SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY THIRUVANANTHAPURAM

DEPARTMENT OF CARDIOLOGY

COMPARISON OF OXIMETRY WITH CARDIAC MAGNETIC RESONANCE IMAGING FOR ESTIMATION OF FLOW IN BIDIRECTIONAL GLENN SHUNT

A THESIS SUBMITTED FOR THE DEGREE OF

DM CARDIOLGY

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JANUARY 2021

DECLARATION

I, Dr. Gayathri Bhuvaneswaran Kartha, hereby declare that the project in this book, titled "Comparison of oximetry with Cardiac Magnetic resonance imaging for estimation of flow in bidirectional Glenn shunt" was undertaken by me under the supervision of the faculty, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

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Date: 30/1/2021 — DM Trainee

CERTIFICATE

I hereby certify that the work in this dissertation titled "Comparison of oximetry with Cardiac Magnetic resonance imaging for estimation of flow in bidirectional Glenn shunt" is a certified record of original research work undertaken by Dr. Gayathri Bhuvaneswaran Kartha in the Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology in partial fulfilment of requirement for the purpose of award of D.M. Cardiology degree.

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TITLE

"COMPARISON OF OXIMETRY WITH CARDIAC MAGNETIC RESONANCE IMAGING FOR ESTIMATION OF FLOW IN BIDIRECTIONAL GLENN SHUNT"

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ACKNOWLEDGEMENTS

This dissertation would never have materialized into its present shape if not for the kind help and enduring support of a lot many people. So, it is with great pleasure that I convey my heartfelt gratitude.

First and foremost, I express my immense gratitude to my teacher and guide, Dr. Ajit Kumar VK for his guidance and constant encouragement throughout the study period. I thank him for having confidence in me and guiding me through each and every step in this endeavor. His great clinical acumen, constructive criticism and desire for perfection have always inspired me to strive harder in my pursuit.

I would like to express my appreciation to my co guides, Dr. Abhilash S. P. and Dr Anoop A., for their valuable and constructive suggestions during the planning and development of this research work.

I am extremely indebted to my teacher Dr. Krishnamoorthy, Professor and head, Department of Cardiology, SCTIMST for his guidance and constant motivation.

It is with immense gratitude that I acknowledge the support and help offered by Dr Sivasankaran S, Dr Deepa S Kumar and Dr Arun Gopalakrishnan. Their valuable inputs are greatly appreciated.

I would also like to sincerely thank all the faculty members of Department of Cardiology, SCTIMST for their guidance.

It is with immense gratitude that I acknowledge the support and help offered by my seniors and juniors.

I am extremely thankful to the technicians and my colleagues in Radiology for the help offered at all stages of this endeavor.

Also, I thank Dr Harikrishnan K N, for his timely assistance and valuable suggestions throughout the study.

No words can express my gratitude to my family. My deepest gratitude goes to my father, Dr Bhuvaneswaran K P Panicker to whom I owe all the dreams I shall ever realize. The unstinting support and constant words of encouragement of my mother, Dr Vinaya G Kartha has been the pillar of my strength and my guiding light when the going was tough.

My husband Dr. Arun Govind, for his tireless encouragement and for being a source of constant support and strength which helped me tide over all ups and downs during my journey towards the completion of my dissertation.

I shall be failing in my duty, if I do not acknowledge the contributions of the patients and their parents involved in this study, as without their co-operation this dissertation would never have seen the light of the day.

I now, with a high sense of gratitude, offer my sincere thanks to the Almighty, the Creator and the Preserver for blessing me with goodness all around.

Dr Gayathri Bhuvaneswaran Kartha

ABBREVIATIONS

Qp/PBF	Pulmonary blood flow
Qs/SBF	Systemic blood flow
BDGS	Bidirectional Glenn shunt
AVSD	Atrio Ventricular septal defect
DORV	double-outlet right ventricle
SV	single ventricle
SCPC	superior cavo-pulmonary connection
PAVM	pulmonary arteriovenous malformations
AVVR	atrioventricular valve regurgitation
APCA/APC	aortopulmonary collaterals
SAT	saturation
APBF	Antegrade pulmonary blood flow
IVC	Inferior Vena Cava
LSVC	Left superior vena cava
Qp/Qs	pulmonary blood flow to systemic blood flow ratio
PV	Pulmonary Vein
SVC	superior vena cava
TCPC	Total Cavo Pulmonary Anastomosis
PC MRI/CMR	Phase-contrast cardiac magnetic resonance imaging
PA	Pulmonary artery
PVRI	indexed pulmonary vascular resistance
VO2	Oxygen consumption
MvO2	Mixed venous oxygen saturation
SaO2	Systemic arterial oxygen saturation
LVed	Left ventricular end diastolic pressure
TPG	Transpulmonary gradient

SYNOPSIS

Introduction: Fontan pathway is the destination therapy in single ventricle palliation. Multiple anatomic and hemodynamic parameters are assessed to ensure optimal candidacy for Fontan surgery. Estimation of PVRI & Qp/Qs is of vital importance. Despite its limitations due to the assumptions involved, cardiac catheterization has classically been the pre-operative investigation of choice in BDGS patients. Recently, cardiac MRI and newer techniques like phase-contrast CMR have shown good accuracy in simple shunt assessment. There is a scarcity of literature comparing the two modalities in this subset of patients.

Aim: We aimed to compare cardiac catheterisation-(Fick-principle) derived estimates of pulmonary and systemic blood flows and Qp/Qs with measurements obtained using Cardiac MRI.

Methods: We prospectively analysed the demographic, clinical, hemodynamic, and CMRI data from 30 patients with bidirectional Glenn shunt who had undergone both cardiac MRI & cardiac catheterisation. Qp, Qs, Qp/Qs, and PVRI derived from both the modalities were compared and assessed for correlation. The baseline aortic saturation was 81 (±5) % with a mean SVC saturation of 64 (± 8)%. The mean BDG pressure, LV end diastolic pressure & transpulmonary gradient were 11.93 (± 2.77) mmHg, 9.9 (± 2.54) mmHg and 3.77(± 1.74) mmHg respectively.

Results: The mean (± SD) age of the study population was 108.83 (± 26.72) months with 43.33% of the population comprising of Tricuspid atresia with Ventricular septal defect with pulmonary stenosis. CMR derived Qp was significantly higher than catheterization derived values, especially when CMR Qp was taken as total PV flows (2339.12 ± 758.25 vs 1890.09±599.10 ml/min). Whereas catheterisation derived Qs proved to be an overestimate when compared to CMR derived Qs, irrespective of the formula used (4192.21 ± 2198.92 vs 2801.65 ± 903.06 ml/min). Catheterisation derived Qp/Qs by Fick-principle based formulae were comparable with each other (mean Qp/Qs of 0.47 ± 0.13 vs 0.48 ± 0.17 vs 0.63 ± 0.18 vs 0.54 ± 0.28). The CMR derived mean Qp/Qs was 0.88 ± 0.30 & significantly higher than corresponding catheterisation derived values. Patients with CMRI derived Qp/Qs ≥ 0.7 had significantly higher systemic to pulmonary artery collateral flow when compared with those with Qp/Qs <0.7, but did not differ significantly in terms of other parameters.

Catheterization derived PVRI was numerically higher than CMR derived values (1.88 ± 1.34 vs 1.44 ± 0.90 WUm^2). There was no correlation between Qp, Qs, Qp/Qs, and PVRI by cardiac catheterisation with that derived from PC MRI.

Conclusions: Qp & Qp/Qs from PC MRI is consistently higher than Qp & Qp/Qs by cardiac catheterization while the opposite is true of Qs & PVRI. There was no correlation between Qp, Qs, Qp/Qs, and PVRI by cardiac catheterisation with that derived from PC MRI. Patients with CMRI derived Qp/Qs ≥ 0.7 had significantly higher systemic to pulmonary artery collateral flow when compared with those with Qp/Qs <0.7, but did not differ significantly in terms of other parameters. In our study aortic saturation reflects Qp/Qs (as derived by catheterisation) and not SVC or collateral flow.

What is already known? Calculation of systemic & pulmonary flows and PVRI in BDGS population through the Fick principle is challenging and has a margin of error as it involves multiple assumptions. Different authors have suggested different formulae to calculate flows & Qp/Qs in the BDGS circuit. CMR derived Qp is an estimate of total pulmonary blood flow while catheterisation derived Qp reflects effective pulmonary blood.

This study adds: Previously proposed formulae for Qp/Qs are comparable numerically. Though superior and inferior caval circulations are separate in BDGS circulation, assuming a separate oxygen consumption for the upper body circulation to estimate Qp & Qp/Qs may not be prudent or relevant. Data from a combined catheterization- CMR may be most informative of the complex physiology in BDGS patients.

INTRODUCTION

The functional single ventricle is a condition where the two circulations, pulmonary and systemic, are connected in parallel with the circulation being driven by the single ventricle pump & relative impedance offered by the two circuits. Children with this severe subtype of congenital heart defect, are subjected to staged palliative procedures to increase longevity & improve their life quality. Essentially this results in an intermediate stage, the bidirectional Glenn shunt (BDGS), wherein the superior caval vein is anastomosed to the pulmonary artery, resulting in a passive flow of systemic venous return through the pulmonary circulation and a functional single ventricle supporting the systemic circulation (1). This is followed up with the destination procedure, Fontan palliative operation, where the inferior caval vein is diverted to the pulmonary arteries, thereby effectively separating the pulmonary & systemic circulations. The Fontan heart supports a series circulation; however, unlike the normal cardiovascular system, the pulmonary circulation lacks a muscular pump to propel blood into the pulmonary arteries. Thereby making this circulation fragile with an inherent potential to fail. (2) Hence, careful selection of patients who might benefit most from Fontan completion is crucial. Anatomic & hemodynamic data is obtained from cardiac catheterisation & imaging studies to aid the selection of optimal Fontan candidates (3).

Cardiac catheterization, an invasive procedure, is routinely done in BDGS patients during pre-Fontan assessment & in the evaluation of hypoxemia. However, BDGS physiology poses inherent challenges in applying the Fick principle. Systemic-to-pulmonary arterial collaterals are an additional source of pulmonary blood flow (PBF) which is not accounted for in conventional oximetry calculations. Furthermore, there is no true mixed venous blood available for sampling, as superior & inferior vena caval circuits are separate. (3)

According to a large multicentre study, the reported risk of adverse outcomes of catheterization in this group is 11% (4). Hence, even though routinely used, it might not be the most accurate or safest tool available.

CMR gives an accurate anatomic assessment of cardiac anatomy. Previous studies have demonstrated that developments in phase-contrast cardiac MRI (PC-CMR) techniques have clinically acceptable accuracy for simple flow assessment. (5)

Hence, we planned to study the agreement between cardiac catheterisation-(Fick-principle) derived estimates of pulmonary and systemic blood flows with measurements obtained using PC-CMR in this subset of patients. If a good correlation is found between cardiac catheterisation and cardiac MRI flow assessment, then this may lead to CMR being the initial modality of choice for evaluation of BDG patients, with the necessity of invasive cardiac catheterisation being limited to obtaining fewer hemodynamic measurements. Thereby invasive cardiac catheterisation may become abbreviated to a limited study.

