr. Syam K
Dr. Varghese T. Panicker
Dr. K. Shivakumar (Member Secretary)

Dr. Varghese T Panicker, Dr. Rupa Sreedhar, Dr. Jayadevan ER, Dr. Syam K, Dr. Krishna Kumar K, and Dr. Bijulal S stayed away from the proceedings when the projects in which they are involved as investigator were discussed (#762, 768, 769, 772, 775, 776, 778, 782, 784, 785).

Risk Classification of the project (Minimum/ Moderate/ High): Minimum

Requirement of DSMB: No

Recommended members of DSMB: Not applicable

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

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

Signature of the Member Secretary, TAC (Clinical Studies)

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

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)
Grams : Chitramat, Phone : +91-471-2443153, Fax : +91-471-2553728 / 2446433, E-mail : sct@sctimst.ac.in, Website : www.sctimst.ac.in

Institutional Ethics Committee
(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1242/AUGUST-2018 07.09.2018

Dr. Neeraja Ajayan
Senior Resident
Department of Ananesthesiology
SCTIMST, Thiruvananthapuram

Dear Dr. Neeraja Ajayan,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "COMPARISON OF HEMODYNAMICS AND CARDIAC FUNCTION BEFORE AND AFTER NEUROSURGERY IN PATIENTS WITH AND WITHOUT RAISED INTRACRANIAL PRESSURE: A PILOT OBSERVATIONAL STUDY WITH TRANSTHORACIC ECHOCARDIOGRAPHY (IEC/1242)" on 17th August, 2018.

The following documents were reviewed:

Original submission

1. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 19.07.2018 with checklist*
2. *TAC Approval Letter*
3. *List of Abbreviations*
4. *IEC Application Form*
5. *Project Proposal*
6. *Proforma*
7. *Patient Information Sheet and Consent Form in English and Malayalam*
8. *CV of Principal Investigator and Co- Principal Investigators*

Revised submission

1. *Covering letter addressed to the Member Secretary, IEC, SCTIMST with checklist*
2. *Forwarding Letter from the HOD*
3. *TAC Approval Letter*
4. *List of Abbreviations*
5. *IEC Application Form*
6. *Project Proposal*
7. *Proforma*
8. *Patient Information Sheet and Consent Form in English and Malayalam*
9. *CV of Principal Investigator and Co- Principal Investigators*

The following members of the Ethics Committee were present at the meeting held on 17th August, 2018 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

Sl. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. R V G Menon	M Tech, PhD	Male	Lay Person (Chairman)	No
2.	Dr. V. Raman Kutty	M D, M Phil, M P H	Male	Health Sciences Expert/Clinician	Yes
3.	Dr. K R S Krishnan	M.E., Ph.D.	Male	Medical Technology	Yes
4.	Dr. Rema M. N	MD	Female	Basic Medical Scientist	No
5.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

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

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

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

Sincerely,

Mala Ramanathan
Member Secretary, IEC

URKUND

Document Information

Analyzed document	Full thesis -F.docx (D78146426)
Submitted	8/25/2020 11:05:00 AM
Submitted by	kanmanisethu
Submitter email	kanmanis@sctimst.ac.in
Similarity	0%
Analysis address	kanmanis.sctims@analysis.urkund.com

Sources included in the report

W	URL: https://academic.oup.com/ehjcimaging/article-pdf/18/suppl_3/iii319/22296974/jex298.pdf Fetched: 3/22/2020 4:07:49 PM	1
W	URL: https://www.science.gov/topicpages/a/absolute+left+ventricular Fetched: 6/2/2020 6:14:13 AM	1
J	**Right ventricular function in patients with acute anterior myocardial infarction: tissue Doppler echocardiographic approach** URL: d0201002-e0af-4944-af48-b16b51b2f6ed Fetched: 3/13/2019 5:00:53 AM	1
SA	**PLAGIARISM.docx** Document PLAGIARISM.docx (D61726714)	1
W	URL: https://iaimjournal.com/wp-content/uploads/2017/06/iaim_2017_0406_12.pdf Fetched: 8/25/2020 11:14:00 AM	1

