ESTIMATION OF RIGHT VENTRICLE TO PULMONARY ARTERY PRESSURE GRADIENT IN PATIENTS SUBJECTED TO INTRACARDIAC REPAIR FOR TETRALOGY OF FALLOT- A COMPARISON OF ECHOCARDIOGRAPHIC METHODS VERSUS DIRECT PRESSURE MEASUREMENT

Thesis submitted to the faculty of Sree Chitra Tirunal Institute For Medical Sciences and Technology, Thiruvananthapuram

In partial fulfillment of the requirement for the degree of DM, Cardiothoracic and Vascular Anaesthesia

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DECLARATION

I hereby declare that this thesis entitled, "**Estimation of right ventricle to pulmonary artery pressure gradient in patients subjected to intracardiac repair for tetralogy of Fallot-a comparison of echocardiographic methods versus direct pressure measurement**" has been prepared by me under the capable supervision and guidance of Dr. Suneel. P. R, Dr Unnikrishnan K P, Division of Cardiothoracic and Vascular Anesthesiology, Department of Anesthesiology, Dr. Thomas Mathew, Department of Cardiothoracic and Vascular Surgery, and Dr. Venkateswaran S, Department of Cardiology, at Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram.

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CONTENTS

INTRODUCTION

Tetralogy of Fallot is a complex congenital cardiac lesion consisting of an unrestrictive VSD, RVOT obstruction, right ventricular hypertrophy and overriding of the aorta[1]. The main symptoms of this condition arise due to reduced pulmonary blood flow as a result of the right ventricular outflow tract obstruction. The surgical correction of tetralogy of Fallot (TOF) involves the resection of muscle bundles that obstruct the right ventricular outflow tract (RVOT), thereby widening the RVOT and thus increasing the pulmonary blood flow[2]. Residual RVOT obstruction is a significant problem following corrective surgery for Tetralogy of Fallot[3]. Residual lesions of any nature would lead to higher postoperative morbidity, suboptimal RV and LV functions, higher reoperation rate, subnormal lung function, and increased risk of ventricular arrhythmias and sudden death[4,5,6,7].

The assessment of the adequacy of this resection is done by comparison of the pressure measurements taken by direct puncture of the right ventricle (RV) and the pulmonary artery (PA) after the surgical repair. Conventionally, this measurement is done in the orperating room by the surgeon once the repair is completed and the patient has been weaned from CPB and has stable hemodynamics. The surgeon employs a hypodermic needle, which he first

inserts into the RV, and then the same needle is inserted into the PA. These pressures are noted down and the difference is recorded as the RV-PA gradient. An ideal repair for TOF would have a minimal gradient. Obtaining the RV-PA gradient by means of a needle inserted into RV and PA is a time honored method and is even considered to be the method of choice by many surgeons.

There are however, less invasive and easily reproducible methods that can obtain RV-PA gradient. Epicardial echocardiography and transesophageal echocardiography are two such tools.

Epicardial echocardiography was first used in clinical practice in patients undergoing mitral commissurotomy. Epicardial echocardiography provides superior imaging of the heart since the probe is in direct contact with the surface of the heart[8]. Kaushal et al[3] have utilized epicardial echocardiography as a means to determine the RVOT gradient in patients who have undergone corrective surgery for Tetralogy of Fallot and found this technique to be useful in gradient determination.

Transesophageal echocardiography is a widely employed tool during cardiac surgical procedures of various kinds[1]. It has been used in TOF repair in the post bypass period to identify residual RVOT gradient [3]and has been found to help in identifying residual lesions.

We hypothesize that TEE and epicardial echo measurements can provide equally valid results as compared to needle transducer measured pressure gradients. For the purpose of the study, the TEE assessment of the RV-PA gradient was done through the ascending aortic short axis view, the aortic arch short axis view and the transgastric right ventricular outflow view[9]. Thereafter the surgeon did the epicardial echo, the RVOT was profiled by epicardial echo and the RVOT gradient measured. Correlations were calculated for the various echocardiography derived gradients and the needle gradients.

REVIEW OF LITERATURE

Tetralogy of Fallot

The initial description of the lesion complex was done by Neils Stenson in 1671[10] and the first precise anatomical description was illustrated by William Hunter in 1784[11]. Etienne-Louis Fallot in 1888 in his description of *L'anatomie pathologique de la maladie blue* [12]refined the anatomical description and its resulting physiology and the condition has been named after him. The term Tetralogy of Fallot refers to a tetrad of (i) ventricular septal defect with (ii) overriding of the aorta (iii) right ventricular outflow obstruction and (iv) right ventricular hypertrophy.

Tetralogy of Fallot constitutes 3-5% of all congenital heart lesions which corresponds to one in 3600 live births and has an equal gender distribution[13].

The ventricular septal defect in Tetralogy of Fallot is almost always non restrictive, resulting in equalization of pressures in both the ventricles. The severity of the lesion is determined by the degree of obstruction of the right ventricular outflow tract. The more severe the obstruction at the level of the right ventricular outflow tract or in extreme cases where there is atresia of the right ventricular outflow tract, a large right to left shunt exists at the level

of the VSD and the patient presents with severe cyanosis requiring intervention early on[14]. Most cases of tetralogy of Fallot have adequate pulmonary blood flow at birth but develop increasing cyanosis during the first few weeks and months of life.

Transthoracic echocardiography provides a comprehensive description of the intracardiac anatomy of the lesion and remains the mainstay of diagnosis.

Surgical management of Tetralogy of Fallot

Surgical treatment of Tetralogy of Fallot was first performed by Blalock, Thomas and Taussig in 1945[15], by performing anastomosis of the subclavian artery to the pulmonary artery, the classic Blalock Taussig shunt. Various modifications of the shunt surgeries were introduced by various surgeons[16,17,18,19] and all of them improved the level of oxygenation, reduced the hypercyanotic episodes and allowed the patients' development. Till 1955, palliative shunt surgeries were the only surgical option for Tetralogy of Fallot. It was Lillihei[20] who in 1955 who first did the total correction of the tetralogy using the "cross circulation" technique in a patient aged ten months. Since then rapid progress has been made in operative techniques and in the methods of extracorporeal perfusion. Since the initial mortality for single stage total correction was very high, a 2 stage correction was followed; a shunt surgery in

infancy flowed by a total correction at a later age[21,22]. The results of single stage total correction improved considerably after 1990 when the transatrial/ transpulmonary correction was introduced by Hudspeth[23] and Edmunds[24]. This technique obviated the need for a large ventriculotomy and incision of the pulmonary annulus and resultant right ventricular dysfunction and pulmonary valve insufficiency. Ever since the introduction of this surgical technique, mortality has fallen to less than 5% and surgery is being offered to younger patients[25].

In the earlier era, mortality was used as the benchmark to assess the success of a procedure. In the present day where cardiac surgical techniques have undergone a lot of refinements, the focus has shifted from mortality to bringing down the morbidity associated with the procedure. This includes avoidance of reoperations, preservation of the ventricular function and preservation of the pulmonary valve integrity whenever possible[26].

Complications after total correction for Tetralogy of Fallot

Even though the introduction of total correction for TOF was a surgical breakthrough and was considered a curative procedure, long term follow up results have shown that there are some sequelae following this surgical technique[27,28,29]. The most important of these is progressive right ventricular dysfunction arising due to pulmonary regurgitation. This is especially

prominent in those patients who have undergone right ventriculotomies and transannular incisions which lead to loss of integrity of the pulmonary valve leading to significant pulmonary regurgitation. PR is one of the main reasons for reoperations in these subset of patients and if left uncorrected, leads to progressive RV dysfunction and eventually to RV failure[30].

Restrictive RV diastology is another commonly encountered complication following total correction for TOF. This occurs due to the failure of reverse remodeling of the RV and thus, these patients have persistent RV hypertrophy. The filling pressures of the RV are elevated and the coronary flow will be phasic, occurring predominantly in diastole, similar to the left ventricle. Persistent RVH also sets the stage for the development of ventricular arrhythmias which are persistent and refractory to medical management. Residual RVOTO plays a significant role in the late development of this condition[31,32].

RV ischemia as a result of damage to the coronary arteries is a commonly encountered problem, especially in the region of the conus. As a result, those regions of the RV become akinetic and undergo fibrosis contributing significantly to RV dysfunction and development of arrhythmias[26].

Progressive dilatation of the aortic root and aortic incompetence are recognized late complications of total correction for TOF[33,34].

Residual RVOT obstruction as a significant postoperative problem

Residual RVOT obstruction after total correction for TOF is a well-documented problem especially after the transatrial/transpulmonary approach and specifically in cases wherein a pulmonary valve sparing operative technique has been implemented. Unidentified RVOTO in the immediate perioperative period leads to persistence of RV hypertension, prevents the reverse remodeling of the right ventricular hypertrophy and contributes significantly to right ventricular diastolic as well as systolic dysfunction and acts as a substrate for generation of arrhythmias[35,36]. Residual RVOTO could be due either to incomplete surgical resection which often results in a fixed obstruction wherein there is no change in the RVOT dimensions with various phases of the cardiac cycle, or it could be due to a dynamic obstruction wherein the RVOT clamps itself shut in systole and results in RVOTO[3]. Identification of the presence, nature and degree of RVOTO is extremely important to prevent postoperative adverse sequelae. Unidentified significant RVOTO leads to significant morbidity as well as mortality in the immediate as well as the late postoperative period.

Utility of intraoperative echocardiography

In the current era, TEE probes of several sizes are available which facilitates the examination across the entire age spectrum of patients with TOF. Intraoperative TEE has demonstrated an overall favorable safety profile[37,38,39]. Currently available TEE probes incorporate all the modalities that are available in TTE. TEE provides diagnostic information in CHD by overcoming limitations due to poor echo windows and suboptimal image quality.

In the prebypass period, the main aims of intraoperative TEE are to confirm and/or exclude preoperative diagnoses. The prebypass examination also serves as the reference for comparison with the post bypass examination. Intraoperative TEE has changed the surgical plan or set the stage for major modifications thereof in multiple instances[40,41,42].

Intraoperative TEE also is instrumental in guiding the hemodynamic management intraoperatively, thus influencing the anaesthetic management significantly. This is especially useful in the setting of TOF where conditions like tachycardia, hypovolemia and increased inotropy can precipitate a hypercyanotic spell[43].

The prebypass TEE examination should ideally be comprehensive although only limited studies might be feasible in those situations where the patients' hemodynamics are deteriorating. The comprehensive prebypass TEE examination should focus on the examination of the VSD, the RVOT obstruction, aortic override, right ventricular hypertrophy and other associated anomalies.

Examination of the VSD

The VSD should be assessed in terms of its location, size and margins. The classically described VSD in TOF is a large unrestrictive VSD and is generally a malaligned, conoventricular defect. The direction of shunt across the VSD depends on the degree of right ventricular outflow tract obstruction: the greater the obstruction, the more the degree of right to left shunt. The VSD is generally assessed through the midoesophageal 4 chamber view, the midoesophageal long axis view, the midoesophageal aortic valve short axis view, midoesophageal right ventricular inflow outflow view and the deep transgastric view. Colour Doppler examination of the defect can help to identify the direction of the shunt and also the presence of any additional shunts. Many a times, the presence of additional VSDs cannot be recognized preoperatively because of the preferential shunting through the large conoventricular defect[44].