REVIEW OF LITERATURE

Background

Univentricular hearts are characterised by a functional single ventricle, with the second ventricle being a rudimentary chamber. There is a mixing of blood between the pulmonary and systemic circulations. This is manifested postnatally as cyanosis with the severity dependent on the relative proportions of pulmonary & systemic blood flow. Babies with concomitant systemic outflow tract obstruction may present with lethargy, rapid breathing & acidosis because of reduced cardiac output to the systemic circulation. The morphology of the main ventricle may be left (more common) or right ventricular or, in rare cases, indeterminate. The classical examples include hypoplastic left heart syndrome, double-inlet left ventricle, and tricuspid atresia. Univentricular hearts also include several congenital heart defects where a biventricular repair is not possible. The examples include unbalanced AtrioVentricular septal defect (AVSD), double-outlet right ventricle (DORV) with a non-routable Ventricular septal defect (VSD), AV valve straddling, or a very large or multiple VSDs amounting to a single ventricle (SV). These defects together come under the group of "functional univentricular heart", as their management parallels that of SV(6)(7). The prevalence of single ventricle is 2.3/10,000 live births, corresponding to 2.8% of all congenital heart defects. (8) (9)

Staged palliation

Univentricular palliation ultimately aims to unload the volume and pressure overloaded functional single ventricle and restore pumping of blood fully oxygenated blood to the systemic circulation. In the process, the pulmonary circulation loses its muscular pump and becomes a passive circuit where the flow is dependent primarily on the transpulmonary gradient and ventricular suction effect. This unloading of the single ventricle is, hence done sequentially, with the superior cavo-pulmonary connection (SCPC) done after the fall in pulmonary vascular resistance (PVR) to acceptable levels. (10)

Bidirectional Glenn Shunt (BDGS)

In the late 1950, Dr. Glenn for the first time envisaged the idea of a cavopulmonary shunt, wherein the SVC was anastomosed to the transected right pulmonary artery (RPA) while working on the concept of partial right heart exclusion expounded by Carlon et al.(11). However, the classic Glenn shunt as described above led to the formation of pulmonary arteriovenous malformations (PAVMs) in the lung ipsilateral to the Glenn shunt and difficulty in subsequent complete surgical repair (12). Therefore this was largely replaced by the bidirectional Glenn shunt, in which the superior vena caval blood is shunted to bilateral pulmonary arteries. This resulted in an improvement in the systemic arterial saturation by increasing the effective pulmonary blood flow and in the unloading of the single ventricle with subsequent favorable alteration in the ventricular geometry (12–15). Intuitively, the success of BDGS depended on the pulmonary impedance, which must be suitably low to allow forward flow from the superior caval vein. Presently mean pulmonary artery (PA) pressures of 15mmHg or below are considered suitable for BDGS. This is usually achieved around 3 months after the regression of neonatal pulmonary resistance. In the hypoplastic left heart variant of single ventricle, usually an early BDGS at 4-6 weeks after birth is considered. (16)

Additional procedures such as atrial septectomy, repair of branch pulmonary artery stenosis, atrioventricular valve regurgitation (AVVR), and Total anomalous pulmonary venous connection (TAPVC) repair may have to be done at the time of bidirectional Glenn procedure. (7).

Fontan

The Fontan strategy refers to the landmark surgery for tricuspid atresia by Fontan and Baudet (17). Fontan strategy involves directing inferior vena caval blood to the PA thereby achieving separation of the systemic and pulmonary circulation with subsequent reduction in ventricular volumes (18). This comes at the expense of the lack of a muscular pump propelling blood into the pulmonary arteries. After TCPC, patients have a pre-load deprived ventricle with nearly non-pulsatile PA with raised central venous pressures. These abnormalities characterise the Fontan circulation(19). Cardiac output in this circulation critically depends on the PVR and

SV function. Hence, careful selection of patients who might benefit most from Fontan completion is crucial. This is done through a series of anatomic & hemodynamic measurements obtained from cardiac catheterisation & imaging studies. The surgical caval–pulmonary connections, the PAs, the pulmonary capillary network, and the pulmonary veins with their atrial connections should be assessed. Any degree of pulmonary hypoplasia, stenosis, distortion, pulmonary vascular disease, collateral flow may lead to failure of this circulation. (2). Before the destination palliation of Fontan shunt, few patients require interim procedures like coiling of large aortopulmonary collaterals(APCAs) and PAVMs to reduce the pulmonary pressures and systemic desaturation respectively.

Timing of Fontan

In normal neonates, SVC flow accounts for 49% of CO; it peaks to a maximum of 55% at the age of 2.5 years and thereafter its contribution diminishes to 35% by the age of 6 years (20). In those patients with BDGS serving as the sole pulmonary blood supply, the saturations are initially 85% or above as the SVC return constitutes around 50-60% of total systemic venous return. As the child starts standing & walking, the relative proportion of systemic venous return from the SVC decreases to around 40%, and resting saturations fall with age (21). Salim et al.(22) subjected 29 BDGS patients to cardiac catheterisation (mean ± SD age of subjects- 2.95 ± 1.65 years). They concluded that in children under 3 years, the contribution of SVC to total venous return is >50%. Eyskens et al. (23) carried out CMR & cardiac catheterization study in 18 BDGS patients to assess the contribution of superior caval venous flow to total cardiac output. No significant difference could be found in the ratios of superior-to-inferior caval venous flow, nor of superior caval venous-to-systemic flow could be found across ages of 8 to 48 months. This suggests that the ratio does not significantly decrease with age till 4 years of age, as it does in otherwise healthy children. They proposed that following BDGS, there is a redistribution of blood flows, with a proportionally higher flow in the upper body compared to the lower body. A similar distribution with higher SVC flows has been observed by Houlind et al. (24) in his study of 7 TCPC patients with a mean age 9 (4–18) years.

However Whitehead et al. (25) concluded that IVC contribution to total flow increases as a function of body surface area(BSA) & age and could be defined by the following formula:

$y = 0.2 \ln(x) + 0.57$ (Pearson $r = 0.72$, $P < 0.05$)

(where y= IVC fraction and x=BSA)

This has been tabulated below (Table 3.1).

Table 3.1: Contribution of Vena Caval Flow to Total Cardiac Output

Author	N, age	Method	Conclusion
Salim et al(20)	145 healthy children, mean age 1.6 ± 2.0 y (1 day to 6.6 years)	Doppler echocardiographic study	SVC flow accounts for 49% of CO in normal neonates; it peaked to a maximum of 55% at 2.5 years and thereafter it diminished to 35% by 6 years
Salim et al(22)	29 BDGS mean ± SD, age 2.95 ± 1.65 years	cardiac catheterisation	in children < 3 years, ratio of SVC to total venous return is >50%.
Eyskens et al(23)	18 BDGS patients, (ages of 8 to 48 months)	CMR & cardiac catheterisation	No significant difference in the ratios of SVC to IVC flow, nor of SVC: SVC+IVC flow across ages of 8 to 48 months
Whitehead et al.(25)	105 Fontan patients, (aged 2–24 years)	PC MRI	IVC contribution to total caval flow was 59% ± 15%. Age (r = 0.60) and BSA (r = 0.74) correlated with IVC contribution.
Mohiaddin et al(26)	13 healthy subjects	cine magnetic resonance velocity mapping	SVC flow in normal adults was equal to 35% of the systemic CO
Houlind et al. (24)	7 lateral tunnel TCPC patients, mean age 9 (4–18) years	CMR & Cath	Following a standard lateral tunnel TCPC, flow returning via the SVC is not lower than flow returning via IVC as otherwise seen in healthy subjects

SVC-Superior Vena Cava, IVC-Inferior vena cava, CO-cardiac output, BSA-body surface area, CMR - cardiac MRI, TCPC-Total Cavo Pulmonary Anastomosis, BDGS -bidirectional Glenn shunt, cath-catheterisation

Even though the Fontan surgery is currently recommended by the age of 3 to 7 years (7), the timing of TCPC surgery is still a matter of debate. Fontan circulation is non-physiological and imposes twin problems of central venous hypertension and reduced cardiac output (CO). Over course of time diastolic dysfunction, hepatic dysfunction, and less commonly, protein-losing enteropathy set in(27). The proponents of late surgery cite these reasons to advocate delayed surgery. However, data from few studies indicate poorer outcomes in older patients (28) and better survival in younger patients (29–34). This may be in part attributed to delayed surgical timing, however, it might, more importantly, be related to poor patient selection. (27).

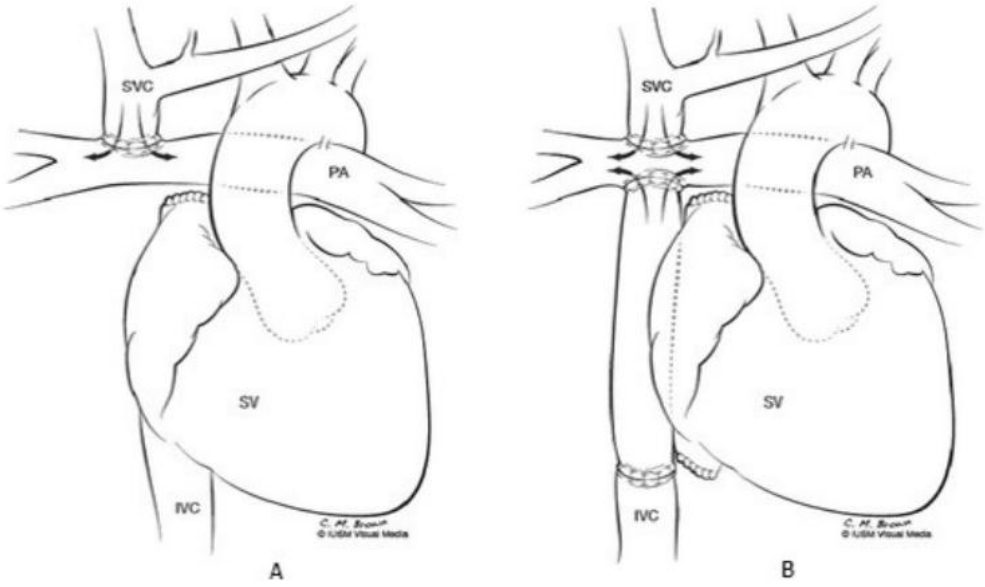


Figure 3.1 Illustration of the anatomic relationships following bidirectional Glenn shunt (A) and total cavopulmonary connection (B) palliation. IVC-inferior vena cava; PA-pulmonary artery; SV-single ventricle; SVC-superior vena cava.

Selection of ideal Fontan candidate involves preliminary assessment of pulse oximetry, chest X-ray, detailed echocardiography, and recording of weight to determine initial counseling and potential future management. (21) This is followed by more specialised investigations of cardiac catheterisation and imaging.