Master Chart

General								Preop Data							
Sl. No.	Group	Age	Gender	Weight	Height	BSA	BMI	Symptoms	GCS	CT findings	Osmotherapy	ASA Grading	ECG Change	Preop HR	Preop BP
1	1	18	M	60	165	1.66	22.0	N	15	N	N	1	N	80	110/70
2	1	36	M	75	176	1.91	24.2	N	15	N	N	1	N	80	120/70
3	1	21	M	75	175	1.91	24.5	N	15	N	N	2	N	70	110/80
4	1	18	F	56	162	1.59	21.3	N	15	N	N	2	N	65	100/70
5	1	36	M	60	156	1.61	24.7	N	15	N	N	1	N	64	130/80
6	1	31	F	60	156	1.61	24.7	N	15	N	N	1	N	70	100/70
7	1	23	F	45	160	1.41	17.6	N	15	N	N	1	N	74	110/70
8	1	44	M	70	164	1.79	26.0	N	15	N	N	2	N	80	120/70
9	1	55	F	57	145	1.52	27.1	N	15	N	N	1	N	82	136/86
10	1	40	F	47	160	1.45	18.4	N	15	N	N	1	N	80	120/70
11	1	50	M	68	168	1.78	24.1	N	15	N	N	2	N	65	100/70
12	1	36	F	70	168	1.81	24.8	N	15	N	N	1	N	70	110/70
13	1	38	M	72	175	1.87	23.5	N	15	N	N	2	N	70	100/70
14	1	48	F	68	160	1.74	26.6	N	15	N	N	2	N	64	110/70
15	1	42	F	84	171	2.00	28.7	N	15	N	N	1	N	74	130/80
16	1	36	M	72	156	1.77	29.6	N	15	N	N	1	N	76	124/76
17	1	44	F	75	170	1.88	26.0	N	15	N	N	1	N	64	116/80
18	1	28	F	64	164	1.71	23.8	N	15	N	N	1	STDEP	62	110/70
19	1	30	F	60	170	1.68	20.8	N	15	N	N	1	N	73	124/72
20	1	46	M	50	164	1.51	18.6	N	15	N	N	2	N	71	96/54
21	1	41	M	69	170	1.81	23.9	N	15	N	N	2	N	69	100/70
22	1	24	F	70	156	1.74	28.8	N	15	N	N	1	N	80	110/70
23	1	36	F	59	160	1.62	23.0	N	15	N	N	1	N	92	120/70
24	1	28	M	69	170	1.81	23.9	N	15	N	N	1	N	74	124/76
25	1	40	M	72	165	1.82	26.4	N	15	N	N	2	N	70	117/80
26	1	32	M	56	158	1.57	22.4	N	15	N	N	1	N	85	116/72
27	1	33	F	72	165	1.82	26.4	N	15	N	N	1	N	74	125/85
28	1	24	M	70	164	1.79	26.0	N	15	N	N	1	N	98	130/82
29	1	46	M	69	165	1.78	25.3	N	15	N	N	1	N	66	110/71
30	1	40	F	78	172	1.93	26.4	N	15	N	N	2	N	68	130/81

Key to Masterchart (Units & Abbreviations):

Units: Age(years),Gender (M-Male,F-Female),Weight (Kgs), Height(cms), BSA(m^2), BMI(kg/m^2); Heart rate (HR)–bpm ; BP-Blood pressure(mm Hg)

Symptoms-:Raised ICP(Y- Yes,N-No);Osmotherapy(Y- Yes,N-No);ECG changes(STDEP-ST depression, TINV-Twave inversion,N-Normal ECG),

General								Preop Data							
Sl. No.	Group	Age	Gender	Weight	Height	BSA	BMI	Symptoms	GCS	CT findings	Osmotherapy	ASA Grading	ECG Change	Preop HR	Preop BP
31	2	41	F	54	155	1.52	22.5	Y	15	Y	N	2	STDEP	56	136/86
32	2	60	F	60	156	1.61	24.7	Y	15	Y	N	2	N	70	130/80
33	2	32	F	40	140	1.25	20.4	Y	15	Y	Y	2	STDEP	60	120/70
34	2	23	F	44	150	1.35	19.6	Y	15	Y	N	1	N	86	110/70
35	2	41	M	66	170	1.77	22.8	Y	15	Y	N	1	N	70	120/70
36	2	30	M	70	175	1.84	22.9	Y	15	Y	N	1	N	56	146/80
37	2	37	F	73	158	1.79	29.2	Y	15	Y	Y	2	TINV	76	130/90
38	2	56	M	57	160	1.59	22.3	N	15	Y	N	1	N	78	130/80
39	2	41	M	75	180	1.94	23.1	Y	15	Y	N	1	STDEP	60	150/90
40	2	41	F	70	156	1.74	28.8	Y	15	Y	N	2	TINV	80	150/80
41	2	23	M	56	180	1.67	17.3	N	15	Y	N	1	N	76	110/70
42	2	23	F	60	150	1.58	26.7	Y	15	Y	N	1	N	76	110/80
43	2	50	M	70	165	1.79	25.7	y	15	Y	N	2	N	90	140/80
44	2	53	M	52	156	1.50	21.4	y	15	Y	N	2	N	66	130/76
45	2	32	M	65	170	1.75	22.5	y	15	Y	y	1	N	58	126/72
46	2	40	M	79	175	1.96	25.8	N	15	Y	N	1	N	64	143/98
47	2	28	F	56	164	1.60	20.8	Y	15	Y	Y	1	N	56	100/70
48	2	49	M	65	170	1.75	22.5	Y	15	Y	N	2	N	70	130/80
49	2	38	F	53	158	1.53	21.2	Y	15	Y	Y	1	N	72	110/70
50	2	37	F	68	170	1.79	23.5	Y	15	Y	Y	1	N	56	110/70
51	2	42	F	54	148	1.49	24.7	Y	15	Y	Y	1	TINV	76	110/70
52	2	39	F	64	160	1.69	25.0	Y	15	Y	Y	2	N	60	150/90
53	2	32	M	72	160	1.79	28.1	Y	15	Y	N	2	N	66	130/76
54	2	26	M	60	159	1.63	23.7	Y	15	Y	Y	1	N	76	130/90
55	2	42	M	82	170	1.97	28.4	Y	15	Y	Y	2	N	78	130/80
56	2	45	F	56	160	1.58	21.9	Y	15	Y	Y	1	STDEP	72	136/82
57	2	39	M	67	165	1.75	24.6	Y	15	Y	Y	2	N	76	140/80
58	2	42	F	54	148	1.49	24.7	Y	15	Y	Y	1	TINV	76	110/70
59	2	39	F	64	160	1.69	25.0	Y	15	Y	Y	2	N	60	150/90
60	2	32	M	72	160	1.79	28.1	Y	15	Y	N	2	N	66	130/76

Key to Masterchart (Units & Abbreviations):

[Units: Age(years),Gender (M-Male,F-Female),Weight (Kgs), Height(cms), BSA(m^2), BMI(kg/m^2); Heart rate (HR)–bpm ; BP-Blood pressure(mm Hg)