Right ventricular outflow tract obstruction

The nature and severity of right ventricular outflow tract obstruction plays a key role in determining the severity of TOF. The essential pathology in TOF is a malaligned conal septum which encroaches on the right ventricular outflow tract, thus narrowing it. The infundibular region is the most commonly affected region of the RVOT in TOF, but obstruction due to narrowing of the pulmonary valve and the main or branch pulmonary arteries could also exist, either in combination with infundibular obstruction or in isolation.

The TEE views employed to assess the right ventricular ouflow tract include the midoesophageal right ventricular inflow outflow view, the midoesophageal ascending aortic short axis view, the upper oesophageal aortic arch short axis view and the transgastric right ventricular outflow tract view. Colour Doppler assessment of the RVOT helps to identify the site of obstruction and serves as a guide for the placement of the spectral Doppler. Spectral Doppler assessment helps to quantitate the degree of obstruction and the Doppler waveform characteristic helps to identify the nature of obstruction: a late peaking dagger shaped systolic signal is typical of dynamic obstruction whereas fixed valvar obstruction is associated with a rounded contour of the spectral Doppler envelope[43,44].

Aortic override

Aortic override is one of the components of the tetralogy and it occurs due to the underdevelopment of the subpulmonary infundibulum. This is best imaged and its extent quantified in the midoesophageal long axis view, transgastric long axis view and the deep transgastric long axis view. Assessment of the aorta should also include assessment of the aortic root size and the presence and degree of any aortic valve incompetence.

Right ventricular hypertrophy

The right ventricle in TOF hypertrophies as a result of pressure overload on it both because of the right ventricular outflow tract obstruction and the unrestictive nature of the VSD which facilitates equalization of pressures in both the ventricles. This is best assessed in the midoesophageal 4 chamber view, the midoesophageal RV inflow outflow view and the transgastric RV inflow view.

Post bypass TEE examination

In the post bypass period, TEE allows for the continuous monitoring of intracardiac air, ventricular function and assessment of loading conditions.

In the post bypass TEE examination, the key issues to be addressed include the presence of a residual VSD, presence of residual RVOT obstruction, presence of pulmonary regurgitation and ventricular dysfunction.

Residual VSD

A residual VSD post TOF repair could be due to patch dehiscence or due to the presence of additional VSDs. If a residual defect is present, its size, location, direction and magnitude of shunting should be assessed. Any residual VSD which measures more than 5 mm in size when measured from the LV side of the septum requires immediate surgical reintervention. Residual VSDs measuring between 3-5 mm in size require reintervention if the Qp:Qs is more than 1.5:1[43].

Residual RVOT obstruction

RVOT should be assessed at the level of the infundibulum, the pulmonary valve and the main and branch pulmonary artery level so as to look for any residual obstruction. Its location, nature (whether dynamic or fixed) and its severity should be assessed. Residual obstruction is generally considered significant if the peak velocity of flow is more than 3m/s.

Pulmonary regurgitation

This is an especially common problem in those patients who require a transannular patch since the pulmonary valve integrity is lost following its placement[45]. The grade of pulmonary regurgitation must be quantitated as pulmonary regurgitation can have long term sequelae on right ventricular function[46].

Kaushal et al[3] emphasized the utility of intraoperative echocardiography in the post bypass decision making in TOF. In their study population of patients undergoing TOF repair through the transatrial approach, a significant number had RVOT obstruction which was deemed hemodynamically relevant requiring reintervention based on the conventional criteria: a peak RVOT gradient more than 40 mm Hg and/or an RV/LV pressure ratio of 85% or more. But, only a minority of patients in this study population had a fixed obstruction as assessed by TEE and therefore, no intervention was done in most. In their follow up of these patients, they noted that the dynamic gradients decreased considerably irrespective of their severity.

Utility of intraoperative echocardiography has also been highlighted by Ungerleider et al[47] who noted that patients who leave the operating room with uncorrected residual defects had a higher mortality in the post operative period and a significant number of these patients required a reoperation. Intraoperative echocardiography obviates these problems by setting the stage for immediate identification of any residual problems which requires reintervention.

Challenges associated with intraoperative TEE

The main limitation of TEE is that the probe lies within the confines of the oesophagus and therefore the availability of imaging windows are limited. Imaging of structures in the far field like the pulmonary valve could also be suboptimal with TEE. Optimal alignment of the Doppler signals of the RVOT could be especially challenging using TEE and it therefore requires multiple views to ascertain the findings.

Epicardial echocardiography

Epicardial echocardiography was introduced into clinical practice in the 1970s during open mitral valve commissurotomy. Even though its utility gained popularity during valve surgeries; with the advent of perioperative transoesophageal echocardiography, this diagnostic entity lost its unique status in the perioperative period. This underutilized clinical entity does have some

unique advantages over TEE: it can be utilized in those patients who have some contraindication to the use of TEE (eg: patients with oesophageal strictures), the imaging planes are not limited to the confines of the oesophagus, anterior structures of the heart can be very clearly imaged, optimal Doppler alignment is possible by adjustment of the echo probe and the "blind spots" in TEE can be visualized by this entity[42].

The utility of perioperative epicardial echocardiography in congenital cardiac surgery has been attested to by Ungerleider[48] in his series of patients who underwent surgery for correction of atrioventricular septal defect.

The role of epicardial echocardiography as a useful clinical adjunct was reiterated by Gussenhoven[49] citing his center's vast experience with the technology in patients undergoing congenital cardiac surgical procedures.

AIMS AND OBJECTIVES

Primary objectives

- To assess whether TEE and epicardial echocardiography can provide reliable estimate of the RVOT gradients in patients with TOF.
- To compare the RVOT gradients obtained via TEE as well as epicardial echocardiography with preoperative TTE measured RVOT gradients in the preoperative phase.
- To compare the RVOT gradients obtained via epicardial as well as transoesophageal echocardiography with needle-saline-transducer measured gradients in patients undergoing intracardiac repair for Tetralogy of Fallot in the post bypass phase after surgical correction.

Secondary objectives

- To assess which is the TEE view that provides the most accurate estimate of RVOT gradient in patients with TOF.
- To assess whether there is any correlation between the level of obstruction in the RVOT and the TEE view which would aid us in reliably measuring the gradient at that particular level.

MATERIALS AND METHODS

The study was conducted in the Department of Cardiovascular and Thoracic Anaesthesia, SCTIMST, after departmental, institutional (TAC) and ethics committee clearance.

61 patients who were scheduled for elective total correction for Tetralogy of Fallot were included in the study after obtaining informed consent.

Study design

Prospective observational study

Inclusion Criteria:

Age: 5 months - 40 years

Gender: both

Intracardiac repair for the correction of tetralogy of Fallot

Patients undergoing redo surgeries were included

No bias against caste, gender, ethnicity, race, class.

Exclusion criteria:

Weight less than 5 kg

Contraindications to TEE probe insertion which include: Esophageal spasm, Esophageal stricture, Esophageal laceration, Esophageal perforation, Esophageal diverticula (e.g. Zenker's diverticulum), Large diaphragmatic hernia, Atlantoaxial disease , patients who received extensive radiation to the mediastinum, Upper gastrointestinal bleeding, significant dysphagia and odynophagia.

Emergency surgery

Patient with infective endocarditis or any evidence of infection.

Patients undergoing other concomitant cardiac procedures.

Conduct of the study

- Patients undergoing ICR for TOF who satisfied the inclusion – exclusion criteria were enrolled in the study.
- After induction of anesthesia and endotracheal intubation, TEE probe was inserted in all recruited patients.
- Preoperative echocardiographic evaluation was conducted using the ultrasound system IE 33 (Philips Medical Systems, Bothell, WA).

During the preoperative phase the RV-PA gradient was obtained from the midoesophageal ascending aortic short axis view (Image 1), upper oesophageal aortic arch short axis view (Image2) and the transgastric RV outflow view (Image 3) and the gradients so obtained were compared with the preoperative TTE values. Epicardial echocardiographic assessment of the RVOT gradients was done with assistance from the surgical team and these were also compared to the TTE values. Epicardial echocardiographic examination was done by inserting either the S8 or S12 TTE probes into a plastic sheath filled with ultrasound jelly (Images 4 &5). The level of maximal obstruction was noted by 2D and colour Doppler examination.

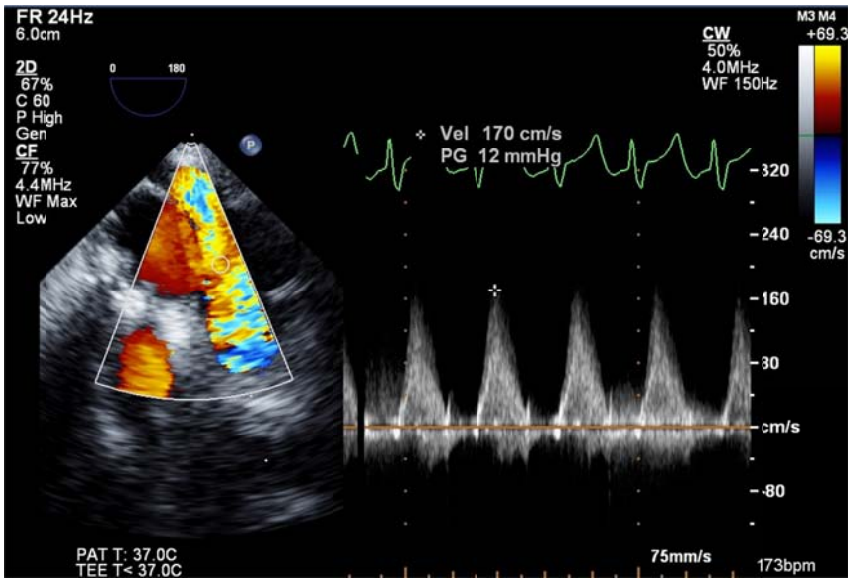

Image 1: Midoesophageal ascending aortic short axis view & its spectral Doppler profile