Cardiac catheterization

This initial assessment is followed by cardiac catheterization wherein pressure measurements and oximetry samples are taken from within the ventricle, the pulmonary veins, pulmonary venous atrium, the SVC, pulmonary arteries, the aorta, and the IVC. Angiography is done to delineate adequacy of pulmonary circulation, identify the presence of collaterals & define ventricular function, morphology, and atrioventricular valvar regurgitation (AVVR). (8)

Principle of flow assessment by cardiac catheterisation

Adolph Fick in 1870, described the theoretical principle for measurement of the cardiac output using catheterization. This principle states that the flow of blood for a specified time period is equal to the amount of substance entering the bloodstream divided by the difference between the blood concentrations of the substance upstream and downstream from its point of entry into the circulation during that time period.

$$CO = \frac{VO_2}{C_a - C_v}$$

CO = cardiac output
VO_2 = oxygen consumption in ml of pure gaseous oxygen per minute
C_a = oxygen content of arterial blood
C_v = oxygen content of mixed venous blood

Pulmonary blood flow can be determined by measurement of oxygen uptake and the arteriovenous difference of oxygen across the pulmonary circulation. Similarly, systemic blood flow is calculated by measurement of oxygen uptake and the arteriovenous difference of oxygen across the systemic circulation

Therefore in people without cardiac defects, the flow in pulmonary (Qp) and systemic circulation (Qs) is determined respectively by

$$Qp = \frac{\dot{V}O_2}{CpvO_2 - CpaO_2}$$

$$Qs = \frac{\dot{V}O_2}{CaoO_2 - CmvO_2}$$

Where VO2 is oxygen consumption

CpvO2- oxygen content in pulmonary veins

CpaO2- oxygen content in pulmonary artery

CaoO2- oxygen content in aorta

CmvO2- oxygen content in mixed venous sample

Therefore, the ratio of flows in both circulation can be determined by:

$$QP/QS^1 = \frac{Sat\ (aorta) - Sat\ (mixed\ venous^2)}{Sat\ (pulmonary\ vein^3) - Sat\ (pulmonary\ artery)}$$

(35)(36)

Cardiac catheterisation though widely accepted has attendant risk of errors; as multiple assumptions are involved. These include assuming that patient is in a steady-state throughout the study and represents his baseline state. This may not be true under anesthesia and sedation. Also, the obtained oximetry value may not be truly representative of the chamber sampled from due to streaming & incomplete mixing effects. Additionally, the whole body oxygen consumption is an estimated value, which is usually adopted from weight & age-based charts.

Fick's principle in BDGS circulation

Pulmonary circulation

Here the primary source of blood to pulmonary circulation is the BDGS, which is the SVC- unilateral or bilateral that is anastomosed end- to- side to the ipsilateral PA. Additional sources of pulmonary blood supply include preserved antegrade pulmonary blood flow through the patent pulmonary valve and systemic-to-pulmonary arterial collaterals. These collaterals may communicate with the PA or may supply the lung segment in an individual direct manner. Hence in the presence of multiple sources of blood supply to lungs, the calculated Qp varies depending on the site of sampling. Collateral supply is usually not accounted for in conventional oximetry calculations. The precise site of oximetry sampling for the pulmonary blood is not known. The presence of APC in single ventricle may reach more than 80% (37–40). Furthermore, the values may be contaminated by streaming effects of associated lesions. Additionally, oxygen consumption(MVO2) of upper body, which is then drained by SVC is not known. (21,41)

Systemic circulation

Aorta supplies the systemic circulation & it is drained by the SVC & IVC in a combined manner. Hence for calculation of Qs, mixed venous blood is taken. However in BDGS , there is no true mixing of systemic venous blood from SVC & IVC as superior & inferior vena caval circuits are separate (3).

Invasive hemodynamics is usually obtained under general anesthesia (GA) with positive pressure ventilation (PPV). In BDGS patients, one of the major driving forces of the cavopulmonary circulation is self-ventilation; the generation of negative intrathoracic pressure during inspiration increases the systemic venous return from the body. (21). PPV may decrease the cardiac output and alter pulmonary vascular resistances depending on positive end-expiratory pressure (PEEP) & fraction of inspired oxygen (FiO2) used respectively. Therefore the hemodynamic study is not representative of true basal state of the patient. Hoskote et al. (42) studied the effects of permissive hypercapnia strategy in 9 post BDGS patients who were less than 2 years. They demonstrated that after BDGS, systemic oxygenation, Qp, Qs, and cerebral blood flow increased and indexed systemic vascular resistance (SVRI)

decreased at CO_2 tensions of 45 and 55 mm Hg compared with 35 mm Hg. Hypercarbia results in a fall in SVRI but Qp/Qs, Qp /IVC, and PVRI values were not affected (42). Fogel et al. drew similar conclusions from their study on 12 BDGS patients aimed at understanding carbon dioxide feedback in this unique patient subset. (43)

Considering these shortcomings of cardiac catheterisation, studies have been done to determine whether a subset of patients who have undergone a BDGS could be identified in whom cardiac catheterisation was of little benefit and whether TCPC could be done based on non-invasively obtained data alone. Ro et al. described 2 clinical criteria (pulse oximetry <76%, haemoglobin content >18 g/dl) and 6 echocardiographic criteria (Left pulmonary artery visualized without stenosis, No significant atrioventricular valve insufficiency (≤1+), No significant ventricular dysfunction (qualitative), No aortic coarctation, An unrestrictive atrial communication, and no evidence of a decompressing vessel) to identify low risk TCPC candidate. They concluded that catheterization before Fontan could be avoided in a large percentage of patients who fulfilled all the criteria without adversely affecting outcomes (44). Similar studies were done by Ait-Ali et al., Yassin et al., Fogel et al. and Nijres et al. utilising clinical, echocardiographic & CMR data. (45–48). They concluded that a non-invasive diagnostic algorithm could be used as an effective screening tool to detect patients in whom pre-Fontan cardiac catheterization could be avoided.

Despite its significant limitation in its ability to calculate flows with accuracy, cardiac catheterisation continues to be mandatory before TCPC completion (49). It is the only modality that allows us to quantify pressure with accuracy. Determination of transpulmonary gradient, mean pulmonary artery pressure & single ventricle end-diastolic pressure is of prime importance while planning TCPC completion (41,50). It also has therapeutic value whereby catheter-mediated interventions directed at stenosis of the pulmonary branches, vascular anomalies (aortopulmonary and veno-atrial collateral vessels, pulmonary arteriovenous fistulas), etc are carried out to prepare the patient for a future TCPC completion. (50). Other disadvantages of cardiac catheterisation include its invasive nature and exposure to radiation

Hemodynamic calculations in BDGS circulation

Several authors have attempted to devise a formula to define pulmonary to systemic flow ratio in children post-BDGS. Inuzuka et al have calculated Qp/Qs from combining data from the 2 modalities of lung perfusion scintigraphy & cardiac catheterisation. (51). Salim et al.(22) suggested that Pulmonary/systemic flow ratio = (Systemic saturation- IVC saturation) / (PV saturation- IVC saturation)

$$Q_S = Q_P + Q_{IVC}; \qquad Q_{IVC} = Q_S - Q_P. \qquad [1]$$

Systemic blood oxygen transport = Pulmonary venous blood oxygen transport + Inferior vena cava blood oxygen transport. Thus, Oxygen-carrying capacity of blood × Systemic arterial saturation × Systemic blood flow = (Oxygen-carrying capacity of blood × Pulmonary venous saturation (PV_{sat}) × Pulmonary venous return) + (Oxygen-carrying capacity of blood × Inferior vena cava saturation (IVC_{sat}) × Inferior vena cava flow):

$$\begin{aligned} &Q_S \times (O_2\text{-carrying capacity}) \times SA_{sat} \\ &= Q_P \times (O_2\text{-carrying capacity}) \\ &\times PV_{sat} + Q_{IVC} \\ &\times (O_2\text{-carrying capacity}) \times IVC_{sat}. \end{aligned} \qquad [2]$$

Substituting equation 1 in equation 2 yields:

$$\begin{aligned} &Q_S \times (O_2\text{-carrying capacity}) \times SA_{sat} \\ &= Q_P \times (O_2\text{-carrying capacity}) \\ &\times PV_{sat} + (Q_S - Q_P) \\ &\times (O_2\text{-carrying capacity}) \times IVC_{sat}. \end{aligned}$$

The oxygen-carrying capacity is constant for the same hemoglobin in the same patient during catheterization and cancels out of the formula as follows:

$$\begin{aligned} Q_S \times SA_{sat} &= Q_P \times PV_{sat} + Q_S \times IVC_{sat} \\ &\quad - Q_P \times IVC_{sat}; \end{aligned}$$

$$Q_S \times SA_{sat} - Q_S \times IVC_{sat} = Q_P \times PV_{sat} - Q_P \times IVC_{sat};$$

$$Q_S \times (SA_{sat} - IVC_{sat}) = Q_P \times (PV_{sat} - IVC_{sat});$$

$$\frac{Q_P}{Q_S} = \frac{SA_{sat} - IVC_{sat}}{PV_{sat} - IVC_{sat}}. \qquad [3]$$

$$Q_P = \frac{\text{Oxygen consumption}}{(PV_{sat} - PA_{sat}) \times \text{Blood oxygen-carrying capacity}}; \quad [4]$$

$$Q_S = \frac{\text{Oxygen consumption} \times (PV_{sat} - IVC_{sat})}{\text{Blood oxygen-carrying capacity} \times (PV_{sat} - PA_{sat}) \times (SA_{sat} - IVC_{sat})}. \quad [5]$$

Fang et al. (52) designed a mathematical model of the oxygen delivery kinetics of the bidirectional Glenn (BDG) shunt circulation and validated it using data from 98 BDGS patients undergoing cardiac MRI and catheterization. They concluded that in the absence of aortopulmonary collateral (APC) flow, Qp/Qs calculated using cardiac catheterization data closely matched that obtained with cardiac MRI. In the presence of APC flow, cardiac catheterization derived Qp/Qs underestimated CMR Qp/Qs. In the absence of an additional source of PBF, they suggest

$$Qp/Qs = [SaO_2 - S_{SVC}O_2]/[SpvO_2 - S_{SVC}O_2]$$

Downing et al.(3) defined

$$Qp/Qs = \frac{\text{Ao sat - Mixed Venous sat}}{\text{PVsat - PAsat}}$$

Where MV was defined as the lowest SVC or PA. This formula also doesn't take the contribution of systemic to pulmonary collaterals into consideration.

Stumper et al.(21) utilise the following formula in their catheterisation lab in BDGS patients

$$Q_P/Q_S = \frac{Ao_{Sat} - IVC_{Sat}}{PV_{Sat} - SVC_{Sat}}$$

Subsequently, many authors have incorporated these formulae in their research in this population subset. (42,51,53–55)

CMR in univentricular heart

Since the early 1980s, CMR techniques have advanced considerably. It is presently the imaging modality of choice for extracardiac anatomy, including veno-

atrial and ventriculo-arterial connections and quantification of ventricular volumes and function. Detailed morphological information on intracardiac anatomy can also be obtained. (50). ECG-gated cine Steady-State Free Precession (SSFP) sequences help visualize the ventricular anatomy and aid in quantitative assessment of ventricular dimensions, function, and stroke volume (45).