Symptoms-:Raised ICP(Y- Yes,N-No);Osmotherapy(Y- Yes,N-No);ECG changes(STDEP-ST depression, TINV-Twave inversion,N-Normal ECG)]

	Intraop								
Sl. No.	Brain full	Brady	Tachy	Hypo	Hyper	Vasopressor	Vasodialator	Blood transfusion	Fluid
1	N	N	N	N	N	N	N	N	500
2	N	N	N	N	N	N	N	N	300
3	N	N	N	Y	N	N	N	Y	400
4	N	Y	N	N	N	N	N	N	350
5	N	Y	N	N	N	N	N	N	370
6	N	N	N	Y	N	Y	N	Y	420
7	N	N	N	Y	N	N	N	Y	200
8	N	N	N	N	N	N	N	N	500
9	N	N	N	Y	N	Y	N	N	650
10	N	N	N	N	N	N	N	N	300
11	N	N	N	N	N	N	N	N	250
12	N	N	N	N	N	N	N	N	650
13	N	y	N	N	N	N	N	N	800
14	N	N	N	Y	N	N	N	Y	650
15	N	N	N	N	N	N	N	N	400
16	N	N	N	N	N	N	N	N	350
17	N	N	N	N	N	N	N	N	450
18	N	N	N	Y	N	N	N	Y	600
19	N	N	N	N	N	N	N	N	250
20	N	y	N	N	N	N	N	N	100
21	N	N	N	Y	N	N	N	Y	150
22	N	Y	N	N	N	N	N	N	600
23	N	N	N	N	N	N	N	N	400
24	N	N	N	N	N	N	N	N	300
25	N	N	N	N	N	N	N	N	450
26	N	N	N	N	N	N	N	N	420
27	N	N	N	N	N	N	N	N	0
28	N	N	N	N	N	N	N	N	160
29	N	N	N	N	N	N	N	N	180
30	N	N	N	N	N	N	N	N	200

Key to Masterchart (Units & Abbreviations):

[Brain full= Intraoperative brain bulge(Y-Yes,No); Brady=Bradycardia; Tachy=Tachycardia, Hypo=Hypotension;Hyper=Hypertension;vasopressor-intraoperative vasopressor use; vasodilator=intraoperative vasodilator use; Fluid- intraoperative fluid (ml)]

	Intraop								
Sl. No.	Brain full	Brady	Tachy	Hypo	Hyper	Vasopressor	Vasodialator	Blood transfusion	Fluid
31	Y	N	N	Y	N	Y	N	Y	1000
32	N	N	N	Y	N	Y	N	Y	500
33	Y	N	N	Y	N	Y	N	N	0
34	N	N	N	Y	N	Y	N	Y	600
35	N	N	N	Y	N	Y	N	Y	400
36	Y	Y	N	Y	N	Y	N	Y	300
37	Y	Y	N	Y	N	Y	N	Y	400
38	Y	Y	N	Y	N	Y	N	Y	400
39	Y	N	N	Y	N	N	N	Y	450
40	Y	Y	N	Y	N	Y	N	Y	600
41	N	N	N	N	N	N	N	N	550
42	N	N	N	N	N	y	N	N	600
43	y	N	N	y	N	y	N	N	200
44	y	N	N	y	N	y	N	y	350
45	y	y	N	y	N	y	N	y	200
46	y	N	N	N	N	N	N	y	400
47	Y	Y	N	Y	N	Y	N	Y	400
48	N	N	N	N	N	y	N	N	600
49	N	N	N	Y	N	Y	N	Y	600
50	y	N	N	N	N	N	N	y	540
51	N	N	N	Y	N	Y	N	Y	390
52	N	N	N	N	N	y	N	N	450
53	y	N	N	y	N	y	N	N	600
54	y	N	N	y	N	y	N	y	750
55	Y	Y	N	Y	N	Y	N	Y	850
56	Y	N	N	N	N	N	N	N	750
57	Y	N	N	Y	N	Y	N	N	650
58	N	N	N	Y	N	Y	N	Y	390
59	N	N	N	N	N	y	N	N	450
60	y	N	N	y	N	y	N	N	600

Key to Masterchart (Units & Abbreviations):

Brain full= Intraoperative brain bulge(Y-Yes,No); Brady=Bradycardia; Tachy=Tachycardia, Hypo=Hypotension;Hyper=Hypertension;vasopressor-intraoperative vasopressor use; vasodilator=intraoperative vasodilator use; Fluid- intraoperative fluid (ml)