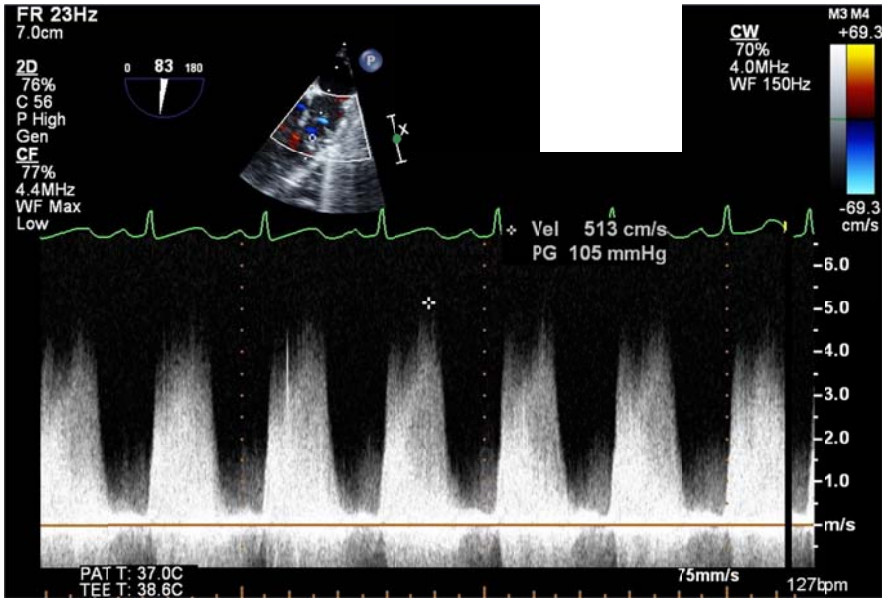

Image 2: Upper oesophageal aortic arch short axis view & CW Doppler interrogation of this structure

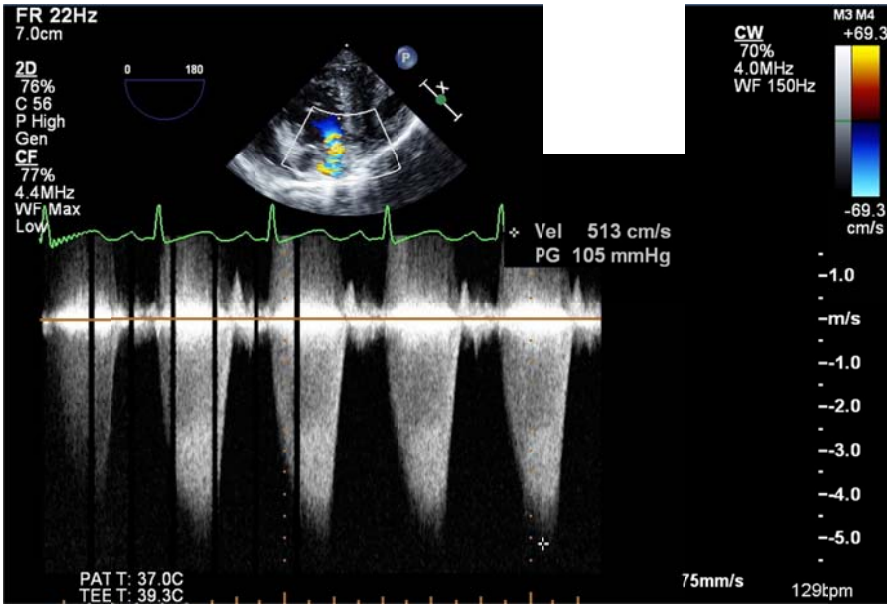

Image 3: Transgastric Right ventricular outflow view & CW Doppler interrogation of the structure

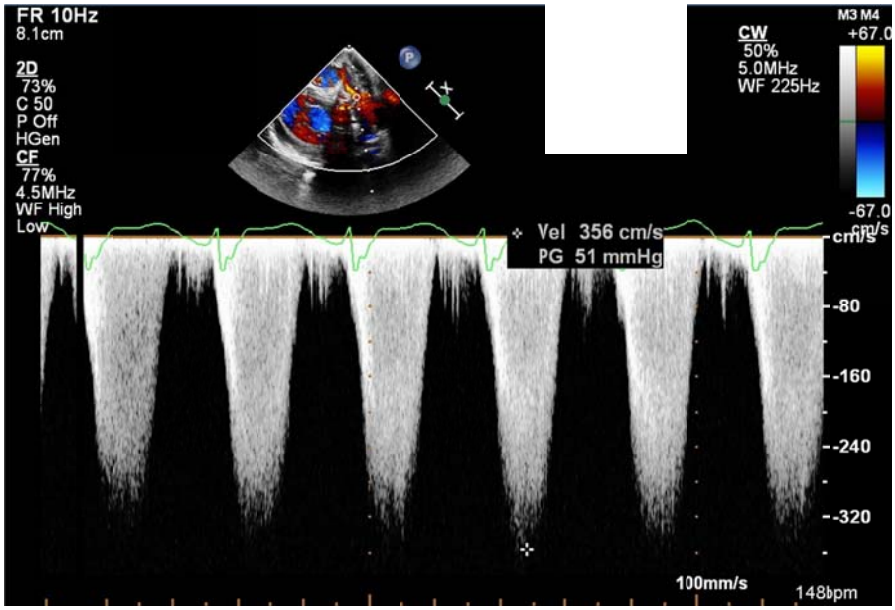

Image 4: Epicardial RVOT view with CW Doppler interrogation

Image 5: Epicardial echocardiography imaging being done.

- Upon completion of the surgery and successful weaning from cardiopulmonary bypass, the anesthesiologist measured the RV-PA gradient from the ascending aortic short axis view, the aortic arch short

axis view and transgastric RV outflow view. Thereafter with surgical assistance an epicardial echo was done and the RV-PA pressure gradients again obtained. The surgeon then obtained the needle pressures from RV and PA using a saline filled pressure transducer system.

Data collection:

Demographic Data including age, sex, weight, height and body surface area of all the participants were noted.

Variables measured included inotropic support, preoperative TTE RVOT gradient, whether transannular patch repair was done/not, Dopppler RVOT gradients as obtained via epicardial echo and TEE, systemic hemodynamics at the time of documenting the RVOT gradient, RVOT gradient as obtained via a saline filled pressure transducer system, duration of aortic cross clamp and cardiopulmonary bypass, degree of pulmonary regurgitation.

Statistical analysis

As descriptive statistics, percentages for categorical variables and means (SD) for quantitative variables were presented. Associations between quantitative variables were assessed by Pearson's correlation coefficients. Associations were studied for the total sample of patients as well as for

stratified data by age-group and levels of obstruction in the RVOT also. P values <.05 were considered to conclude statistical significance. MS Excel and IBM SPSS Statistics version 21 for Windows were used for data entry and analysis.

RESULTS

Sixty-one patients scheduled for elective intracardiac repair for tetralogy of Fallot were included in this prospective observational study. Intraoperative demographic, hemodynamic as well as echocardiographic data were recorded as described in the Materials and Methods section.

Demographic parameters

The mean and standard deviation and the range of values of the demographic parameters of all the patients in the study were analyzed and are represented in a tabular form hereunder.

Table 1: Table showing the demographic parameters and their mean, standard deviation and ranges

Parameter	Minimum	Maximum	Mean	Std. Deviation
Age (yrs)	.45 (5 months)	37.00	5.9	7.6
Wt (kg)	5.0	59.0	16.3	13.8
Ht (cm)	56.0	173.0	96.88	32.05
BSA (m^2)	.280	1.68	.640	.37

Age, height, weight and body surface area.

Our study population had a total of 61 patients, 35 males (57.4%) and 26 females (42.6%). The mean age of the study population was 5.9 years (±7.6), the age range being 0.45-37 years. The mean weight of the population was 16.3 kg (±13.88), the range being 5-59 kg. The mean height was 96.88cm (±32.05), with a range of 56-173 cm.

Table 2: Table showing the gender distribution of the study population

Gender	Percent (%)
Female	42.6
Male	57.4

Diagnosis and level of obstruction in the RVOT

Preoperative diagnosis: 83.6% of the study population was diagnosed with classic Tetralogy of Fallot whereas 8.2% and 4.9% were diagnosed respectively with VSD, PS and DORV, VSD, PS. TOF with PA and TOF in association with AV canal defect were the other diagnoses accounting for 1.6% each.

Table 3: Table showing the preoperative diagnosis of the patients included in the study

Diagnosis	Frequency	Percent
Classic TOF	51	83.6
VSD,PS	5	8.2
DORV,VSD, PS	3	4.9
TOF with PA	1	1.6
TOF+ AVcanal	1	1.6
Total	61	100.0

Level of obstruction in the RVOT: Isolated infundibular obstruction was the predominant cause of RVOT obstruction in the study population accounting for 49.2% of the study population followed by combined infundibular and valvar obstruction which constituted 27.9% of the study population. The level of obstruction in the RVOT and the number of patients in each category is represented in Table 4 and is diagrammatically represented in Figure 1.

Table 4: Table showing the various levels of obstruction in the RVOT and the number of affected patients in each group.

Level of Obstruction	Frequency	Percent
Valvar	1	1.6
Infundibular	30	49.2
Infundibular + valvar	17	27.9
Infundibular+ valvar+ supravalvar	12	19.7
Valvar+ Supravalvar	1	1.6
Total	61	100.0

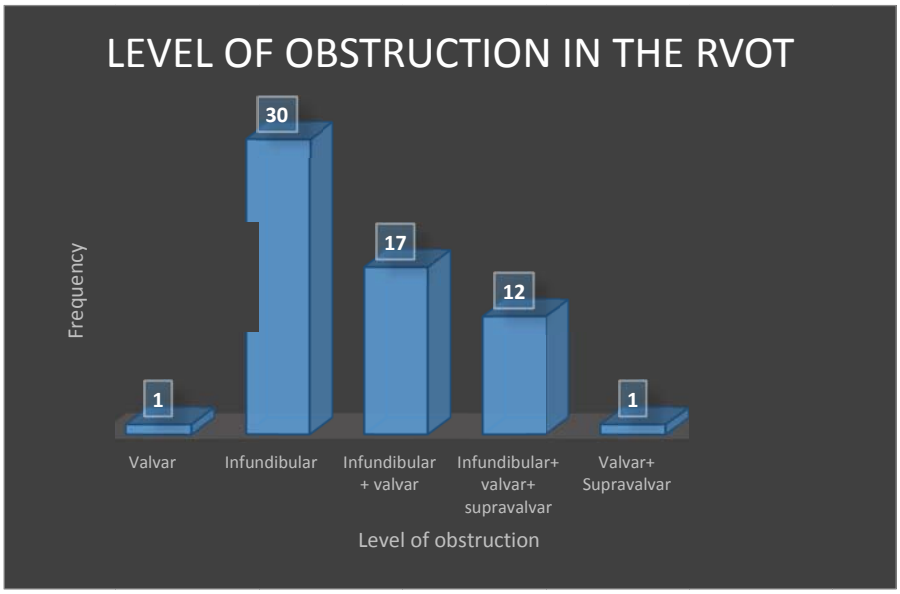

Figure1: Chart showing the frequency distribution of the various levels of RVOT obstruction in the study population

Pre CPB hemodynamic parameters

Heart rate, systolic, diastolic and mean blood pressures, oxygen saturation, CVP and end tidal carbon dioxide concentration and the delivered inspired oxygen concentration were noted in the pre CPB period and results are tabulated in table 5.

Table 5: Table showing the various hemodynamic parameters in the pre CPB period, their means and standard deviations and their ranges.