A contrast-enhanced three-dimensional Magnetic Resonance Angiography with 3D spoiled gradient-echo (GE) sequences defines mediastinal vessels, as well as potential aorto-pulmonary and veno-venous collaterals well (45). Late Gadolinium Enhancement (LGE) after 10 minutes of contrast administration can be used to detect potential myocardial fibrous tissue (45).

CMR is also the gold standard in cardiac output measurement. Relative flows to the pulmonary arteries, systemic collaterals, and fenestration flow can also be quantified (50,56–58). PC MRI provides a non-invasive technique to quantify blood flow that is not limited by the imaging window or image angle-dependent (48,59,60).

Phase-contrast MRI: technique

ECG-gated phase-contrast sequences perpendicular to the SVC, IVC ascending aorta, branch pulmonary arteries, and pulmonary veins are obtained for flow assessment (3,45). Here MRI signal is used to quantify velocity. It relies on phase data, & uses bipolar gradients. The degree of phase shift in the direction of the gradient corresponds directly to the flow velocity. Therefore, for a given gradient, there is a maximal velocity that can be measured before aliasing occurs. This velocity is called the encoding velocity (v_{enc}). Hence, knowing the approximate velocities to be measured is very important for selecting the most appropriate and accurate v_{enc} for a phase-contrast sequence. Flow measurements are most accurate when the imaging plane is perpendicular to the vessel of interest with an appropriate $v_{enc.}$ Flow curves are then generated by tracing a region of interest around the vessel contour during all phases by using one of the many commercially available analysis software (61) (5).

PC MRI technique relies on several assumptions (such that venous vessels do not change calibre during the respiratory or cardiac cycle). It is also limited by its inability to measure flow in small vessels like pulmonary veins accurately, as this

technique limited spatial resolution and requires the flow curves to be traced during the non-breathhold acquisition. (21)

Lastly, as compared to cardiac catheterisation CMRI is less commonly available, takes longer time, and requires familiarity with potential loopholes & expertise in interpretation of data. CMR fails to visualize very small APC that, according to some groups, may alter outcomes after Fontan (37,38,62). Current limitation of hemodynamic assessment by CMRI lies in its inability to accurately estimate pressure data (41). Also, the long procedural times and the need for the patient to lie still to avoid motion artifacts often necessitates the use of general anesthesia.

Accuracy of PC MRI in flow assessment

Investigators have used ventricular stroke volume, thermodilution, Fick principle, indicator dilution, and flow probe measurements as reference standards, showing strong correlations with PC MRI (63–68). Hundley et al. (69) found that ascending aorta flow in 23 adults was within 4% of flow measurements by the Fick method and within 5% measured by thermodilution. Beerbaum et al. (60), in a study of 50 children with atrial or ventricular septal defects (VSDs) who underwent concomitant cardiac catheterization, reported a mean difference between PC MRI and oximetry of 2% (2SD = −20% to +26%). Powell et al. (70) in a study of 20 patients with atrial septal defect (ASD), found a mean difference between PC MRI and oximetry of 2.3% with reproducibility of repeat PC MRI flow measurements to the tune of 1.1 ± 4.2% in the main pulmonary artery and 0.7 ± 5.4% in the ascending aorta.

Hemodynamic calculations in BDGS circulation

Downing et al. and Whitehead et al. (3,53) defined Q_P as the total PV flow, and Q_S was defined as the total caval (SVC+IVC) flow. APC flow can be calculated as the difference between PV and PA flow or the difference between aortic and caval flow. They defined it as the average of these 2 measures. CMR derived Qp & Qs was estimated by Grosse-Wortmann et al.(56,71) by the following formula.

Qp=sum of Q_{PV}

$Q_s=Q_{SVC}+Q_{DA}$ (where DA is descending aorta flows; when there was no significant systemic venous collaterals) $(Q_s)=Q_{SVC}+Q_{DA}+Q_{runoff}$ (when there was obvious systemic venous collaterals). The APC flow is obtained by subtracting the flow of both pulmonary arteries from the Qp.

Kappanayil et al. (41) estimated CMR flows in a case of complex cyanotic congenital heart disease post-Kawashima surgery as follows. Qs= aortic outflow (in the absence of significant APC). They suggest that alternately Qs can be calculated from the sum total of the systemic venous return (RSVC + LSVC + hemiazygous vein + hepatic vein in the absence of significant decompressing veins. (Qp) = total PV flow. Qp equals the sum of flows across the RSVC, LSVC, hemiazygous vein, and the antegrade PA flows. Qp can also be derived as a sum of the aortic outflow and the hepatic venous return. Pulmonary blood flow would be equal to RPA + LPA flows.

Correlation of CMRI with cardiac catheterisation

Downing et al. compared CMRI & cardiac catheterisation data obtained from 30 BDGS patients with a median age of 2.6 years(Range: 11 mo-7y). *Qp* by oximetry underestimated CMR-measured *Qp* by 32% of the CMR value ($P<0.0001$). Whereas Qs by oximetry was an overestimate when compared to CMR value by 15%($P=0.009$). Q_p:Q_s by Fick and CMR ($\rho_c=0.01$) did not correlate. The error in the Fick Q_p correlated moderately with the measured APC flow ($r=0.39$). The median total oxygen consumption calculated using combined CMR and oximetry data was 173 mL/min per m^2, higher than the assumed values used to calculate flows by the Fick equation. The upper body circulation received on average about 51% of systemic blood flow while conducting only 39% of total body metabolism. (3). Similar study was done by Fang et al.(52) & they too drew conclusions similar to Downing et al. In 37 BDGS patients who underwent CMR & cardiac catheterisation, Fogel et al (48) examined agreement of CMR with cath and intraoperative findings. They found good accuracy with no significant quantitative difference between CMR and cath with surgical findings.

Calculation of pulmonary vascular resistance(PVR)

Total PVR was calculated using transpulmonary gradients and pulmonary vein flow for each lung separately.

Downing et al.(3) described this as

$$\frac{1}{R_T} = \frac{1}{R_R} + \frac{1}{R_L}$$

where R_T=total PVR, R_R=right lung PVR, and R_L=left lung PVR.

AIMS AND HYPOTHESIS

Aim:

To compare cardiac catheterisation-(Fick-principle) derived estimates of pulmonary and systemic blood flows and Qp/Qs with measurements obtained using Cardiac MRI.

Hypothesis:

We hypothesise that Cardiac MRI derived estimates of pulmonary and systemic blood flows and Qp/Qs have a good correlation with cardiac catheterisation-(Fick-principle)-derived measurements.

Objectives:

To compare cardiac catheterisation-(Fick-principle) derived estimates of pulmonary and systemic blood flows and Qp/Qs with measurements obtained using Cardiac MRI.

MATERIALS & METHODS

Design: prospective observational study

Setting: Study was done in Sree Chitra Tirunal Institute for Medical Sciences and Technology -a tertiary referral centre.

Inclusion criteria:

All patients with bidirectional Glenn shunt (BDGS) who underwent cardiac MRI & cardiac catheterisation between December 2018 to January 2021 as part of routine evaluation of hypoxemia or workup for TCPC (the next stage in the staged palliative surgery).

Exclusion criteria:

Patients with interrupted inferior vena cava, large systemic to pulmonary or venous collateral vessels, Pulmonary Vein stenosis, Pulmonary artery hypertension, severe atrio-ventricular valve regurgitation, severe ventricular dysfunction, coarctation of aorta significant preserved antegrade pulmonary blood flow as estimated by the treating team from echocardiographic, MRI and catheterisation data, or contraindication to CMRI was be excluded.

Sample size: A preliminary review of hospital records; revealed that approximately 2 patients undergo CMRI & cath study in a month. Therefore in 2 years, approximately 50 patients were expected to be enrolled. However in view of the COVID-19 pandemic & lockdown, elective admissions were reduced and deferred, resulting in fewer case enrollments. We enrolled 30 patients in this study. A similar study by Downing et al.(3) done in a retrospective fashion had enrolled 30 patients.

Methodology:

All patients with BDGS who underwent cardiac MRI & cardiac catheterisation was be identified during their hospital admission for cardiac MRI & cardiac catheterisation. Informed consent to use clinical data was obtained from participants before enrolment. Data collection of all patients will be done by the principal investigator by using a standard data collection form (See Annexures). Collection of

demographic details was done during hospital admission and collection of data from cardiac catheterisation and cardiac MRI was done from the hospital records. Flow assessment was done by both phase-contrast cine MRI as well as by oximetry (performed during cardiac catheterisation), the details of which are described below. It was aimed to minimise the time between both the assessments to as close as possible. The catheterisation personnel was blinded to the MR investigators and vice versa. The observations during both the studies were systematically recorded.

CMRI protocol:

Our Institute's cardiac anesthesia team assessed each child before CMRI and general anaesthesia was administered on a case to case basis. CMR images were acquired on a 1.5-T MRI Scanner (Avanto fit, Siemens). Localization of velocity mapping image planes was performed using multiplanar reformatting of a static balanced steady-state free precession (SSFP) axial stack gated to late diastole. Multiplanar reformatting was used to set the position and angle of the imaging plane for anatomical and PC-MRI cines. Retrospectively gated, through-plane, phase-contrast cines (PC-MRI) were performed in the PAs, PVs, vena cavae (SVC and IVC), and aorta. Right and left PA measurements were obtained individually, and the right PA measurement was performed proximal to the origin of the right upper lobe PA. In patients with proximal right PA branching, the right upper lobe PA was measured separately. When possible (based on whether all the pulmonary veins on one side formed a common vein of sufficient length before entering the atrium), all the pulmonary veins on one side were measured in one velocity map. This was more common for the left pulmonary veins, which often form a single confluence before joining the left atrium. When necessary, the upper and lower pulmonary veins, and occasionally a middle pulmonary vein, were measured separately.

Table No 4.1 : *MRI Parameters used in the 1.5 T Seimens Avanto MR Scanner*	
FOV	220×165 mm
Matrix	192×144
Slice Thickness	3- to 4-mm
Echo Time (TE)	2.82 ms
Bandwidth	501 Hz/px
Repetition Time (TR)	34 ms
Flip Angle	25°
Measured Phases	14
Calculated Phases	24
Segments	3
Averages	3
Acquisition time	Ranged from 55 to 110 seconds per velocity map and 12 to 18 minutes overall

Table No 4.2 : *VENC setting in the PC MR assessment as part of the study*	
Aorta	150 cm/s
SVC, IVC, right PA, and left PA	60 cm/s
Pulmonary vein	80 cm/s

The imaging MR parameters were chosen on the basis of clinical experience, which suggest that spatial resolution is more critical than temporal resolution in resolving flow. This is particularly true with the low-frequency venous flows that predominate the protocol.