General		Postop							LVIDd		LVIDs		IWIDd		IWIDs		IVSd		IVSs		RWT		LV Mass	
Sl. No.	GCS	Brady	Tachy	Hypo	Hyper	Vasopressor	Vasodialator	Blood transfusion	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop
1	15	N	N	N	N	N	N	N	4.5	4.2	2.4	2.7	0.7	0.8	1.3	1.4	0.9	0.7	1.4	1.1	0.31	0.38	113.63	93.04
2	12	N	N	N	N	N	N	N	3.1	3.7	1.9	2.2	1.6	1	1.9	1.3	0.9	1.2	1.1	1.1	1.03	0.54	121.93	129.33
3	15	N	N	N	N	N	N	N	4.9	4.8	3	3	0.9	1.2	1.8	2	1.2	1.2	1.4	1.1	0.37	0.50	188.09	219.13
4	15	N	N	N	N	N	N	N	3.8	3.6	2.7	2.5	0.7	0.7	1.1	1	0.5	0.6	0.8	0.8	0.37	0.39	58.95	59.67
5	15	N	N	N	N	N	N	N	4.6	4.3	2.7	1.8	1.1	1.6	1.5	2.6	1.1	1.5	1.7	1.9	0.48	0.74	181.22	271.60
6	15	N	N	N	N	N	N	N	3.3	4.1	2.2	2.8	0.9	0.7	1.2	1.4	1.3	2.1	1.2	2.4	0.55	0.34	109.12	216.58
7	15	N	N	N	N	N	N	N	4.4	4.1	2.9	2.6	0.5	0.7	0.9	0.9	1	0.9	1.2	1.5	0.23	0.34	100.60	97.34
8	15	N	N	N	N	N	N	N	4.7	4.6	3.4	3.2	1.2	1.1	1.5	1.4	0.5	0.6	0.9	1	0.51	0.48	132.32	127.66
9	15	N	N	N	N	N	N	N	4	4.3	3	3.2	0.8	0.7	1	1	0.7	0.9	0.8	0.9	0.40	0.33	85.78	105.33
10	15	N	N	N	N	N	N	N	4	4.1	3	2.8	1.2	1	0.9	0.9	1.2	0.8	0.8	0.8	0.60	0.49	165.46	114.13
11	15	N	N	N	N	N	N	N	4.4	4.3	3.4	2.6	0.9	0.9	0.8	0.8	1.1	1	1.7	1.7	0.41	0.42	147.83	132.74
12	15	N	N	N	N	N	N	N	4.3	4.4	3.2	3.2	0.8	0.8	1	0.9	1.1	1	1.2	1.2	0.37	0.36	132.74	128.02
13	15	N	N	N	N	N	N	N	3.6	3.9	2.5	2.9	0.9	0.9	1.1	1	1.1	1.1	1.2	1.2	0.50	0.46	107.89	122.12
14	15	N	N	N	N	N	N	N	4.2	4.1	3	2.9	0.9	0.9	1	1.1	1.2	1.2	0.8	0.8	0.43	0.44	147.00	141.55
15	15	N	N	N	N	N	N	N	3.6	3.8	2.6	2.8	0.9	0.9	1	1.2	0.9	1	1.1	1.1	0.50	0.47	92.79	109.03
16	15	N	N	N	N	N	N	N	4.3	4.3	3.1	3.1	1	0.9	0.9	1	0.8	1.1	1.2	1.1	0.47	0.42	123.30	142.49
17	15	N	N	N	N	N	N	N	4.4	4.3	3.2	3.2	0.9	0.9	0.9	1	0.9	1.2	1.4	1.3	0.41	0.42	128.02	152.55
18	15	N	N	N	N	N	N	N	4.4	4.4	3.2	3.2	0.7	0.8	0.8	1.1	1.1	1	1.3	1.2	0.32	0.36	128.02	128.02
19	15	N	N	N	N	N	N	N	4.4	3.8	2.9	2.6	0.9	0.9	1	1.2	0.96	0.9	1.1	1.1	0.41	0.47	133.83	101.06
20	15	N	N	N	N	N	N	N	4.5	4.2	2.9	3	1.1	1	1	1.1	1.2	1.1	0.9	0.8	0.49	0.48	186.39	147.00
21	15	N	N	N	N	N	N	N	4.9	4.3	3.4	3.1	0.9	0.9	0.9	1	1.1	1	0.9	1	0.37	0.42	176.04	132.74
22	15	N	N	N	N	N	N	N	4.1	4	2.7	2.9	0.9	0.9	0.9	1	1	0.9	0.8	0.9	0.44	0.45	122.97	109.69
23	15	N	N	N	N	N	N	N	4.2	4.1	2.9	3	0.8	1.1	1	1.2	1.1	1	1	1	0.38	0.54	127.81	141.55
24	15	N	N	N	N	N	N	N	4.3	4.5	2.6	3.1	0.9	0.9	1	1	0.8	0.7	0.7	0.7	0.42	0.40	114.16	113.63
25	15	N	N	N	N	N	N	N	4.1	4	2.6	2.8	0.7	0.9	0.7	1	0.9	0.96	1.1	1.2	0.34	0.45	97.34	114.78
26	15	N	N	N	N	N	N	N	4.4	4.3	3	3.4	0.9	0.8	0.8	1	1.1	1.2	1.2	1	0.41	0.37	147.83	142.49
27	15	N	N	N	N	N	N	N	4.1	4.2	3	3.1	1.2	0.9	1	1.1	1.1	1.1	1	1.2	0.59	0.43	161.36	137.25
28	15	N	N	N	N	N	N	N	4	4.2	3	3.1	0.9	0.7	0.8	1	1.2	1.2	1.1	1	0.45	0.33	136.20	127.81
29	15	N	N	N	N	N	N	N	4.8	4.4	3.5	3.2	0.8	1.2	1.1	1.3	1.3	1.3	1.1	1	0.33	0.55	181.91	203.05
30	15	N	N	N	N	N	N	N	4.2	4.3	2.8	3.1	0.9	0.9	1	1.2	1.1	1	1	1.2	0.43	0.42	137.25	132.74