Parameter	Minimum	Maximum	Mean	Standard deviation
Preop HR	64	150	108.25	17.8
Preop SBP	70	142	94.89	17.05
Preop DBP	37	94.0	53.87	13.83
Preop MAP	49	101	70.25	12.54
Preop CVP	4	15	8.87	2.65
Preop FiO2	.39	1.00	.52	.11
Preop EtCO2	16	41	31.67	4.39
Preop SpO2	56	100	89.54	10.89

Pre CPB echocardiographic data

The mean RVOT gradients obtained from the ascending aortic short axis view, aortic arch short axis view, transgastric RV outflow view and epicardial echo are tabulated in table 6. The mean preoperative TTE derived RVOT gradient is also tabulated alongside for comparison.

Table 6: Table showing the various echocardiographic measurements of the preCPB RVOT gradient, the mean values of each with the respective standard deviation and the upper and lower limits.

Echo view	N	Minimum	Maximum	Mean	Standard deviation
Preop TTE gradient	61	16	105	66.11	20.52
Preop AA sax	58	5	110	49.88	24.87
Preop Arch sax	45	10	115	56.49	24.80
Preop TG RV	47	9	104	53.66	20.96
Preop epicardial	52	6	105	57.15	21.22

Correlations between the intraoperative echocardiographic views and preoperative transthoracic echo gradients

The overall correlation between the highest intraoperative echocardiographic gradient (which refers to the intraoperative echo gradient obtained either using any of the TEE views or using epicardial echo which was the highest) in each case when compared to the preoperative TTE value revealed a correlation coefficient of 0.360 which shows a not so strong correlation. This value was found to be statistically significant with a p value of 0.004. This is represented in Table 7 and diagrammatically represented in Figures 2 and 3.

Table 7: Table showing the Pearson's correlation coefficient of the highest preoperative echo gradient and the preoperative TTE gradient.

Correlation to preoperative TTE gradient		
Highest preop gradient	Pearson Correlation	.360
	P Value	.004
	N	60

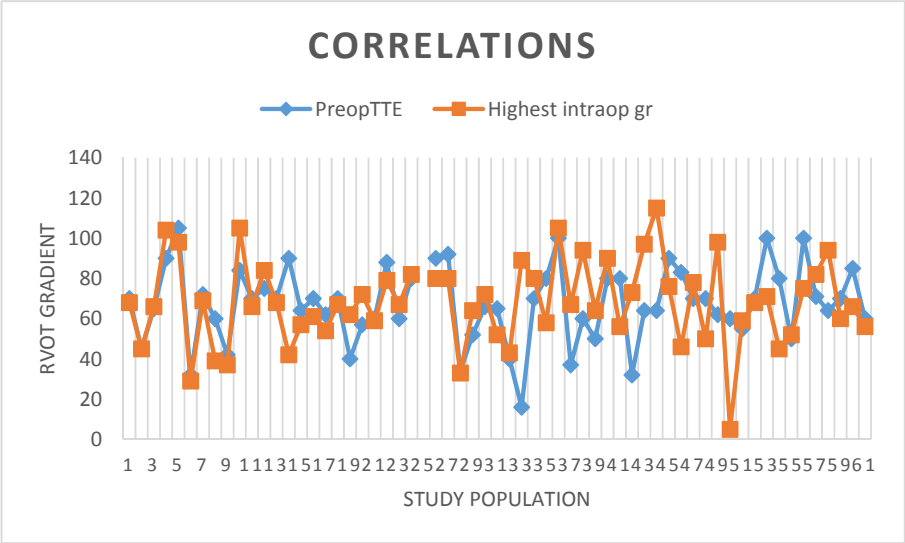

Figure 2: Chart showing the correlations between the preoperative TTE gradient (blue line) vs. the intraoperative gradient (orange line) for the study population.

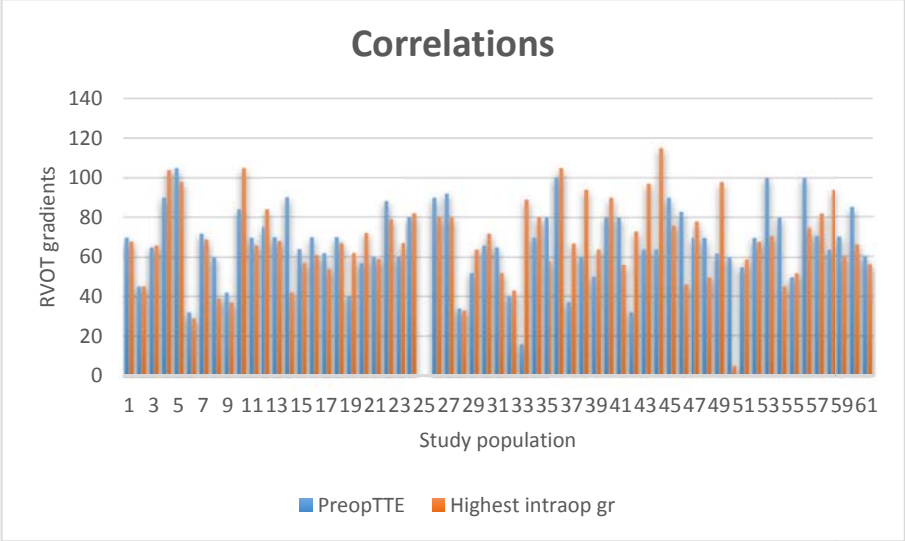

Figure 3: Clustered column chart showing the RVOT gradients as measured by preoperative TTE (represented in blue) and intraoperative echocardiography (represented in orange) in each patient in the study.

However, the correlation coefficients for the individual transoesophageal echocardiographic views when compared to the preoperative TTE value did not reveal a strong correlation, although all of them did show a positive correlation coefficient. Epicardial echocardiography derived RVOT gradient was the preoperative echocardiography mode that was found to have a statistically significant positive correlation in the preoperative period. The individual correlation coefficients and their corresponding p values are tabulated in Table 8.

Another notable fact is that in the preCPB period, the UE aortic arch short axis view was reliably obtained in only 73% of patients and the

transgastric RV outflow view was obtained in 77% of the patients, while the ME ascending aortic short axis view could be documented in 95.08% patients. Epicardial echocardiography could document the RVOT gradient in 85.24% patients.

When the highest preoperative TEE gradient (the value amongst the 3 TEE views which was the highest) was compared with preoperative TTE value, a correlation coefficient of 0.217 was obtained as against an r value of 0.459 which was the correlation coefficient obtained when the epicardial gradient was compared with the preoperative TTE value. It was TEE which provided the highest preoperative echo gradient in 75% of the instances.

Table 8: Table showing the correlation coefficients (r) of the various intraoperative echocardiographic views to the preoperative TTE derived RVOT gradient and their respective p values.

Correlations to preoperative TTE gradient		
Preop AA sax	r	.192
	P Value	.150
	n	58
Preop Arch sax	r	.116
	P Value	.447
	n	45
Preop TG RV	r	.148
	P Value	.322
	n	47
Preop epicardial	r	.459
	P Value	.001
	n	52
Highest TEE gradient	r	0.217
	P value	0.107
	n	60

Subgroup analysis: Correlations between the intraoperative echo data and the preoperative TTE values in age groups <5 years and < 10 years

When subgroup analysis was performed to assess the correlation of the highest intraoperative echocardiography derived RVOT gradient to the preoperative TTE gradient in patients aged 5 or less (n=45), a correlation coefficient of 0.488 was obtained which suggests a moderately strong positive correlation, both clinically as well as statistically (p value <0.001). Subgroup

analysis was also performed for the age group <10 years, which also showed a moderately strong positive correlation between the intraoperative echo data and the preoperative TTE values, the Pearson's correlation coefficient being 0.499 in this group (n=50). These data are tabulated in Table 9.

Table 9: Table showing the Pearson's correlation coefficient for age groups < 5 years and < 10 years.

Correlations to preoperative TTE gradient		
Highest preop gradient; age < 5 years	Pearson Correlation	.488
	P Value	<.001
	N	45
Highest preop gradient; age < 10 years	Pearson correlation	0.499
	P value	<0.001
	N	50

CPB and ACC duration

The mean CPB duration was 137.97 min (±72.8) and the mean ACC duration was 94.48 min (±48.6). The mean temperature on CPB was 29.29°C(±2.74). The type of cardioplegia delivered was cold blood cardioplegia using a BCDS in 62.3% of patients; Del Nido cardioplegia was used to arrest the heart in 37.7%.

Transannular patch

A transannular patch was required in 44.3% of the study population whereas 55.7% of the patients could be repaired with a pulmonary valve sparing technique. The data is represented in table no:10.

Table 10: Table showing the frequency and corresponding percentages of patients who did and did not require a transannular patch.

Transannular patch.	Frequency	Percent
TAP	27	44.3
No TAP	34	55.7
Total	61	100.0

Inotrope requirement

Dobutamine was the most frequently used inotrope in the study population, being used as the sole inotropic agent in 75.4% of the study population followed by a combination of Dobutamine and Noradrenaline which was used in 16.4% of the study population. The various inotropic agents or combinations thereof, along with the frequency of their use is represented diagrammatically in Figure 4.

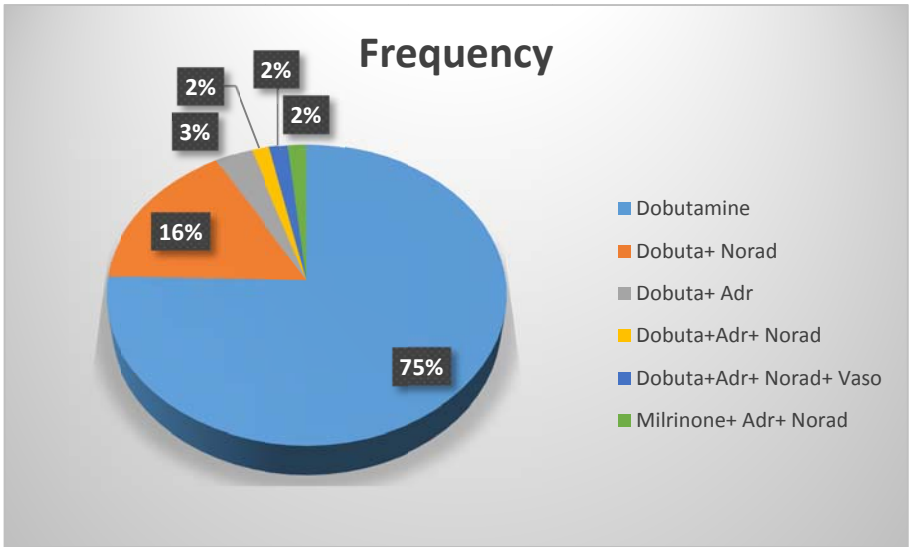

Figure 4: Pie diagram showing the frequency distribution of inotrope use in the study population.

Post CPB hemodynamic parameters

The hemodynamic parameters that were noted in the post CPB period included heart rate (HR), systolic, diastolic and mean arterial pressures (SBP, DBP and MAP), central venous pressure (CVP), arterial oxygen saturation (SpO_2), fraction of inspired oxygen concentration (FiO_2) and endtidal CO_2 concentration ($EtCO_2$) monitoring. The mean values are tabulated in Table 11 along with their standard deviations and upper and lower limits.