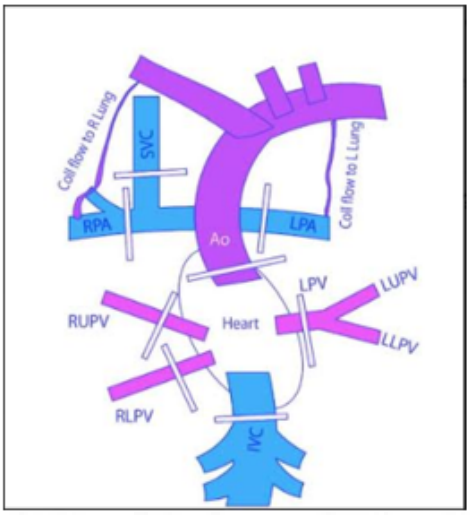
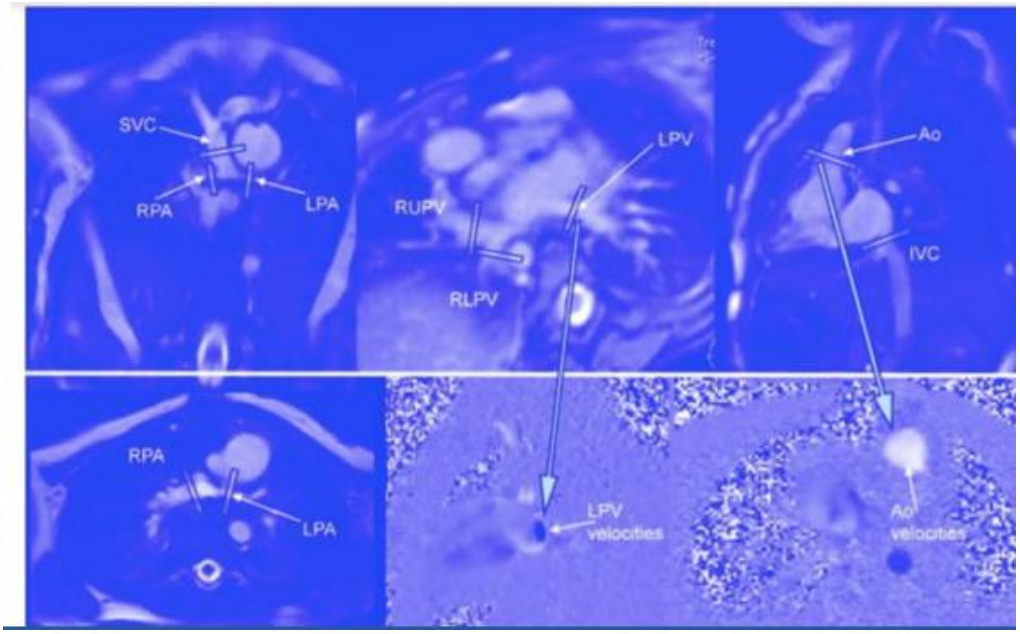


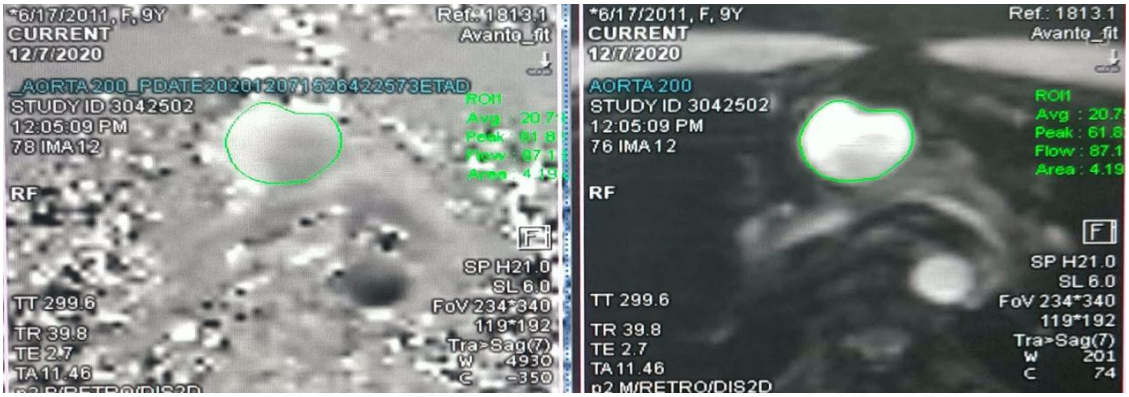
Figure 4.1 (a) *Diagram showing areas of interrogation for obtaining velocity data from SVC, IVC, RPA, LPA, Aorta and Pulmonary veins.* **(b)***Corresponding sections are shown in the MR imaging planes*

(a)



(b)

Figure 4.2: Magnitude, phase image and time velocity curve in aorta



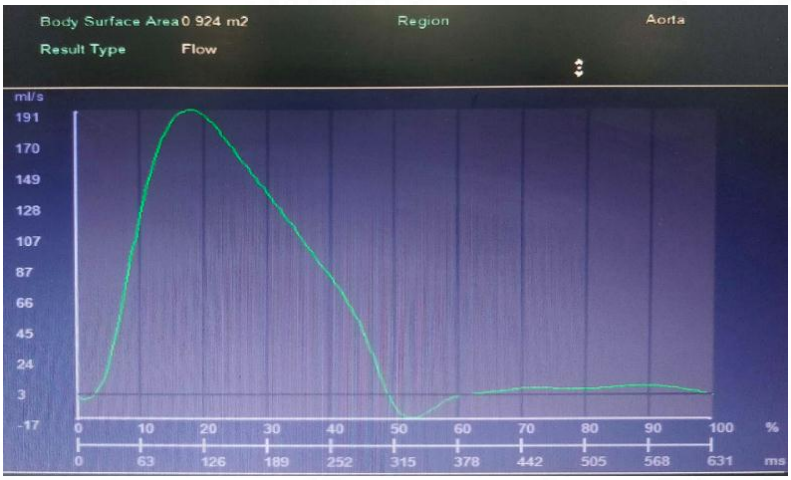


Figure 4.3: Magnitude, phase image and time velocity curve in RPA

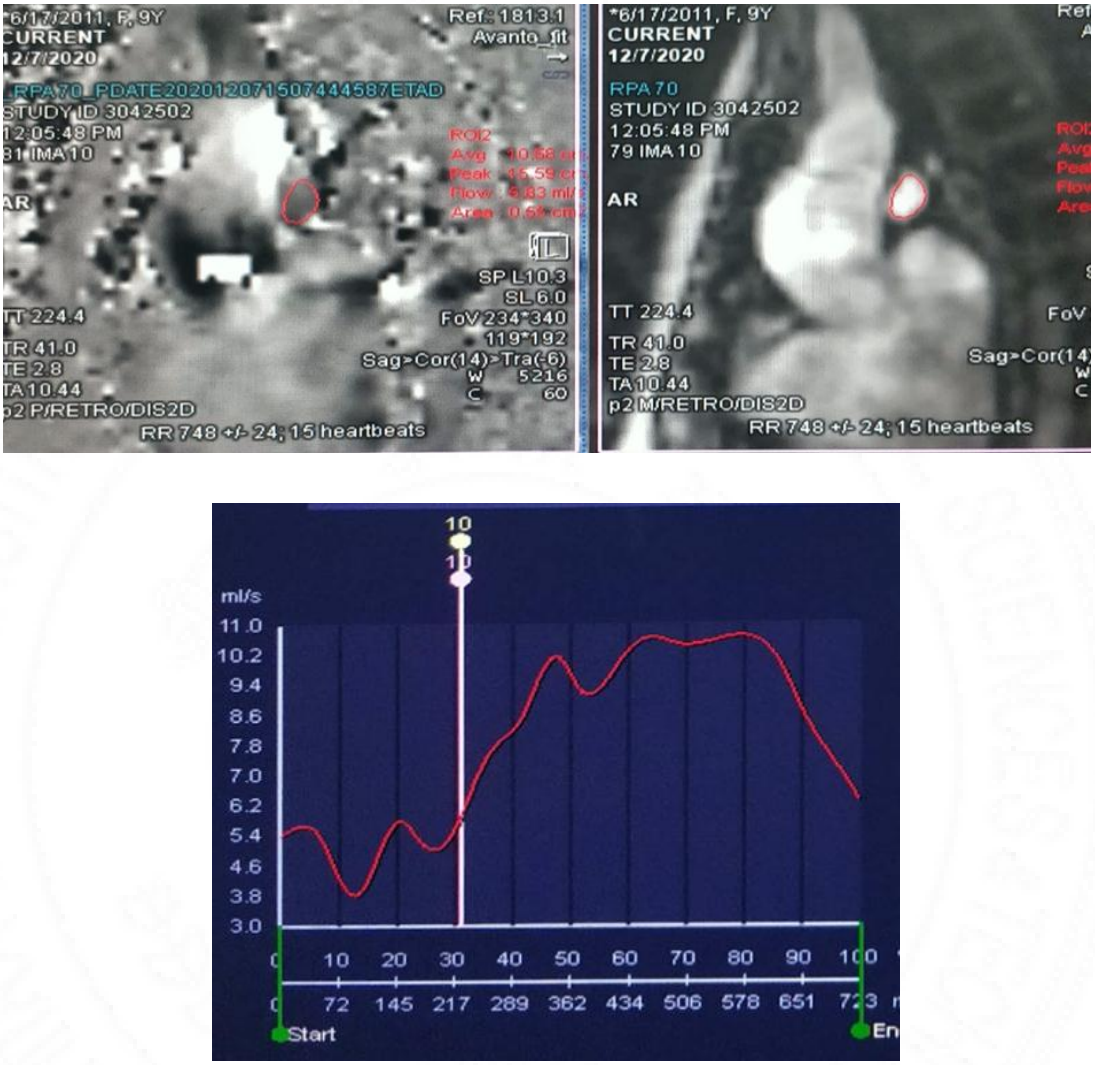
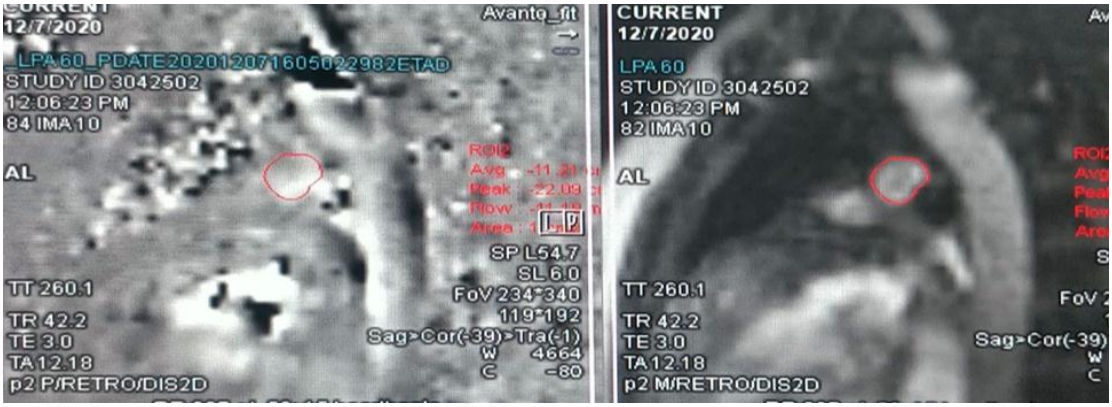