General		Postop							LVIDd		LVIDs		IWIDd		IWIDs		IVSd		IVSs		RWT		LV Mass	
Sl. No.	GCS	Brady	Tachy	Hypo	Hyper	Vasopressor	Vasodialator	Blood transfusion	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop
31	15	N	N	N	N	N	N	N	2.8	3.9	1.5	2.9	0.9	1.1	1.2	1.3	1	1.1	1.2	1	0.64	0.56	68.72	140.09
32	15	N	N	N	N	N	N	N	4.8	4.9	3	2.9	1.2	1.3	1.5	1.6	0.8	0.9	1.6	1.6	0.50	0.53	170.19	200.50
33	12	N	N	N	N	N	N	N	3.3	4	2	2.1	1.1	1	1.4	1.2	0.8	0.9	1.1	1	0.67	0.50	87.69	118.23
34	15	N	N	N	N	N	N	N	3.5	3.9	2.2	2.8	0.7	0.5	1.3	0.9	0.7	0.6	1	0.8	0.40	0.26	62.81	55.25
35	15	N	N	N	N	N	N	N	2.5	4.1	1.1	1.4	2	2.4	1.9	3.1	0.9	1.5	0.5	1.8	1.60	1.17	118.61	369.24
36	15	N	N	N	N	N	N	N	4.3	4.4	3	2.9	0.6	1.1	1.5	1.4	0.7	1	0.8	1.4	0.28	0.50	80.56	158.21
37	15	N	N	N	N	N	N	N	4.7	4.4	3.5	3.2	0.8	0.8	1.4	1.2	0.8	0.9	1	1	0.34	0.36	122.26	118.58
38	13	N	N	N	N	N	N	N	2.8	3.1	1.3	2	1.8	1	2.1	0.8	1.2	1.3	2.1	1.4	1.29	0.65	144.67	106.82
39	15	N	N	N	N	N	N	N	4.9	5	2.7	2.4	1	0.8	1.2	1.4	0.8	1.1	0.8	1.4	0.41	0.32	152.95	169.92
40	12	N	N	N	N	N	N	N	3.9	3.9	2.7	2.6	1	0.9	1.2	1.2	0.6	0.5	0.9	0.7	0.51	0.46	89.67	75.11
41	15	N	N	N	N	N	N	N	4.7	2.2	2.8	1.1	0.8	1	0.9	1.1	1.4	0.9	1.9	1.1	0.34	0.91	187.54	49.08
42	15	N	N	N	N	N	N	N	3.6	2.6	2.5	2	1.3	2.5	1.3	2.5	0.9	0.8	1.1	0.7	0.72	1.92	124.12	156.85
43	12	N	N	N	N	N	N	N	4.5	3.1	2.6	1.8	0.6	1.1	1.4	1.4	0.9	1.3	1.4	1.2	0.27	0.71	104.50	114.24
44	14	N	N	N	N	N	N	N	1.4	2.3	0.9	1.3	1.5	0.9	1.4	1.4	2.2	1	1.8	0.9	2.14	0.78	108.68	52.12
45	13	N	N	N	N	N	N	N	5.5	5.7	3.9	4.6	0.8	0.9	1.8	1	1.7	1	1.4	1.1	0.29	0.32	288.16	211.75
46	13	N	N	N	N	N	N	N	3.7	4.2	1.9	2	1.3	1.2	1.9	1.8	1.5	1.6	2.1	2	0.70	0.57	186.94	224.33
47	14	N	N	N	N	N	N	N	3.6	3.9	2.2	2.8	0.6	0.5	1.2	0.9	0.7	0.5	1	0.9	0.33	0.26	59.67	49.13
48	13	N	N	N	N	N	N	N	4.6	2.2	2.8	1.1	0.9	1	0.9	1.1	1.3	0.9	1.9	1.2	0.39	0.91	181.22	49.08
49	15	N	N	N	N	N	N	N	4.8	5	2.7	2.4	0.9	0.8	1.2	1.5	0.8	1.1	0.9	1.4	0.38	0.32	137.08	169.92
50	14	N	N	N	N	N	N	N	3.9	3.7	2.2	2.1	1.3	1	0.8	0.7	0.9	0.8	1.1	1.1	0.67	0.54	140.09	96.88
51	13	N	N	N	N	N	N	N	4.9	4.5	4.2	4.1	0.9	1	1.4	1.2	0.8	0.7	0.7	0.6	0.37	0.44	141.91	123.07
52	15	N	N	N	N	N	N	N	4	3.9	2.9	2.8	1.4	1.5	1.7	1.6	1.4	1.5	1.5	1.5	0.70	0.77	208.96	224.57
53	14	N	N	N	N	N	N	N	4.6	4.4	3	3.1	1.3	1.2	2.1	2	1	0.9	1.3	1.2	0.57	0.55	192.94	158.21
54	15	N	N	N	N	N	N	N	4.5	4.4	3	2.9	1	0.9	1.2	1.3	0.9	0.8	1	1.1	0.44	0.41	142.89	118.58
55	15	N	N	N	N	N	N	N	3	3.1	2.1	2.2	1.2	1.2	1.3	1.3	0.7	0.7	0.7	0.7	0.80	0.77	76.02	79.81
56	12	N	N	N	N	N	N	N	5	5.1	3.5	3.6	1	1	1.5	1.5	1.2	1.1	1.7	1.6	0.40	0.39	207.14	200.78
57	14	N	N	N	N	N	N	N	3.7	3.9	1.7	1.6	1.6	1.6	1.7	1.7	0.8	0.9	1.5	1.6	0.86	0.82	147.30	169.35
58	13	N	N	N	N	N	N	N	4.9	4.5	4.2	4.1	0.9	1	1.4	1.2	0.8	0.7	0.7	0.6	0.37	0.44	141.91	123.07
59	15	N	N	N	N	N	N	N	4	3.9	2.9	2.8	1.4	1.5	1.7	1.6	1.4	1.5	1.5	1.5	0.70	0.77	208.96	224.57
60	14	N	N	N	N	N	N	N	4.6	4.4	3	3.1	1.3	1.2	2.1	2	1	0.9	1.3	1.2	0.57	0.55	192.94	158.21