Table 11: Table showing the various hemodynamic parameters of the study population in the post CPB period with their means and standard deviations, upper and lower range limits.

Parameter	Minimum	Maximum	Mean	Standard deviation
Postop HR	80	156	121.43	16.515
Postop SBP	59	140	87.85	15.299
Postop DBP	31	76	49.34	9.799
Postop MAP	22	95	63.61	12.391
Postop CVP	7	25	11.89	3.184
Postop FiO_2	.40	1.00	.6826	.19238
Postop $EtCO_2$	27	44	33.18	4.129
Postop SpO_2	91	100	99.30	2.044

Post CPB RV and PA pressures

The mean systolic, diastolic and mean pressures in the RV and PA as measured by a needle-saline-transducer system are represented in Table 12 along with their standard deviations and the value ranges.

Table 12: Table showing the RV and PA pressures of the study population with their means and standard deviations, upper and lower range limits.

Parameter	Minimum	Maximum	Mean	Standard deviation
RVSBP	24	109	51.77	16.36
RVDBP	1	37	11.64	6.27
RVMAP	11	52	28.70	8.07
sPAP	10	55	31.02	10.34
dPAP	2	39	15.98	5.72
mPAP	8	44	22.33	6.26

Post CPB echocardiographic and needle derived RVOT gradients

In the post CPB period, RVOT gradients measured using transoesophageal echocardiography in the ascending aortic short axis view, upper oesophageal aortic arch short axis view and the transgastric RV outflow view as well as using epicardial echocardiography are tabulated in table 13. RVOT gradients derived using a needle-saline-transducer system are also tabulated.

Table 13: Table showing the RVOT gradients as derived by various echocardiography views and by means of the needle saline transducer system with their respective means, standard deviations and range limits represented.

Echo view	N	Minimum	Maximum	Mean	Standard deviation
Postop AA sax	60	6	94	25.98	19.41
Postop arch sax	49	4	71	23.31	15.29
Postop TGRV	55	4	59	20.53	14.37
Postop epicardial	59	3	76	25.97	17.15
Needle gradient	61	0	75	20.77	16.06

Correlations between the post CPB RVOT gradients as measured by echocardiography and needle-saline-transducer system

When the highest of all the echocardiography gradients (3 TEE views and epicardial echo) was compared to the needle-saline –transducer derived

RVOT gradient, a correlation coefficient of 0.679 was obtained which reflects a moderately strong correlation between these two. This was found to be statistically significant with a p value of <0.001. These values are tabulated in Table 14 and diagrammatically represented in Figures 5 and 6.

Table 14: Table showing the correlation coefficient (r) between the highest postoperative echo derived RVOT gradient and the needle gradient.

Correlations to needle gradient		
Highest postop gradient	Pearson Correlation	.679
	P Value	<.001
	N	61

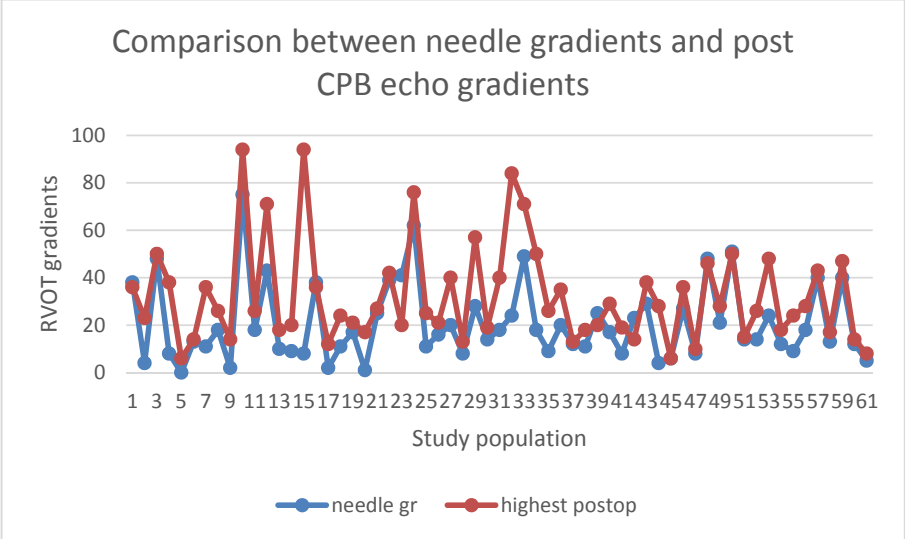

Figure 5: Chart showing the correlations between the intraoperative echo gradient in the post CPB period and the needle gradient.

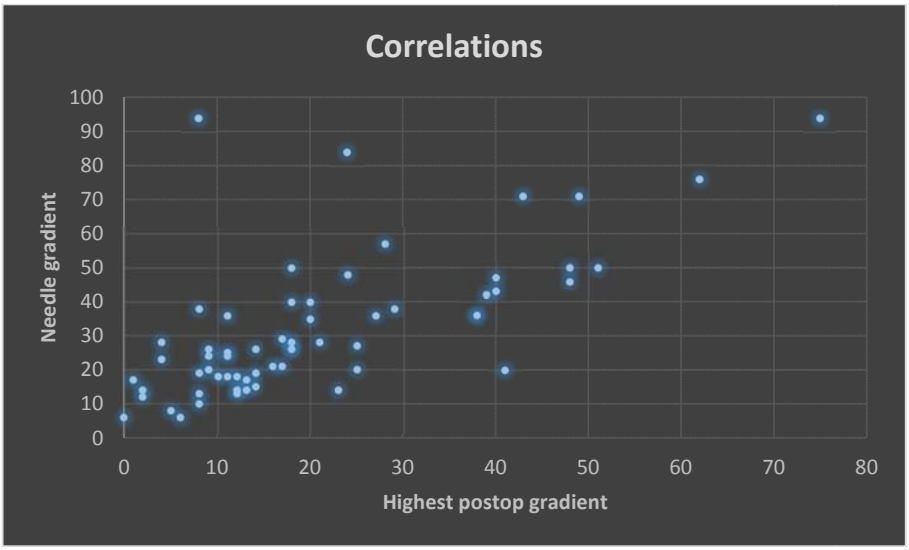

Figure 6: Chart showing the clustering of the RVOT gradient values derived from both the techniques (needle and echo) toward the trendline suggesting a moderately high degree of correlation between the two techniques.

When individual echocardiography views were compared to the needle derived gradient, a statistically significant correlation was found between all the views in predicting the true RVOT gradient, with the highest correlation being that for epicardial echo (Pearson's correlation coefficient of 0.643) followed by the transgastric RV outflow view (Pearson's correlation coefficient of 0.627). The ascending aortic short axis view had the least correlation coefficient (0.584) and the UE aortic arch short axis view had a correlation coefficient of 0.591. When the highest post operative TEE gradient was used for comparison to the needle gradient, a correlation coefficient of 0.663 was obtained which suggests a slightly stronger correlation than that of

epicardial echocardiography (correlation coefficient 0.643). These are tabulated in Table 15.

Also of note was the fact that in our study, echo gradients (the highest of all measured values) were higher than the needle gradients in 78.68% of the patients.

Table 15: Table showing the correlation coefficients between the individual echocardiography views and the needle gradient and their respective p values.

Correlations to needle gradient		
Postop AA sax	r	.584
	P Value	<.001
	n	60
Postop arch sax	r	.591
	P Value	<.001
	n	49
PostopTG RV	r	.627
	P Value	<.001
	n	55
Postop epicardial	r	.643
	P Value	<.001
	n	59
Highest post op TEE gradient	r	0.663
	P value	<0.001
	n	61

Subgroup analysis of correlations between the needle gradient and intraoperative echo gradients in the post CPB period in patients aged <5 years and <10 years.

The RVOT gradients derived via intraoperative echo, the highest value of all measured values, was compared with the needle gradients and correlations derived for age groups <5 years and <10 years. Both the age groups showed moderately strong positive correlation between the 2 sets of measurements, which was significant both clinically and statistically with a p value of <0.001 in both the instances. The Pearson's correlation coefficient was 0.539 in patients aged 5 or less and 0.555 in patients aged 10 or less. The values are tabulated in Table 16.

Table 16: Table showing the correlation coefficients and the p values in the age groups <5 years and <10 years.

Correlation to needle gradient		
Highest postop gradient; age < 5 years	Pearson Correlation	.539
	P Value	<.001
	N	45
Highest postop gradient; age < 10 years	Pearson correlation	0.555
	P value	<.001
	N	50

Requirement of revision surgery

4 patients in the study required an immediate surgical revision, 3 for significant residual RVOT gradients and one for residual VSD. This accounted for a total of 6.6% of patients undergoing immediate revision surgery in the study population.

DISCUSSION

Tetralogy of Fallot is the most common congenital cyanotic cardiac condition in the infant and older child. Intracardiac repair for Tetralogy of Fallot is the preferred surgical procedure for this condition.

Intracardiac repair for Tetralogy of Fallot may be offered to symptomatic patients who present acutely with history of cyanotic spells as well as to patients who are more or less asymptomatic whose cardiac condition gets diagnosed incidentally during a physical exam (eg: pink TOFs). This would explain the wide age range observed in our study (5 months to 37 years). Similar age ranges were reported by Padalino[50] et al and Kaushal[3] et al in their studies involving patients with tetralogy of Fallot undergoing intracardiac repair.

Similarly, the wide variation in the duration of cardiopulmonary bypass (48-450 min) and aortic cross clamp (32-275 min) could be attributed to the complexity of the surgical repair involved (trans RA/ PA ICR vs. requirement of transannular patch and monocusp reconstruction of the PV).

Intracardiac repair for Tetralogy of Fallot confers many advantages over the palliative shunt procedures, being more physiological. Initial attempts at intracardiac repair for TOF involved a right ventriculotomy which extended

from the body of the RV through the RVOT and the PV[51] with the associated problems of right ventricular dysfunction[52], propensity for the development of ventricular arrhythmias[53] and development of pulmonary valve incompetence[54]. Nowadays, more attention is being paid to the preservation of the PV integrity and to RV preservation at the time of surgical repair[55].

Intraoperative echocardiography is assuming more and more importance in corrective surgeries for congenital cardiac conditions. Multiple authors have documented the safety of TEE in the pediatric population[56,57,58]. With the advent of miniaturization of TEE probes, TEE can be safely performed even in neonates[59]. The utility of intraoperative echocardiography has also been documented in the literature[60]. Randolph et al[61] in his prospective assessment of 1002 patients undergoing corrective surgery for congenital cardiac conditions found that intraoperative TEE had a major impact, as defined by a change in the surgical plan preoperatively or to a surgical revision in the post CPB period, in 13.8% of patients. They observed that the procedures which benefited the most from the use of intraoperative echocardiography were valve repairs and complex outflow tract reconstructions. The pediatric council of the American Society of Echocardiography in their guidelines issued in the year 2005[39], on the indications for the performance of TEE in the patient with CHD, also attests to

the benefits that intraoperative TEE can confer to the perioperative team in managing the CHD patient.