Figure 4.4: Magnitude, phase image and time velocity curve in LPA



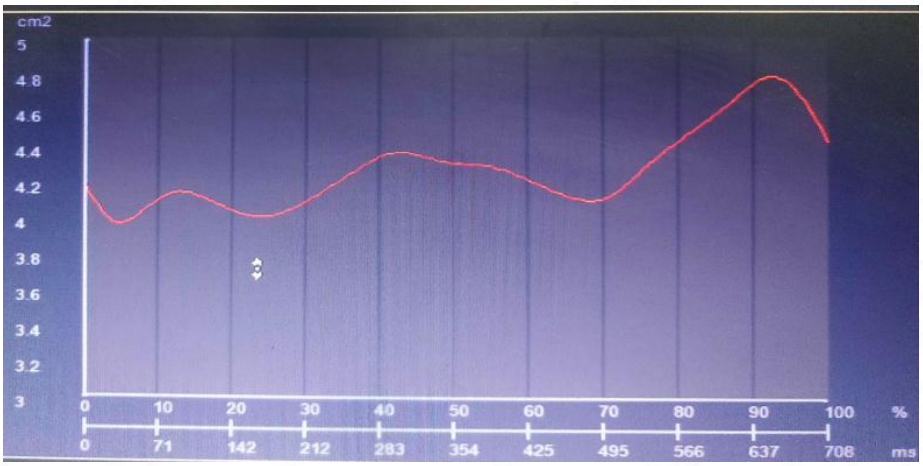


Figure 4.5: Magnitude, phase image and time velocity curve in RSVC

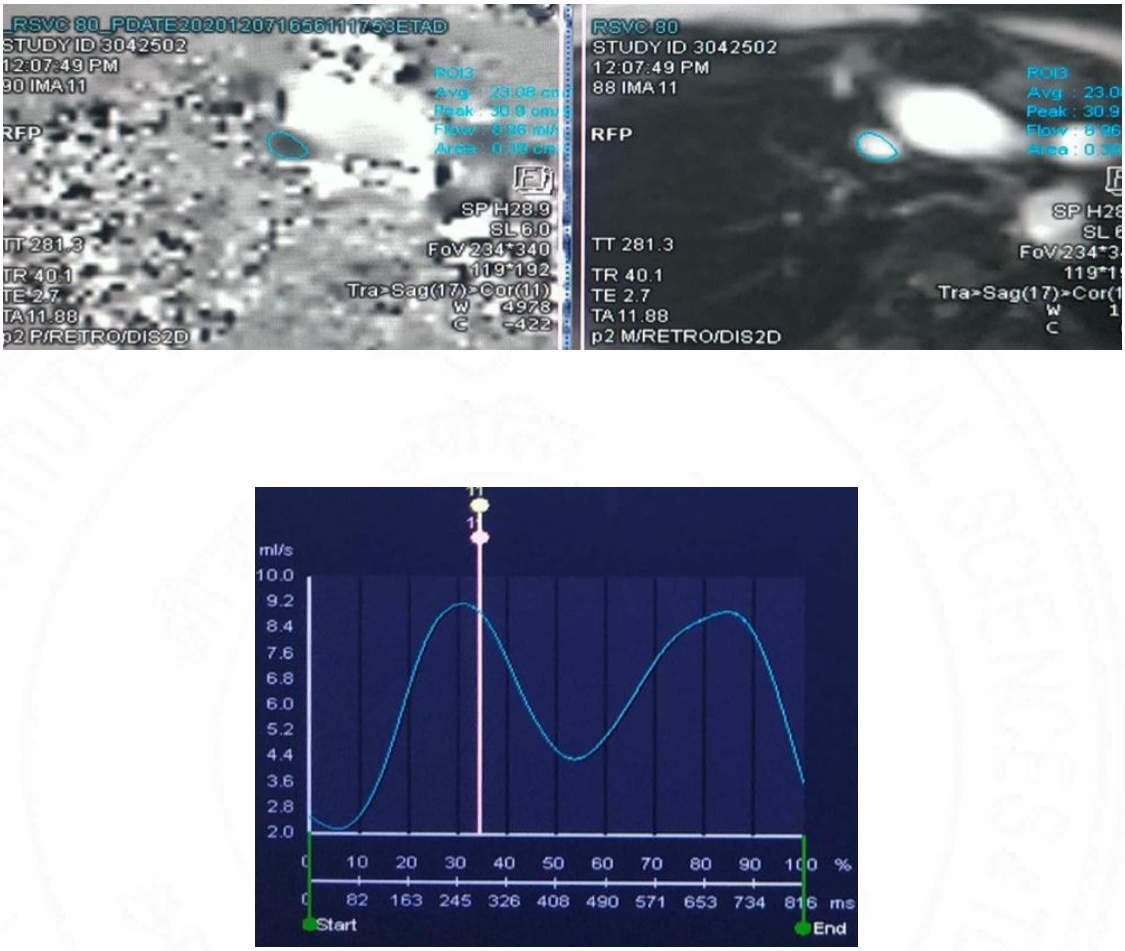


Figure 4.6: Magnitude, phase image and time velocity curve in IVC

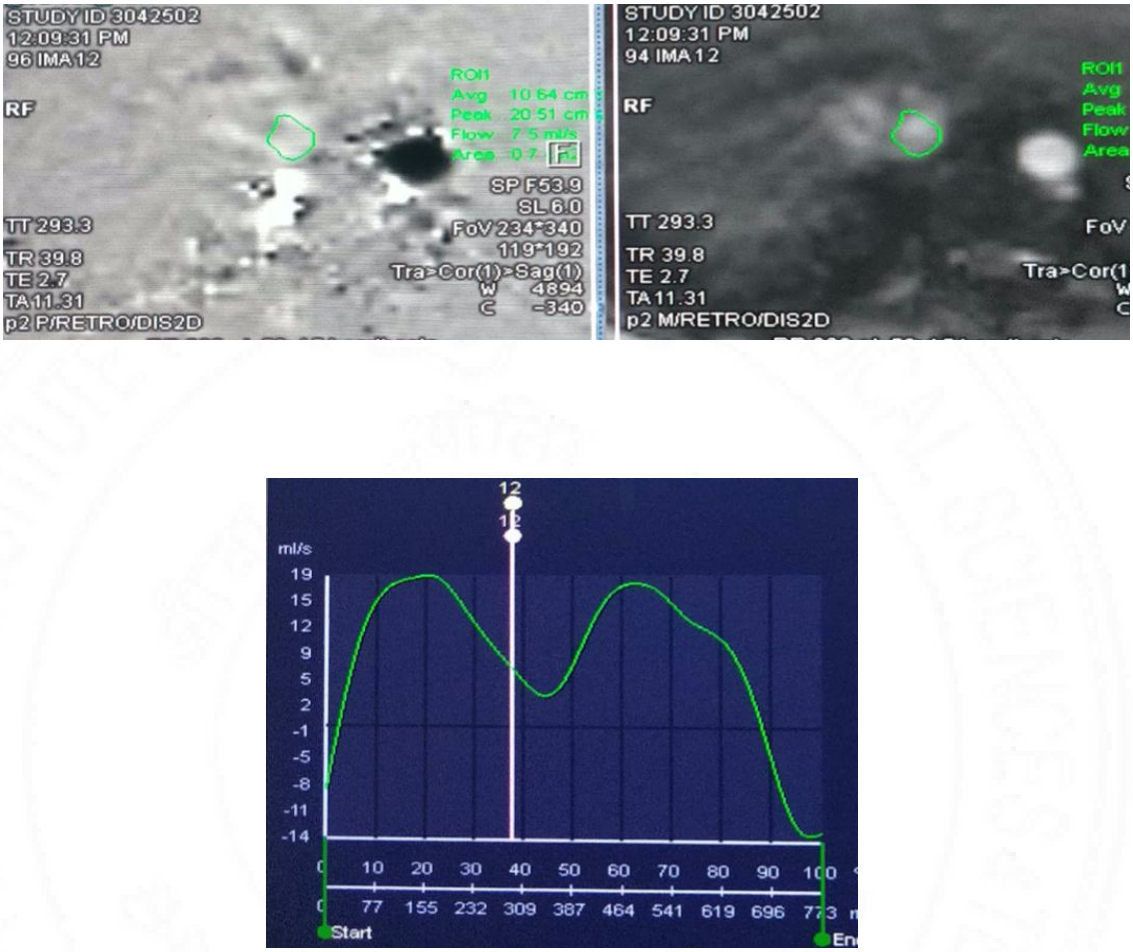


Figure 4.7: Magnitude, phase image and time velocity curve in left pulmonary veins

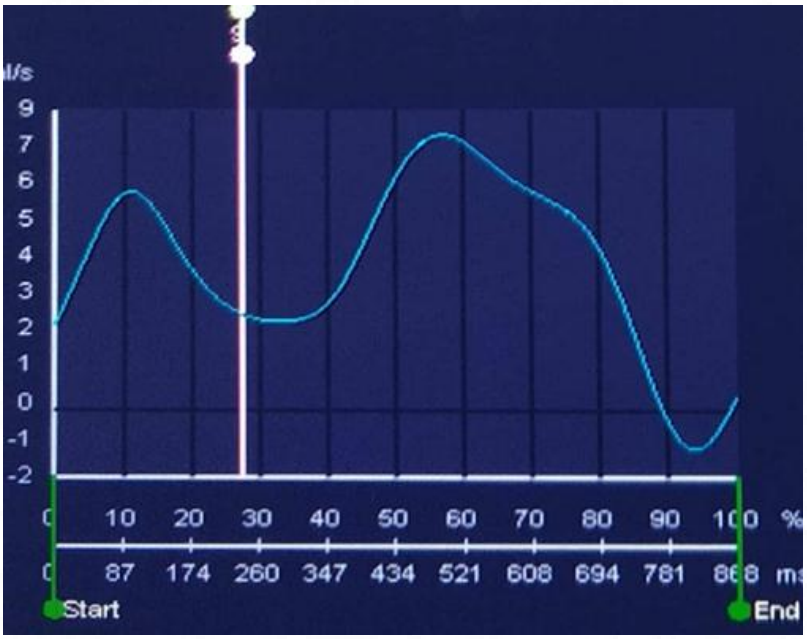
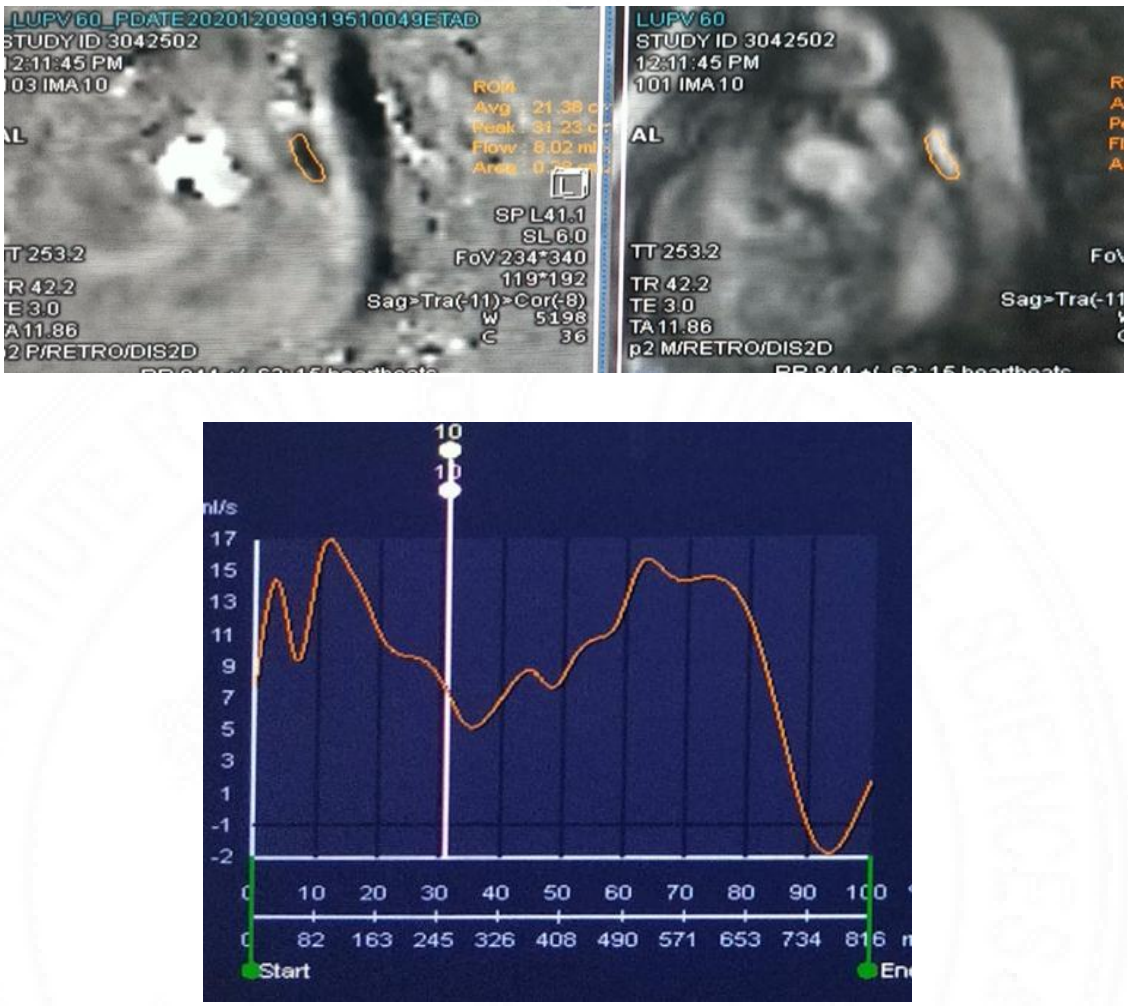