Key to Masterchart (Units & Abbreviations):

Brady=Bradycardia;Tachy=Tachycardia,Hypo=Hypotension;Hyper=Hypertension;vasopressor-intraoperative vasopressor use; vasodilator=intraoperative vasodilator use.
Units for Fluid- intraoperative fluid (ml), LVIDd; LVIDs; IWIDd; IWIDs ;IVSd;IVSs=(cm),Unit for LV Mass(gm)

General															
	LVOT		LVOT area	VTI		SV		LA vol index		LVEF		RWMA		LV Systolic	
Sl. No.	Preop	Postop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop
1	2.4	2.3	4.15	18.4	18.3	83.20	75.99	24	26	66	66	N	N	G	G
2	1.9	2.1	3.46	19.2	25.8	54.41	89.32	22.6	25	73	76	N	N	G	G
3	1.8	1.9	2.83	17.8	18.4	45.27	52.14	24	21	69	67	N	N	G	G
4	2.1	2	3.14	16.5	16	57.12	50.24	21	22	58	60	N	N	G	G
5	2	2.1	3.46	17.4	16.8	54.64	58.16	24	21	72	70	N	N	G	G
6	2.2	2.2	3.80	18.6	23.1	70.67	87.77	17	19	56	55	N	N	G	G
7	1.8	1.9	2.83	18.6	16.4	47.31	46.48	19	21	62	69	N	N	G	G
8	2.3	2.1	3.46	18.9	19	78.49	65.78	22	22	54	55	N	N	G	G
9	2.1	2	3.14	16.2	21.8	56.08	68.45	24	21	68	66	N	N	G	G
10	2.2	2.1	3.46	18.4	19	69.91	65.78	21	24	58	70	N	N	G	G
11	2.1	2	3.14	17.6	18.4	60.93	57.78	23	21	62	65	N	N	G	G
12	1.8	1.9	2.83	19	20	48.32	56.68	24	24	65	68	N	N	G	G
13	2	2	3.14	20.4	21	64.06	65.94	23	26	70	72	N	N	G	G
14	1.8	1.8	2.54	21	20	53.41	50.87	22	25	80	80	N	N	G	G
15	2	2	3.14	20	20.2	62.80	63.43	19	22	74	84	N	N	G	G
16	1.9	1.9	2.83	18.4	18.9	52.14	53.56	20	17	70	78	N	N	G	G
17	1.6	1.6	2.01	19.4	20	38.99	40.19	20	21	68	76	N	N	G	G
18	1.8	1.8	2.54	17.6	21	44.76	53.41	22	24	80	87	N	N	G	G
19	1.6	1.6	2.01	18.6	18	37.38	36.17	23	21	74	72	N	N	G	G
20	2.1	2.1	3.46	20	19	69.24	65.78	24	26	72	70	N	N	G	G
21	2.2	2.2	3.80	18.4	18.4	69.91	69.91	21	22	75	76	N	N	G	G
22	2.1	2.1	3.46	19.4	19	67.16	65.78	22	23	66	70	N	N	G	G
23	2	2	3.14	17.4	18.5	54.64	58.09	24	21	80	75	N	N	G	G
24	1.9	1.9	2.83	21	22	59.51	62.34	22	19	82	85	N	N	G	G
25	1.8	1.8	2.54	22	21	55.95	53.41	25	23	79	80	N	N	G	G
26	2	2	3.14	19	18.6	59.66	58.40	22	21	74	76	N	N	G	G
27	2	2	3.14	18	17.6	56.52	55.26	21	22	65	70	N	N	G	G
28	2.9	2.9	6.60	17.4	18	114.87	118.83	18	19	72	75	N	N	G	G
29	1.6	1.6	2.01	18.9	19	37.98	38.18	18	17	76	72	N	N	G	G
30	1.5	1.5	1.77	19	19	33.56	33.56	16	19	80	78	N	N	G	G