Kamra et a[62] highlights the importance of intraoperative TEE in patients undergoing reparative surgeries for CHD and suggests that intraoperative TEE be made the standard of care for these patients. In their extensive review on the utility of intraoperative TEE, they emphasise the role TEE plays at various stages of cardiac surgery for CHD. In the pre CPB period, TEE helps corroborate the preoperative diagnoses and helps to identify additional information that might have been missed in the preoperative TTE exam. TEE also helps to assess the loading conditions of the heart, ventricular function and shunt fraction thereby guiding the perioperative team in fluid management and in inotropic/vasoactive drug selection. The position of central venous catheters placed percutaneously can also be confirmed by TEE. At initiation of CPB, TEE helps to confirm the placement of venous cannulae and LV venting devices. The major role of intraoperative TEE, however, is in the post CPB period, where it can help identify the presence of any residual lesions which might mandate a return to CPB. Further, it also helps in assessing the adequacy of cardiac deairing and in guiding inotropic and fluid management.

Impact of intraoperative TEE in the perioperative management of TOF has been widely stated by many authors[63,64,65]. Joyce et al[66] confirmed the

accuracy of intraoperative TEE findings with the help of TTE which was done 6 days post repair and concluded that intraoperative TEE predicts the degree of residual RVOT obstruction, degree of PR and the presence of additional VSDs reliably. They found that branch PA stenosis, especially left PA stenosis was the residual lesion which was missed by intraoperative TEE in most of the instances.

Kim et al[65] in their retrospective analysis of patients who underwent corrective surgery for TOF attempted to assess the accuracy and cost effectiveness of intraoperative TEE. They found a high degree of agreement between the findings of intraoperative TEE and early postoperative TTE. In this analysis, they found that intraoperative TEE diagnosed residual lesions in 17.9% of their patients out of whom 10% required a return to CPB. They also conclude that the possible cost savings per patient by using intraoperative TEE is around US$ 1489.

Identification of residual RVOT gradients in the immediate post CPB period is important since it provides a window of opportunity for immediate revision, thus avoiding the added morbidity and costs associated with a redo surgery. Coats et al[67] state that significant residual RVOTO may lead to irrecoverable myocardial dysfunction if the baseline function is poor or exposure to obstruction is more prolonged. Resection of muscle bundles in the RVOT and breach of the PV integrity is not without consequences. It has been

observed by Yoo et al[68] and Van der Hulst and colleagues[69] that an element of residual RVOTO (not more than mild) was protective against development of severe PR and RV dilatation.

Since no studies have been conducted which compared the intraoperative echo (epicardial and TEE) measured RVOT gradients and the needle gradients, this study was designed.

Assessment of RVOT gradients

Obstruction across any cardiac structure can be assessed and quantified using Doppler echocardiography. The Doppler principle was described by the Austrian physicist, Christian Doppler in the year 1842. The change in frequency of the incident ultrasound beam when it hits upon a moving target like RBC is used to gauge the direction and speed of blood flow. In clinical echocardiography, using the modified Bernoulli's principle[70], the pressure gradients across a structure can be calculated by assessing the velocity of blood flowing through it as $\Delta = 4\ v^{2.}$.

In the pre CPB period, assessment of the RVOT gradient assumes importance as this is the lesion which determines the amount of right to left shunt across the VSD and thus, the systemic saturation. In the post CPB period, estimation of the residual RVOT gradient helps to decide on the adequacy of surgical resection and to determine the need for a reintervention.

Correlation between intraoperative echo and preoperative TTE

In the pre CPB period, the observed correlation between intraoperative echocardiography and preoperative TTE was relatively low (r=0.360). This is possibly because of the fact that anesthetic induction produces changes in the loading conditions of the heart as well as a fall in SVR, thus influencing the measured RVOT gradients. This is so because the gradients across the RVOT are dependent on the RV pressures which reflects the systemic pressures which in turn is dependent on the systemic vascular resistance[71]. So also, intraoperative manipulation of the heart is notorious for precipitating a hypercyanotic spell. In the event of a hypercyanotic spell with marked cyanosis, the pulmonary blood flow falls markedly and the measured gradients across the RVOT may be spuriously low. Preoperative TTE is generally conducted under more controlled circumstances which helps estimate the true gradients.

Optimal alignment of the TEE probe to measure RVOT gradients is at times difficult with intraoperative TEE, since TEE is limited by the confines of the oesophagus. RVOT, being an anterior structure, would also limit the image quality and gradient measurement.

The RVOT gradient estimation by echocardiography is also influenced by the fact that TOF generally has multiple levels of RVOT obstruction. If

there is a significant degree of distal obstruction, the proximal gradient would tend to be underestimated. Doppler assessment of the RVOT gradient using intraoperative TEE would depend on the TEE view which is used to interrogate the RVOT since different views would profile different areas of the RVOT well. The branch PAs especially the right PA is best profiled using the midoesophageal ascending aortic short axis view, whereas none of the other TEE views profile the branch PAs with accuracy. Similarly, the infundibular region is amenable to optimal Doppler alignment in the transgastric RV outflow view. The upper oesophageal aortic arch short axis view, although difficult to image in many cases due to obscuring by the bronchial shadow, images the pulmonary valve well and provides for optimal Doppler alignment. Our study did not reveal any strong correlation between the different TEE views and the level of obstruction in the RVOT, but that could be because many patients had multiple levels of obstruction which could have influenced the gradient measurements.

Preoperative RVOT gradients are also affected by the presence of surgically created aortopulmonary shunts and the presence of significant systemic to pulmonary collaterals, the presence of which would underestimate the true RVOT gradients. The pulmonary vascular resistance also affects the estimation of RVOT gradients: the higher the PVR, the lower the measured gradients[72]. This is more of a problem in small infants whose PVR has not

fallen to normal levels after birth. Both these factors would affect the preoperative TTE exam as well as the intraoperative echocardiography equally.

Hutchison et al[73] compared the anatomic imaging and Doppler characteristics of the RVOT and PV using a biplane TEE probe in 22 patients to that of TTE, catheterization data and MRI and concluded that although TEE can delineate the anatomy of the RVOT and PV quite well, the gradients across the RVOT and PV could not be assessed by TEE with accuracy. Their findings could have been limited by the inherent limitations of a biplane TEE probe in obtaining optimal hemodynamic data. Present day multiplane TEE probes overcome these limitations to a great extent.

Post CPB RV and PA pressures.

The mean systolic RV pressure observed in our study was 51.77 mm Hg and the mean sPAP was 31.02mm Hg. Comparable observations were made by Singh et al[74] in their analysis involving TOF patients who underwent ICR. Another important finding is that the RVEDP measured a mean of 11.64 mm Hg in this study population, which is slightly higher than the normal range of 1-7 mm Hg, suggesting reduced compliance and diastolic dysfunction of the RV in these patients. PV incompetence, although not severe in any patient, could also have contributed to the rise in RVEDP. An elevated RVEDP as

defined by a value of 10 or above was noted in 65% of our study population. Another interesting observation in the present cohort of patients was that 14 out of the 61 patients (22.9%) included in this study had a sPAP ≥40 mm Hg, out of which one patient had PAP more than 2/3rd of the systemic pressure. High PA pressures have been reported only rarely after TOF[75,76]. RV/LV pressure ratios of 0.7-0.85 are common in the immediate postoperative phase after TOF correction. Since the obstruction between the RV and PA has been removed surgically, these elevated RV pressures would reflect as elevated PA pressures. The other possible reasons for elevated PA pressures in the post CPB period could be reduced LV compliance, presence of systemic-pulmonary collaterals and unrecognized branch/peripheral pulmonary stenosis. Richmond et al[77] studied the effects of preoperative ventricular shunting on post operative LV mechanics in 11 patients who underwent total correction of TOF. He observed that LV systolic as well as diastolic functions were impaired in the immediate post operative period in patients with TOF, which he attributed to reduced LV compliance caused due to the adynamic VSD patch, myocardial oedema and suboptimal myocardial protection. Ahmad et al[78] also shared similar observations of reduced LV compliance in patients with TOF who had a restrictive RV physiology, in the immediate postoperative period.

Correlation between intraoperative echocardiography and needle gradients in the post CPB period.

We observed a moderately strong positive correlation (Pearson correlation coefficient of 0.679) between the intraoperative echocardiography derived RVOT gradients and the needle gradients in the post CPB period.

Role of Dobutamine

Dobutamine has been implicated as a cause for erroneous estimation of the RVOT gradients perioperatively. Neema et al[79] postulate that the positive inotropy and chronotropy imparted by Dobutamine in conjunction with its vasodilatory properties tend to result in a smaller RV volume and hence, precipitate a dynamic RV obstruction.

The RV infundibulum is more susceptible to the action of inotropic agents than the inflow tract, perhaps as a mechanism to protect the pulmonary vasculature. Hypertrophied RVs in the face of increased inotropy and reduced preload have been found to exhibit dynamic RVOT obstruction to some extent. Since Dobutamine was the predominant inotropic agent used in our study population, being used in almost 98% of the patients, both as a sole agent and in conjunction with other agents, some amount of dynamic RVOT obstruction could also have played a role in our subset of patients. Indeed, the typical dagger shaped spectral Doppler profile was observed in many patients

in the post CPB period (Image 6), in the transgastric RV outflow view which profiles the infundibulum the best.

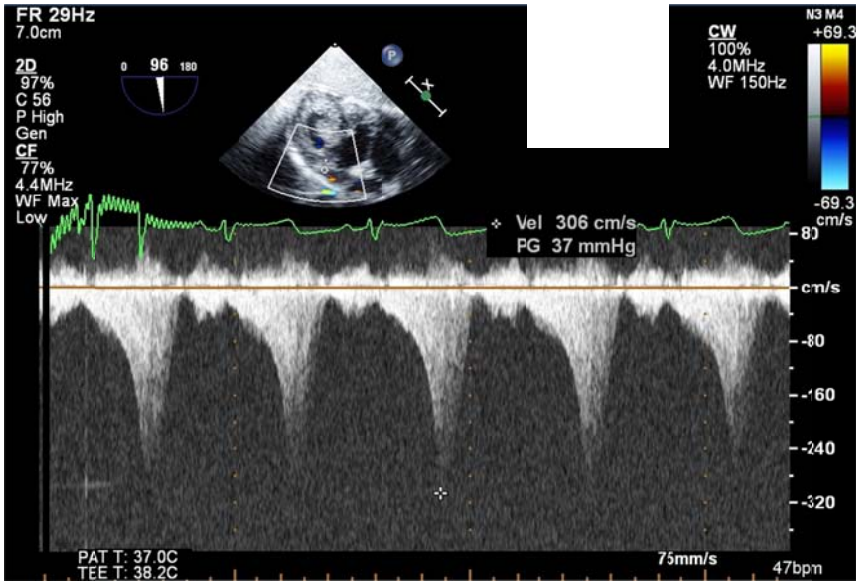

Image 6: Dynamic RVOT obstruction showing the typical late-peaking "dagger shaped" spectral Doppler profile.