Figure 4.8: Magnitude, phase image and time velocity curve in left pulmonary veins



Hemodynamic calculations

Calculations were done primarily based on Downing et al. and Kappanayil et al.studies (3,41)

- *Q*p =the total PV flow, *Q*p =LPA+RPA, *Q*p =RSVC+LSVC
- *Q*s =the total caval (SVC+IVC) flow, Qs= PV+IVC, Qs=aortic flow

In cases, where the vessel flows were unavailable/uninterpretable, primarily pulmonary vein flows due to poor spatial resolution and low frequency flows, Qp was calculated from Qp=LPA+RPA and Qp=RSVC+LSVC.

In cases where, the total PV flow was available, Qp = LPA+RPA and Qp = RSVC+LSVC served to internally validate obtained data and check for the presence of systemic to PA collateral circulation**.**

APC flow was calculated as the difference between PV and PA flow or the difference between aortic and caval flow and calculated as an average of the 2 measurements.

Calculation of pulmonary vascular resistance(PVR)

Total PVR was calculated using transpulmonary gradients and pulmonary vein flow for each lung separately.

Downing et al.(3) described this as

$$\frac{1}{R_T} = \frac{1}{R_R} + \frac{1}{R_L}$$

where R_T=total PVR, R_R=right lung PVR, and R_L=left lung PVR.

Cardiac catheterisation:

Patients enrolled were already scheduled to undergo cardiac catheterization as part of pre-TCPC workup. The procedure was done under general anaesthesia with ventilation at FiO2 of 21-30% as per the standard clinical practice at our institution. Routinely, femoral venous, internal jugular venous and femoral arterial accesses were taken and pressures were recorded in the intracardiac chambers, aorta, BDGS/SVC circuit and bilateral pulmonary arteries.

Oximetry samples was taken in the BDG circuit, both pulmonary arteries, IVC, aorta & pulmonary veins (subject to whether entry into pulmonary vein was feasible). Samples were analysed with an in house ABG analyser. Most patients had multiple PV saturations measured, which were averaged to produce the final value. In 2 patients with no direct measurement, the PV saturation of 96% assumed at the time of the procedure was used in our calculations. Relevant angiograms for cardiac anatomy including the presence of antegrade PBF, venovenous collateral, APCA &

AVVR, were obtained whenever indicated. Qp, Qs, Qp/Qs was calculated using the based on previous study data as follows.(3,22,52)

Calculation of Qp/Qs

$Qp/Qs= Ao_{sat} – IVC_{sat}/PV_{sat} – IVC_{sat}$ (Salim et al.) (22)

This is accurate in the presence of APC flow as the calculation employs PV saturation & not SVC saturation.

$Qp/Qs = AO_{sat}-SVC_{sat}/PV_{sat}-SVC_{sat}$ (Fang et al.) (52)

As most labs do not measure IVC sat, hence $Qp/Qs= Ao_{sat} – SVC_{sat}/PV_{sat} – PA_{sat}$ and in the absence of additional sources of PBF, this is commonly described as aforementioned formula.

$Qp/Qs= Ao_{sat}-MV_{sat}/PV_{sat}-PA_{sat}$ (Downing et al.) (3)

Here MVsat which represents the mixed venous saturation is taken as the lowest SVC or PA saturation.

In addition, we calculated Qp/Qs using 2 additional formulae.

$Qp/Qs= Ao_{sat}-MV_{sat}/PV_{sat}-PA_{sat}$ (conventional formula)

Here mixed venous saturation (MVsat) is calculated from Flamm formula (72) given below:

Where $\mathbf{MV = \frac{3SVC + IVC}{4}}$

Previous authors had noted a decline in the contribution of SVC flow to cardiac output with increasing age (3,20,25). The mean age of our study population was 108 months and considerably higher than most other available studies. On these premises, we proposed that oxygen consumption of the upper body which the SVC traverses is less than total body oxygen consumption. Hence, we assumed an oxygen consumption of the upper body approximately half of the total body oxygen consumption and, Qp/Qs was derived as follows:

- Assumed Qp= MVO2/2

  PV-PA X O2 content ….1

- Assumed Qs= MVO2

  AO-MV X O2 content …..2

Hence, **Qp/Qs = Ao-MV** **(**Alternate formula**)**

(PV-PA)X2

Calculation of Qp & Qs

As done by previous investigators, we too abstracted total body oxygen consumption from age-based charts published by LaFarge and Miettinen. (3,73,74)

Calculation of Qp

Qp= oxygen consumption **(conventional formula)**

(PV_{sat}-PA_{sat})* blood O2 content

Qp= oxygen consumption **(**Alternate formula)

2**(PV_{sat}-PA_{sat})*** blood O2 content

Calculation of Qs

Qs= oxygen consumption x **PV_{sat} – IVC_{sat}** (Salim et al.) (22)

(PV_{sat}-PA_{sat})* (Ao $_{sat}$ – IVC_{sat})* blood O2 content

Qs= oxygen consumption **(conventional formula)**

(**Ao_{sat}-MV_{sat}**) * blood O2 content

Where **MV = 3SVC + IVC** Flamm formula (72)

4

Calculation of pulmonary vascular resistance(PVR)

Total PVR was calculated by using transpulmonary gradients and pulmonary flow (Qp) as follows:

$$PVR = \frac{PAm - LAm}{Qp}$$

Where PAm=mean PA pressure

LAm=mean LA pressure

Qp- pulmonary flow

PVR was calculated separately for conventional formula and alternate formula.

Figure 4.9: BDG angiogram showing good arborisation of bilateral lungs with no evidence of antegrade pulmonary blood flow

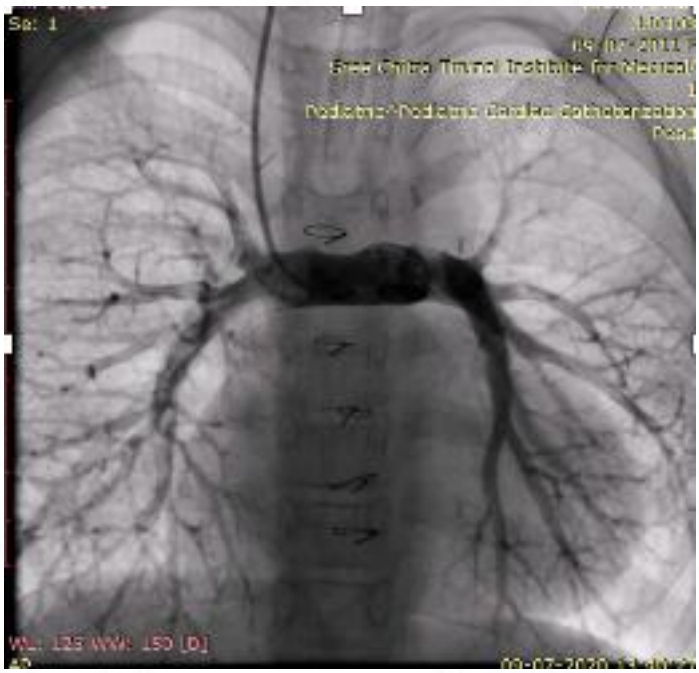


Figure 4.10: BDG angiogram showing veno venous collateral from the BDG

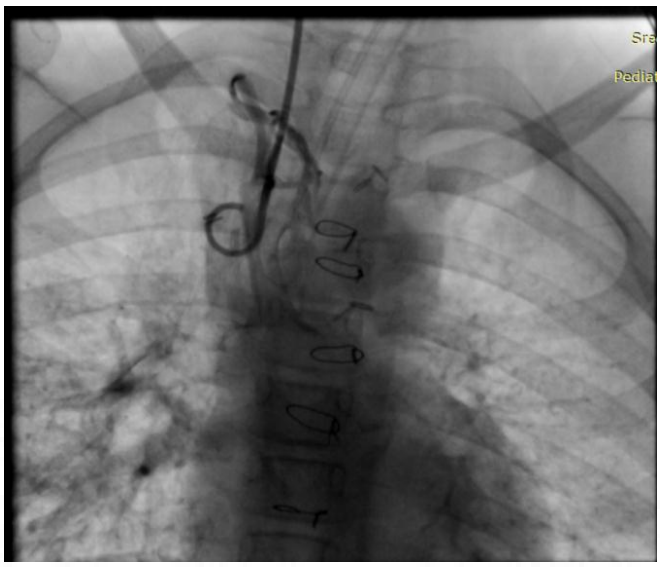
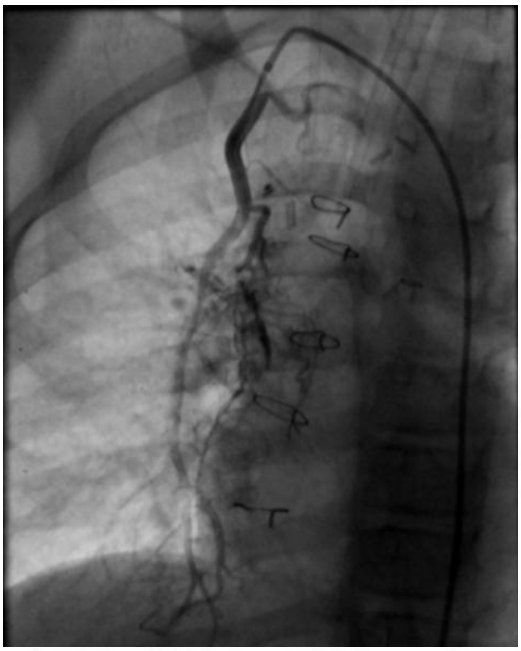


Figure 4.11: Contrast injection into RIMA to delineate aortopulmonary collateral



Data analysis:

The data was analysed by the principal investigator with the help of a statistician. All data was handled with care to maintain patient confidentiality. Records were maintained both in computer and paper formats. Baseline demographic and clinical variables were described using standard descriptive statistics. Normally

distributed variables were described as mean ± SD and skewed variables as median with range. Means were compared using the paired Student t-test for normal variables. Pearson coefficient will be used to measure correlation. Data was not analysed to understand gender, caste, class, ethnicity, race differentials.