General															
	LVOT		LVOT area	VTI		SV		LA vol index		LVEF		RWMA		LV Systolic	
Sl. No.	Preop	Postop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop
31	2	2	3.14	14.1	21.3	44.27	66.88	22	20	41	61	N	N	G	G
32	2	2	3.14	16.2	21.8	50.87	68.45	25	21	50	71	N	N	M	G
33	2.2	2	3.14	25.1	18.6	95.36	58.40	23	26	70	70	N	N	G	G
34	1.4	1.4	1.54	16	12.7	24.62	19.54	24	27	67	71	N	N	G	G
35	2.4	2.2	3.80	17.4	20	78.68	75.99	21	24	81	88	N	N	G	G
36	2.6	2.5	4.91	10.1	20	53.60	98.13	22	26	62	63	N	N	G	G
37	2.4	2.2	3.80	20.6	19.4	93.14	73.71	25	23	55	58	N	N	G	G
38	2.2	2.8	6.15	23.6	16.7	89.67	102.78	22	21	61	59	N	N	G	G
39	2.4	2.3	4.15	16.5	12.8	74.61	53.15	21	22	48	80	N	N	MILD	G
40	2	2.1	3.46	12.2	19.2	38.31	66.47	24	25	60	61	N	N	G	G
41	2.4	2.4	4.52	22.2	23.3	100.38	105.35	25	24	69	82	N	N	G	G
42	1.9	2.3	4.15	14.3	18.2	40.52	75.58	27	24	50	56	N	N	MILD	G
43	2.2	2.4	4.52	23.4	25.7	88.91	116.21	26	27	60	66	N	N	G	G
44	2.2	2	3.14	13.8	16.8	52.43	52.75	22	23	73	79	N	N	G	G
45	2.5	2.5	4.91	11.9	17.7	58.38	86.84	24	24	33	53	N	N	MOD	G
46	2.5	2.4	4.52	23.8	22.4	116.77	101.28	27	25	82	79	N	N	G	G
47	1.5	1.4	1.54	17	12.7	30.03	19.54	22	26	67	72	N	N	G	G
48	2.3	2.4	4.52	22.2	24.5	92.19	110.78	28	25	68	81	N	N	G	G
49	2.5	2.3	4.15	16.5	12.7	80.95	52.74	23	25	48	79	N	N	MILD	G
50	1.3	1.5	1.77	20.9	18.9	27.73	33.38	21	20	47	60	N	N	MILD	G
51	3	2.6	5.31	16.2	18.6	114.45	98.70	20	24	64	66	N	N	G	G
52	2.5	2.6	5.31	18.1	17.1	88.80	90.74	26	25	64	66	N	N	G	G
53	2.4	2.2	3.80	17.6	16.9	79.58	64.21	24	26	66	68	N	N	G	G
54	1.8	1.6	2.01	18	17.9	45.78	35.97	28	26	62	64	N	N	G	G
55	1.9	1.8	2.54	16.1	16	45.62	40.69	26	26	58	58	N	N	G	G
56	2.1	2	3.14	17.2	17	59.54	53.38	28	28	56	58	N	N	G	G
57	2.1	2.4	4.52	16.9	17.2	58.51	77.77	29	30	85	80	N	N	G	G
58	3	2.6	5.31	16.2	18.6	114.45	98.70	20	24	64	66	N	N	G	G
59	2.5	2.6	5.31	18.1	17.1	88.80	90.74	26	25	64	66	N	N	G	G
60	2.4	2.2	3.80	17.6	16.9	79.58	64.21	24	26	66	68	N	N	G	G

Key to Masterchart (Units & Abbreviations):

Units : LVOT(cm);LVOT area(cm^2);VTI(cm);SV(ml);LA vol index(ml/m^2);LVEF(%)
RWMA(Y=Yes,N=No);LV Systolic(G=Good LV systolic function,M=Mild systolic dysfunction,Mod-Moderate Systolic dysfunction)]

General																
	E Vel		E/A		E'		E/E'		DecT		Diastolic dysfunction		TAPSE		RV Systolic	
Sl. No.	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop
1	0.71	0.95	1.9	1.9	0.12	0.12	5.92	7.92	244	220	N	N	1.8	2	G	G
2	0.87	0.8	1.3	1.6	0.12	0.15	7.25	5.33	238	270	N	N	1.8	1.79	G	G
3	0.95	0.92	1.2	1.2	0.11	0.12	8.64	7.67	255	229	N	N	1.8	2.2	G	G
4	0.80	0.7	1.4	1.5	0.15	0.14	5.33	5.00	230	300	N	N	1.6	1.7	G	G
5	0.80	0.7	1.8	1.3	0.15	0.14	5.33	5.00	240	320	N	N	1.5	1.4	G	G
6	0.87	0.89	1.9	1.5	0.09	0.15	9.67	5.93	160	180	N	N	1.7	1.6	G	G
7	0.84	0.89	1.6	1.46	0.11	0.11	7.64	8.09	209	200	N	N	2	2	G	G
8	0.74	0.8	1.65	1.4	0.1	0.12	7.40	6.67	327	300	N	N	1.8	1.6	G	G
9	0.60	0.8	1.2	1.3	0.09	0.1	6.67	8.00	190	200	N	N	1.8	1.6	G	G
10	0.95	0.92	1.2	1.2	0.11	0.12	8.64	7.67	255	229	N	N	1.6	1.8	G	G
11	0.80	0.7	1.4	1.5	0.15	0.14	5.33	5.00	230	300	N	N	1.5	1.6	G	G
12	0.84	0.89	1.6	1.46	0.11	0.11	7.64	8.09	209	200	N	N	2	2.1	G	G
13	0.87	0.8	1.3	1.6	0.12	0.15	7.25	5.33	238	270	N	N	2.1	2	G	G
14	0.80	0.7	1.8	1.3	0.15	0.14	5.33	5.00	240	320	N	N	2	2.2	G	G
15	0.83	0.79	1.4	1.5	0.15	0.14	5.53	5.64	188	190	N	N	1.6	1.8	G	G
16	0.78	0.7	1.8	1.3	0.15	0.14	5.20	5.00	156	166	N	N	1.5	1.6	G	G
17	0.84	0.88	1.9	1.5	0.09	0.15	9.33	5.87	176	194	N	N	1.8	1.9	G	G
18	0.82	0.89	1.6	1.46	0.11	0.11	7.45	8.09	194	199	N	N	2	2	G	G
19	0.76	0.81	1.65	1.4	0.1	0.12	7.60	6.75	164	188	N	N	1.6	1.6	G	G
20	0.69	0.78	1.2	1.3	0.09	0.1	7.67	7.80	205	201	N	N	1.7	1.9	G	G
21	0.89	0.92	1.2	1.2	0.11	0.12	8.09	7.67	246	199	N	N	1.9	2.1	G	G
22	0.82	0.75	1.4	1.5	0.15	0.14	5.47	5.36	215	219	N	N	1.9	1.6	G	G
23	0.82	0.89	1.6	1.46	0.11	0.11	7.45	8.09	164	184	N	N	2.1	2.1	G	G
24	0.86	0.8	1.3	1.6	0.12	0.15	7.17	5.33	240	215	N	N	2.1	2.1	G	G
25	0.80	0.7	1.8	1.3	0.15	0.14	5.33	5.00	230	224	N	N	2.4	2.2	G	G
26	0.78	0.81	1.2	1.4	0.12	0.13	6.50	6.23	220	229	N	N	2.1	2.2	G	G
27	0.82	0.83	1.9	1.6	0.12	1.5	6.83	0.55	210	230	N	N	2.2	2.5	G	G
28	0.69	0.79	1.6	1.8	0.15	1.6	4.60	0.49	190	210	N	N	1.9	2.1	G	G
29	0.84	0.82	1.2	1.5	0.11	0.14	7.64	5.86	173	184	N	N	2.4	2.1	G	G
30	0.82	0.81	1.4	1.2	0.13	0.15	6.31	5.40	190	199	N	N	2.4	2.2	G	G