In their study of restrictive RV physiology in children and adolescents post repair of TOF, Apitz et al[80] noted that the slope of the end diastolic pressure volume relationship (Eed) increased and the PR regurgitant fraction reduced considerably with a Dobutamine infusion (which was kept <10mcg/kg/mt), suggesting that dobutamine increases the stiffness of the RV. In the light of their findings, they advise caution in the use of Dobutamine in the perioperative period in those patients with a restrictive physiology, as diastolic relaxation can be worsened by catecholamines leading to a low cardiac output syndrome.

Branch PA stenosis

Significant branch PA stenosis as a cause of marked outflow tract obstruction was seen in 3 patients in the study. All 3 could be identified with the help of intraoperative TEE. The ascending aortic short axis view consistently showed high gradients in these 3 cases, whereas the other 2 views as well as epicardial echocardiography showed acceptable values. The needle gradients also did not show significance initially in these patients when the RV pressures were compared to the MPA pressures. However, when the measurements were repeated with the pressures in the branch PAs, the true gradient was revealed. Joyce et al[66] observed that branch PA stenosis, especially of the LPA is almost always missed with intraoperative TEE. This is so because the distal LPA and at times, the PA bifurcation are obscured by the bronchial air shadow such that echocardiographic delineation as well as Doppler interrogation of this structure becomes difficult. Colin et al[81] observed that in patients undergoing primary reparative surgeries for congenital heart lesions, the LPA could be visualized and diagnostic information obtained in as many as 71% of patients. However, the quality of images were graded as either good or excellent in only 42% of these patients. That LPA could be visualized on TEE in pediatric patients was reiterated by Tsai et al[82] who described a left paracarinal view for the same.

No intervention was undertaken in these patients since the cause of small branch PA size was attributed to a chronic low flow state and was postulated that the gradients would reduce when the PAs grow in size and get adapted to the increased blood flow. Growth of PA post total correction for TOF has been documented by Sunderland et al[83] in their analysis of post-operative RV hemodynamics using cardiac catheterization wherein they noted an increase of around 50% in PA size as measured by the PA cross sectional area post-operatively. This growth was seen in patients who underwent a transannular patch as well as in those who underwent a valve sparing technique. However, the surgical literature has many case series and reports citing residual branch PA stenosis as a significant post-operative problem requiring intervention at a later date[84,85].

Peak to peak vs. peak instantaneous gradients

In left sided obstructive lesions like AS and HCM, studies have attempted to assess the comparability of peak to peak gradient as is measured in the catheterization lab or using a needle-saline-transducer system perioperatively, and the peak instantaneous gradient which is what is measured echocardiographically. In the first of such studies involving HCM, which has an anatomical substrate similar to that of TOF, Geske et al[86] observed that peak to peak gradients and peak instantaneous gradients correlate well (R^2= 0.98). These authors also observed that peak to peak and

peak instantaneous gradients do not correlate in a similar fashion when a fixed obstruction like aortic stenosis is being assessed. Such comparative studies have not been conducted on right sided obstructive lesions. TOF has components similar to both HCM as well as AS since most of the patients with TOF have multiple levels of obstruction and exhibit fixed as well as dynamic components of RVOTO. Even though conventionally, the peak to peak gradients as measured perioperatively by the surgeon as well as the peak Doppler gradient as measured using echocardiography have been used to quantify RVOTO, the present study suggests that the peak to peak gradients may actually underestimate the true RVOT gradients in many patients. In our study, echo gradients were higher than the needle gradients in 78.68% of the patients.

The concept of pressure recovery as a factor influencing the observed gradients in left sided obstructive lesions especially AS has been documented in literature. In one such study, Baumgartner et al[87] observed that significant overestimation of gradients by Doppler occurs in AS when the aorta was of a small caliber (<3 cm). Even though observations made on the left sided cardiac structures and lesions cannot be extrapolated as such to their right sided counterparts; it is safe to presume that there might be a role for pressure recovery especially when the main and branch PAs are quite small, thus overestimating the true gradients.

Difficulties in image acquisition could be a major obstacle in pediatric patients with congenital heart defects. Abnormalities of situs, anomalous drainage of systemic as well as pulmonary venous systems, variations in the great arterial positions and ventricular morphology make perioperative echocardiography all the more challenging in this patient population. Optimal Doppler alignment for measurement of gradients might not be possible in all the patients in all the TEE views. In the present study, we could not obtain RVOT gradients in many patients using all the TEE views. However, what we did note was that when the best TEE gradient was used for comparison, a significant degree of positive correlation could be obtained, which was higher than that observed with epicardial echocardiography. This emphasizes the importance of performing a comprehensive TEE exam in all the patients whenever possible since important findings may be missed otherwise.

Epicardial echocardiography

The utility of epicardial echocardiography as a perioperative tool to determine residual lesions after repair of congenital heart lesions has been well documented[88]. Epicardial echocardiography provides excellent image quality, the probe being placed directly on the surface of the heart. In the present study also, the images of RVOT obtained by epicardial echocardiography were exceptional. The Doppler signals obtained using epicardial echocardiography also were well defined and optimal beam alignment for gradient measurement

was possible in 85.42% of patients in the pre CPB period and in 96.72% of patients in the post CPB period.

The main disadvantage associated with epicardial echocardiography was the need to interrupt the surgical procedure to obtain the images; thus obviating the possibility of it being a continuous monitor. Other disadvantages noted were incidences of hypotension and generation of ventricular arrhythmias because of placement of the probe directly over the heart. In a small subset of patients, epicardial echocardiography could not align the Doppler beam to the RVOT so as to measure the gradients.

Use of transannular patch

A review of the cardiac surgical literature reveals a trend towards adoption of a pulmonary annulus sparing technique, of late[89]. This is so because loss of integrity of the pulmonary annulus is the leading cause of development of pulmonary incompetence, which in turn is the main cause of late morbidity after total correction for TOF. Pulmonary valve sparing is done at the cost of accepting some amount of residual RVOT obstruction. According to Kaushal et al[3], one of the most important uses of intraoperative echocardiography in patients undergoing ICR for TOF is to identify whether the residual RVOT obstruction is of a fixed or dynamic nature; in their study,

they found that dynamic RVOT obstruction almost always abates over time and does not need to be addressed surgically.

A correlation has been observed between the appearance of anterograde diastolic flow in the pulmonary artery, suggestive of restrictive RV diastology, and the use of a transannular patch[90]. In the present study, the use of transannular patch was relatively high at 44.3%. Comparative surgical literature review reveals that the frequency of use of transannular patch varies between 31 to 68%[91,92].

Attempts to minimize the grade of pulmonary regurgitation is important in the surgical technique for TOF. At our Institute, we routinely fashion a monocusp valve out of PTFE membrane that prevents severe grades of PR in the immediate postoperative period, whenever the pulmonary annulus integrity is breached. Although long term results using a monocusp valve have not been encouraging[93], it definitely helps to tide over the immediate postoperative period without the added burden of volume overloading of the RV. None of the patients in the study had severe grades of PR.

This study provides good evidence that intraoperative TEE is a good monitoring tool in the armamentarium of the perioperative physician caring for the surgical patient with TOF. Since the gradients in the RVOT as measured by TEE were found to correlate well with the observed needle

gradients, we can safely conclude that TEE measured RVOT gradients be used routinely in lieu of the more invasive needle-saline-transducer systems. In addition to providing important insights to patient management in terms of fluid management and inotropic support and diagnosis of other residual lesions, TEE has a major role in predicting the residual RVOT gradients, its nature: whether fixed or dynamic, and the level in the RVOT where the obstruction predominantly is, and thus helps to decide whether a re-intervention is required in an individual patient or not.

SUMMARY

This prospective, observational study included 61 patients scheduled for intracardiac repair (ICR) for Tetralogy of Fallot (TOF) and aimed to assess the accuracy of intraoperative echocardiography: both transoesophageal echocardiography (TEE) and epicardial echocardiography in measuring the pressure gradients across the right ventricular outflow tract (RVOT). The RVOT gradients were measured using the midoesophageal ascending aortic short axis view, upper oesophageal aortic arch short axis view and the transgastric right ventricular outflow tract views. The gradients were measured both in the preCPB period and in the post CPB periods. In the pre CPB period, the RVOT gradients measured intraoperatively were compared to the preoperatively measured TTE gradients. In the post CPB period, the echocardiographic gradients were compared to the intraoperatively measured RVOT gradients measured with the help of a needle-saline-transducer system.

Appropriate statistical analysis of the results revealed the following significant findings:

- TEE can provide reliable estimates of RVOT gradients in patients with TOF, especially in the post CPB period.

- In the pre CPB period, the intraoperatively measured echocardiography gradients showed a relatively weak correlation (Pearson's correlation coefficient of 0.360) when compared to the preoperative TTE values.
- In the post CPB period, relatively strong correlation was observed between the intraoperative echocardiography gradients and the needle gradients, the Pearson's correlation coefficient being 0.679.

Accuracy of echocardiographic views in identifying RVOTO:

- In the pre CPB period, the ascending aortic short axis view was the most reproducible view, being able to measure a gradient in 95.08% of patients, although its reliability in measuring the true gradient was low (Pearson's correlation coefficient being 0.192) in comparison to the preoperative TTE gradients.
- Epicardial echocardiography was the modality which showed the maximum correlation in the pre CPB period when all echocardiographic views were compared individually to the preoperative TTE gradients, the correlation coefficient of this modality being 0.459.
- All the individual TEE views as well as epicardial echocardiography had clinically and statistically significant levels of correlation with the needle gradient; the correlation of epicardial echo being the strongest

among the lot (R=0.643), closely followed by that of the transgastric RV outflow view (R=0.627).

- When the correlation coefficients of TEE (the highest value among the 3 views) was compared with the needle gradients, a slightly stronger correlation than that of epicardial echocardiography was observed (R=0.663).
- **Level of obstruction in the RVOT**: It was observed that the infundibulum could be profiled best in the transgastric right ventricular outflow tract view; the MPA, RPA and occasionally the LPA aligned best in the ascending aortic short axis view and the pulmonary valve seen and aligned best in the upper oesophageal aortic arch short axis view. This finding underscores the importance of performing a comprehensive TEE exam in all cases of TOF wherein multiple levels of RVOT obstruction is possible.

Other significant findings:

- There were 3 patients in this series in whom significant branch PA stenosis was present, the presence of which could be diagnosed only by the transoesophageal midoesophageal ascending aortic short axis view.
- Severe grades of PR was not present in any patient.

CONCLUSION

In conclusion, intraoperative echocardiography provides reliable estimates of the RVOT gradients in patients with TOF undergoing ICR in the post CPB period. Intraoperative echocardiography, especially TEE can be recommended as a less invasive modality to measure the RVOT gradients with accuracy in lieu of the more invasive needle gradient measurements. Intraoperative echocardiography was able to make a significant impact in the post CPB period in 7 patients, 4 of whom required a reintervention. None of the patients in the present study developed any complication attributable to the use of TEE probe or epicardial echocardiography.

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Technical Advisory Committee (Clinical Studies)

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

TAC Registration No: SCT-/S/2013/176 **Date:18.07.2013**

Project title: Estimation of right ventricle to pulmonary artery pressure gradient in patients subjected to intracardiac repair for Tetralogy of Fallot- a comparison of echocardiographic methods Vs direct pressure measurement.

Principal Investigator:
Name: Dr. Sujatha. M Degree: MBBS, MD(Anaesthesiology) Address: DM Cardiothoracic and Vascular Anaesthesia Resident, SCTIMST
Co-Principal Investigator(s)
(1)NAME: Dr. Suneel P. R, Degree: MBBS, MD (Anesthesiology), PDCC Address: Additional professor, Department of Anaesthesiology, Cardiothoracic and Vascular Division, SCTIMST
(2)Name : Dr. Unnikrishnan K.P Degree: MBBS, MD (Anesthesiology), Dip NBE Address: Additional professor, Department of Anaesthesiology, Cardiothoracic and Vascular Division, SCTIMST
(3)Name: Dr. Thomas Mathew Degree: MBBS, MS, MCh Address: Assistant Professor, Department of CVTS, SCTIMST
(4) Name: Dr. Venkateshwaran Degree: MBBS, MD,DM Address: Assistant Professor, Department of Cardiology, SCTIMST

Members who participated in the TAC meeting on 3/07/2013

Dr. J.M. Tharakan (Chairman)
Dr. Bejoy Thomas
Dr. Biju Soman
Dr. Lissy K Krishnan
Dr. Rathore Chaturbhuj Gopalsingh
Dr. K. Shivakumar (Member Secretary)

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. Please 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
तिरुवनन्तपुरम - 695 011, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY
THIRUVANANTHAPURAM - 695 011, INDIA
(An Institute of National importance under Govt. of India)

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

SCT / IEC- 494/ AUGUST-2013

30-08-2013

Dr. Sujatha.M
Resident
DM Cardiothoracic and Vascular Anaesthesia
SCTIMST

Dr. Sujatha.M

The Institutional Ethics Committee reviewed and discussed your application to conduct the clinical trial entitled "ESTIMATION OF RIGHT VENTRICLE TO PULMONARY ARTERY GRADIENT IN PATIENTS SUBJECTED TO INTRACARDIAC REPAIR FOR TETRALOGY OF FALLOT-A COMPARISON OF ECHOCARDIOGRAPHIC V/S DIRECT PRESSURE MEASUREMENT" IEC/494 on 17th August, 2013.

The following documents were reviewed:

1. *Covering letter dated 22.07.2013*
2. *Full proposal, with protocols/instruments for data collection and budget in detail.*
3. *Institutional Ethics Committee – Application for ethics review*
4. *Consent form – English & Malayalam*
5. *Declaration form*
6. *Study proposal & addendum*
7. *TAC Form*
8. *Observation Chart*
9. *Curriculum vitae of investigators*
10. *TAC approval letter*
11. Reply to queries raised by TAC

तार : चित्रमेट | फोन | फाक्स | ई-मेइल
Grams : Chitramet | Phone : 2443152 | Fax : (91)471-2446433 2550728 | E-mail : sct. @sctimst.ker.nic.in

CONSENT FORM

Title of the study:

Estimation of right ventricle to pulmonary artery pressure gradient in patients subjected to intracardiac repair for Tetralogy of Fallot- a comparison of echocardiographic methods Vs direct pressure measurement.

Study number:

You are being requested to enroll your child in a study to compare pressure gradients inside the heart using 2 different techniques-echocardiography and direct measurement of pressures using a needle. We hope to include about 60 people from this hospital in this study.

What is intracardiac repair for tetralogy of Fallot?

Your child is going to have a surgery on his/her heart to repair the congenital heart problem so that his/her symptoms abate.

What are transoesophageal echocardiography and epicardial echocardiography?

Transoesophageal echocardiography is a monitoring device used to image the heart using a tube that is inserted into the mouth of the patient after the patient is anaesthetized. Epicardial echocardiography also images the heart in a similar fashion, but in this, the probe is placed directly on the heart . This helps in assessing the function of the heart during the time of the surgery, identifying any other heart defects if present and also in assessing the adequacy of the surgical repair.

What is a needle-saline –transducer system?

A needle-saline –transducer system is a monitoring tool used to measure pressures within various chambers of the heart as well as blood vessels. The pressure within the required chamber is measured with the help of a needle and a computer and the pressure is recorded on a monitor. In intracardiac repair for Tetralogy of Fallot, reduction of the pressure difference between the right sided cardiac chamber and the blood vessel arising from it is an important determinant of the outcome of the surgery. Therefore, this pressure difference is measured routinely as part of the surgery.

Why are we doing the study?

One of the complications of intracardiac repair is persistence of the primary problem to varying degrees due to inadequate surgical repair. This, if significant and if not identified immediately, warrants a second surgery at a later date. Therefore, recognition of this problem during the time of surgery is very important.

We do echocardiography during the time of surgery hoping to identify this, if present. So also, direct measurement of the pressures are made by inserting a needle directly into the heart. Both these procedures are part of our standard anaesthetic care at SCTIMST . what we propose to do in our study is to obtain various views of echocardiography and compare it with the directly measured pressures so that we can compare the accuracy of echo measurements. If echo is found to be as good as directly measured pressures, then direct measurement of pressures could be avoided in the future.

Is transoesophageal echocardiography , epicardial echocardiography and direct pressure measurement usinga needle safe to be used ?

All three modalities are routinely used as part of the anaesthetic care of most of the patients undergoing cardiac surgery for repair of Tetralogy of Fallot. All of them have a proven safety record and are recommended monitoring tools during cardiac surgery.

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 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 study?

No.

Will your personal details be kept confidential?

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

If you have any further questions, please ask

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DECLARATION

I , _____(father/mother/guardian) of , **Participant's name: Date of Birth / Age (in years)** _____ (Please tick boxes) •
Declare that I have read the above information provided to me regarding the study:

Estimation of right ventricle to pulmonary artery pressure gradient in patients subjected to intracardiac repair for Tetralogy of Fallot- a comparison of echocardiographic methods Vs direct pressure measurement and have clarified any doubts that I had. [ ]

• I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my ward's usual treatment or my legal rights [ ]

• I understand that the study staff and institutional ethics committee members will not need my permission to look at my ward's health records even if I withdraw my ward from participating in the trial. I agree to this access [ ]

• I understand that my ward's identity will not be revealed in any information released to third parties or published [ ]

• I voluntarily agree to take part in this study [ ]

• I received a copy of this signed consent form [ ]

Name:
Signature:
Date:

Name of witness:
Relation to participant:

Date:

(Person Obtaining Consent)

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

_____ _____

Name and Signature of Person Obtaining Consent

Estimation of right ventricle to pulmonary artery pressure gradient in patients subjected to intracardiac repair for Tetralogy of Fallot- a comparison of echocardiographic methods Vs direct pressure measurement.

Name of the patient: Weight (kg):

Age: Height (cm):

Sex: Body surface area

(kg/ cm2):

Hospital number:

Diagnosis and surgery:

Date of surgery:

Preop cardiac drugs

Preoperative RV-PA gradient

CPB time

Cross clamp time

Lowest systemic temperature

Cardioplegia: Type:

Doses:

Transannular patch:

Inotropic support:

Pulmonary regurgitation grade:

Postoperative TTE grade:

Data collection

Parameters	Pre CPB	Post CPB observations		
		1	2	3
HR				
Rhythm				
SBP				
DBP				
MAP				
CVP				
FiO_2				
$ETCO_2$				
Saturation				
Needle pressures				
sPAP				
dPAP				
mPAP				
Echocardiographic data				
AA SAX				
Arch SAX				
TG RV outflow				
Epicardial echo				

Signature of the investigator:

Master chart

sl no	preop gr	preAASAXpre arch		pre TG RV	pre epicar	needle gr	post AASAX	post arch	post TGRV	post epi
1	70	48		68		38	32		16	36
2	45	10	42	45	41	4	23	17	10	10
3	65	66	52	50	42	48	40	34	48	50
4	90	50	90	104		8	14	38	14	24
5	105	23	58	48	98	0	6	4	5	5
6	32	29	14	9	6	13	10	13	9	14
7	72	20	28	59	69	11		26		36
8	60	39	26		20	18	26	24		25
9	42	31	37	17	30	2	14	14	5	13
10	84	105		46	64	75	94	15	10	14
11	70		32	41	66	18	13	17	25	26
12	75	59		72	84	43	71		59	71
13	70	68		55	66	10	16	14	18	18
14	90	16	18		42	9	20	14	12	17
15	64	47	57	44	50	8	94			50
16	70	61			51	38	32		30	36
17	62	12			54	2	8	12	8	8
18	70	67	50	22	50	11	24	18	18	19
19	40	53	58	62	57	17	19	16	14	21
20	57	57		72	62	1	12		17	17
21	60	26		39	59	25	27	15		13
22	88	60	77	42	79	39	42	30	23	28
23	60	20	55	67	45	41	13		20	
24	80	82	81	50	48	62	50	71	55	76
25						11	20	25	15	15
26	90	13	10	80		16	18	21	13	19
27	92	78	62	67	80	20	27	31	27	40
28	34	26	25	33	30	8	9	13	8	3
29	52		64		43	28	36	52	33	57
30	66	72		50	51	14	19	12	15	11
31	65	30	12	52		18	30	38	40	27
32	40	24		43	42	24	84		56	58
33	16	69	87	81	89	49	50	71	54	40
34	70	80	79	71	79	18	26	32	28	50
35	80	51	49	21	58	9	16	26		20
36	100	79	105	76	105	20	26	34	26	35
37	37	46	36	67	64	12	11	9	11	13
38	60	45	45	86	94	11	15	7	12	18
39	50	19		40	64	25	20		18	15
40	80	73	57	90	78	17	28	22	29	19
41	80	46	46		56	8	19	10	6	14
42	32	56	73		8	23	7	9	14	

sl no	preop gr	preAASAXpre arch		pre TG RV	pre epicar	needle gr	post AASAX	post arch	post TGRV	post epi
43	64	73	97	77	85	29	17	38	27	37
44	64	110	115			4	28	26	6	7
45	90	76	48	70	75	6	6	6	5	6
46	83	46		37	43	27	30		18	36
47	70	14	40	78	45	8	10	6	6	7
48	70	43			50	48	35	31	16	46
49	62	98	78	75	74	21	26	24	28	17
50	60	5				51	20		50	50
51	55	43	59			14	15	4	4	4
52	70	68	63	37	60	14	26		19	20
53	100	58	71	38	60	24	22	48	19	36
54	80	45		31	38	12	11		15	18
55	50	38	48	52	32	9	17	24	12	19
56	100	37	40	41	75	18	18	20	21	28
57	71	60	82	42	75	40	40	43	34	42
58	64	87	94	55	58	13	13	17	10	12
59	70	60	60		41	40	42	31		47
60	85	56	66			12	14	13	12	12
61	60	20	56	20	37	5	8	7	6	7