General																
	E Vel		E/A		E'		E/E'		DecT		Diastolic dysfunction		TAPSE		RV Systolic	
Sl. No.	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop
31	1.08	1.08	2.7	1.5	0.12	0.12	9.00	9.00	135	218	Y	N	1.5	2	G	G
32	0.65	0.89	1.5	1	0.07	0.07	9.29	12.71	317	190	N	Y	2	2	G	G
33	1.03	1.1	0.8	1.4	0.15	0.12	6.87	9.17	137	235	Y	Y	2.6	2.4	G	G
34	0.57	0.93	0.7	1.5	0.12	0.15	4.75	6.20	107	270	Y	Y	1.1	1.8	MILD	G
35	1.00	1.1	2	2	0.13	0.17	7.69	6.47	130	165	Y	Y	2.3	2.4	G	G
36	0.54	0.7	0.7	1	0.14	0.12	3.86	5.83	156	160	Y	Y	2.3	2.2	G	G
37	0.76	0.93	1.3	1.4	0.09	0.1	8.44	9.30	136	150	Y	Y	2.1	2.1	G	G
38	0.73	0.8	1.4	1.47	0.11	0.1	6.64	8.00	196	233	N	N	1.6	1.5	G	G
39	1.28	0.7	2.5	1.8	0.12	0.12	10.67	5.83	154	295	Y	N	1.9	1.8	G	G
40	0.61	0.73	1.25	1.4	0.12	0.14	5.08	5.21	185	190	N	N	1.6	1.8	G	G
41	0.66	0.85	2.3	2.16	0.1	0.13	6.60	6.54	309	266	N	N	2.2	2	G	G
42	0.73	0.8	1.8	1.2	0.06	0.09	12.17	8.89	199	180	N	N	1.6	1.5	G	G
43	0.56	0.71	0.8	0.8	0.09	0.08	6.22	8.88	124	237	y	y	1.6	2.2	g	g
44	0.70	0.8	1.62	1.7	0.1	0.12	7.00	6.67	125	150	N	N	1.8	2.4	g	g
45	0.43	0.56	0.8	0.82	0.07	0.08	6.14	7.00	245	250	y	y	1.2	2.6	mild	g
46	0.74	0.72	2	1.98	0.11	0.12	6.73	6.00	136	143	y	y	1.8	1.6	g	g
47	0.56	0.93	0.6	1.5	0.12	0.14	4.67	6.64	107	273	Y	Y	1.1	1.8	MILD	G
48	0.66	0.84	2.3	2.15	0.1	0.14	6.60	6.00	310	265	N	N	2.2	2	G	G
49	1.27	0.6	2.4	1.8	0.12	0.12	10.58	5.00	153	294	Y	N	1.9	1.8	G	G
50	0.78	0.87	1.65	1.73	0.08	0.12	9.75	7.25	313	320	y	y	1.8	2	G	G
51	0.66	0.8	0.8	1.1	0.11	0.12	6.00	6.67	211	240	Y	N	1.6	1.7	G	G
52	0.56	0.55	0.8	0.8	0.05	0.06	11.20	9.17	150	154	Y	Y	2.3	2.2	G	G
53	0.71	0.76	2.5	2.5	0.04	0.05	17.75	15.20	371	380	Y	Y	2.2	2.1	G	G
54	0.76	0.76	2.03	2.2	0.09	0.09	8.44	8.44	314	320	Y	Y	2.1	2	G	G
55	0.50	0.5	1.2	1.3	0.1	0.1	5.00	5.00	301	300	N	N	1.4	1.5	G	G
56	0.54	0.56	0.7	0.7	0.05	0.05	10.80	11.20	101	120	Y	Y	1.6	1.6	G	G
57	0.60	0.6	1.12	1.12	0.04	0.05	15.00	12.00	192	200	Y	N	1.8	1.8	G	G
58	0.66	0.8	0.8	1.1	0.11	0.12	6.00	6.67	211	240	Y	N	1.6	1.7	G	G
59	0.56	0.55	0.8	0.8	0.05	0.06	11.20	9.17	150	154	Y	Y	2.3	2.2	G	G
60	0.71	0.76	2.5	2.5	0.04	0.05	17.75	15.20	371	380	Y	Y	2.2	2.1	G	G

Key to Masterchart (Units & Abbreviations):

Units : E vel (m/sec),E^I (m/sec), Dec T(msec),TAPSE(cm)
Diastolic Dysfunction(Y=Yes,N=No), RV systolic(G=good,Mild=Mild systolic dysfunction,Mod=Moderate systolic dysfunction)]