ETHICAL APPROVAL & INFORMED CONSENT:

The study was approved by the Institutional Ethics Committee of SCTIMST, Thiruvananthapuram (See Annexure). Informed consent was obtained from the study patients after a detailed discussion regarding the nature of the study in their vernacular.

CONFLICT OF INTEREST: None

FINANCIAL SUPPORT: None

RESULTS

Hundred & four children with BDGS underwent catheterisation as part of pre-TCPC evaluation. There were 59 patients with preserved antegrade pulmonary blood flow. Aortopulmonary collaterals, significant atrioventricular valve regurgitation, pulmonary arterio-venous malformations, and venovenous collaterals were seen in 61, 7, 25 and 12 patients respectively. 9 patients underwent concomitant intervention during the index study (MAPCA coiling in 7, PAVM plugging in 1 and balloon dilatation of BDGS anastomotic site in 1). The distribution of patients screened is described in Table 5.1

Table 5.1. Angiographic characteristics of the population screened for the study (n=104)

	Preserved APBF(n= 59)	**No APBF (n=45)**
APCA	32	29
PAVM	7	18
significant AVVR	5	2
Veno-venous collateral	7	5

APCA-Aortopulmonary collaterals, AVVR- atrioventricular valve regurgitation, PAVM -pulmonary arteriovenous malformations, and veno-venous collaterals

Thirty patients had undergone PC MRI and cardiac catheterisation and were included in the study. The mean (± SD) age of the study population was 108.83 (± 26.72) months with 53% comprising of male gender. The baseline characteristics and diagnosis of the study population are described in Table 5.2, Figure 5.1, and Table 5.3.

Table 5.2. Baseline characteristics of the study population (n=30)

age at catheterization (months)	108.83 (± 26.72)
gender*	Male- 16(53%) Female 14 (47%)
BSA at catheterization (m^2)	0.87 (± 0.18)
age at BDGS(months)	21.43 (± 19.08)
systemic ventricle *	right 10 (33.33%) left 19 (63.33%) biventricular 1 (3.33%)
Type of BDGS*	right -17 (56.67%) Left- 4 (13.33%) Bilateral- 9 (30%)
Hemoglobin at catheterization (g/dL%)	18.71 (± 2.51)
Packed cell volume (%)	57.7 (± 9.01)
Aortic saturation (%)	81.13 (±5.3)
Time between CMR & Catheterisation (days)	130.5 (76-426.5)
GA during catheterization (yes:no)(%) *	30:0 (100:0)
GA during CMR (yes:no) *	13:17 (43.33:56.67)

BSA-body surface area. BDGS-bidirectional Glenn shunt surgery. CMR- cardiac magnetic resonance imaging. GA- general anesthesia

All variables expressed as Mean± SD

* Expressed as percentage-n (%)

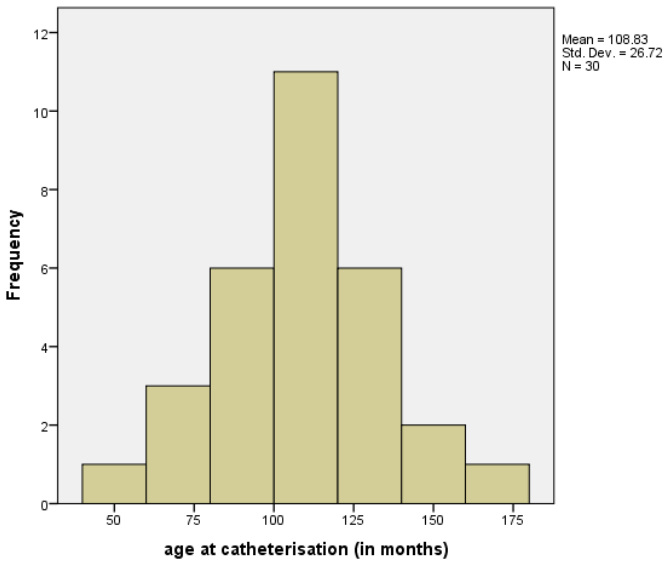


Figure 5.1. Age-wise distribution of the study population

Table 5.3. Diagnosis across the study population (n=30)

Diagnosis	n	%
1- Tricuspid atresia with Ventricular septal defect with pulmonary stenosis	13	43.33
2- Unbalanced Common Atrioventricular canal defects with pulmonary stenosis/ Pulmonary atresia	3	10
3- Ventricular septal defect with Pulmonary atresia	1	3.33
4- Congenitally Corrected Transposition of Great Arteries with Ventricular septal defect with pulmonary stenosis	1	3.33
5- Transposition of Great Arteries with Ventricular septal defect with pulmonary stenosis / Pulmonary atresia	2	6.66
6- Pulmonary atresia with Intact Ventricular septum	1	3.33
7- Double Outlet Right Ventricle with pulmonary stenosis	2	6.66
8- Tetralogy of Fallot with hypoplastic right heart	1	3.33
9- Single Ventricle with pulmonary stenosis/pulmonary hypertension	6	20

The cardiac catheterisation pressure, oximetry & angiographic data has been described in Tables 5.4, 5.5 & 5.6. Five patients had a left ventricular end-diastolic pressure > 12mmHg. The BDGS pressure ranged from 7 mmHg to 16mmHg. There were 5 patients with the lowest PV saturation <96%. The flow data obtained from cardiac MRI has been described in Tables 5.7.

Tables 5.4 Oximetry data obtained during cardiac catheterisation in the study population: (mean ± SD) (n=30)

Sample	Saturation (%)
SVC	63.9 ± 8.08
IVC	66.33 ± 5.72
RPA	66.21 ± 10.17
LPA	66.74 ± 8.30
PV	97.32 ± 3.12
AORTA	81.13 ± 5.29

SVC- Superior Vena Cava, IVC- Inferior Vena Cava, RPA- right pulmonary Artery, LPA- left pulmonary Artery, PV-Pulmonary Vein.

All variables expressed as Mean ± SD

Tables 5.5 Pressure data obtained during cardiac catheterisation in the study population: (mean ± SD) (n=30)

CHAMBER	PRESSURES
SVC	11.93 ± 2.77
RPA	11.80 ± 2.76
LPA	11.77 ± 2.66
LA	8 ± 2.07
RA	8.13 ± 2.19
LVed	9.9 ± 2.54
AORTA systolic	92.14 ± 18.81
AORTA diastolic	54.19 ± 11.68
Aorta mean	69.40 ± 14.33
TPG	3.77 ± 1.74

SVC- Superior Vena Cava, RPA- right pulmonary Artery, LPA- left pulmonary Artery, LA- left atrium, RA- right atrium, LVed- left ventricular end diastolic pressure. TPG- transpulmonary gradient. All variables expressed as Mean ± SD

Table 5.6 Angiographic data obtained during cardiac catheterisation in the study population: (mean ± SD) (n=30)

Variable	n (%)
Aortopulmonary collateral	12 (40)
PAVM	8 (26.66)
Preserved antegrade pulmonary blood flow	6 (20)
Veno venous collateral	-

PAVM- pulmonary arteriovenous malformation

All variables expressed as n (%).

Table 5.7 Flow data obtained from cardiac MRI in the study population. (n=30)

CHAMBER	Flow in mL/min
BDG	1254.5 (965-1603)
IVC	1403 (985-1733)
RPA	774(559-1010)
LPA	582(456-899)
RPV	1170 (888-1450)
LPV	878 (650-1379)
AORTA	2965 (2659-3464)

BDG- bidirectional Glenn, IVC- Inferior Vena Cava, RPA- right pulmonary Artery, LPA- left pulmonary Artery, LPV-Left Pulmonary Vein. RPV- Right Pulmonary Vein.

All variables expressed as Median (IQR)

Internal validation of CMRI data was carried out by comparing aortic flow to the total caval flow. A mean difference of 604 (± 398)mL/min was seen between the 2 with good correlation (Pearson correlation coefficient r=0.681) (p<0.01) (Figure 5.2).

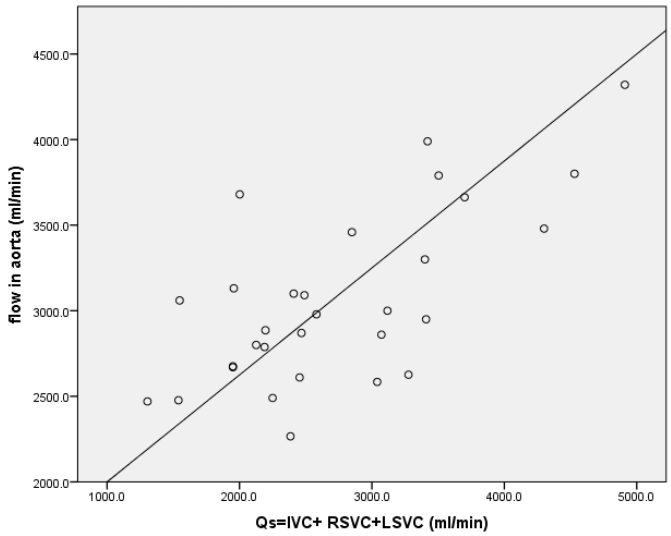


Figure 5.2. Scatter plot comparing aortic flow to the total caval flow in the study population. Pearson correlation coefficient r=0.681 (p<0.01), suggestive of good correlation.

CMR flow trends were compared in different vessels as shown in Figures 5.3, 5.4, 5.5. Table 5.8 describes the age wise contribution of superior vena cava flow to the total caval flow. In the absence of aortopulmonary collateral, this is a measure of Qp/Qs. The mean (± SD) superior vena cava flow to the total caval flow is 0.48 (±

0.07). No particular trend in the age-wise contribution of superior vena cava flow to the total caval flow could be appreciated.

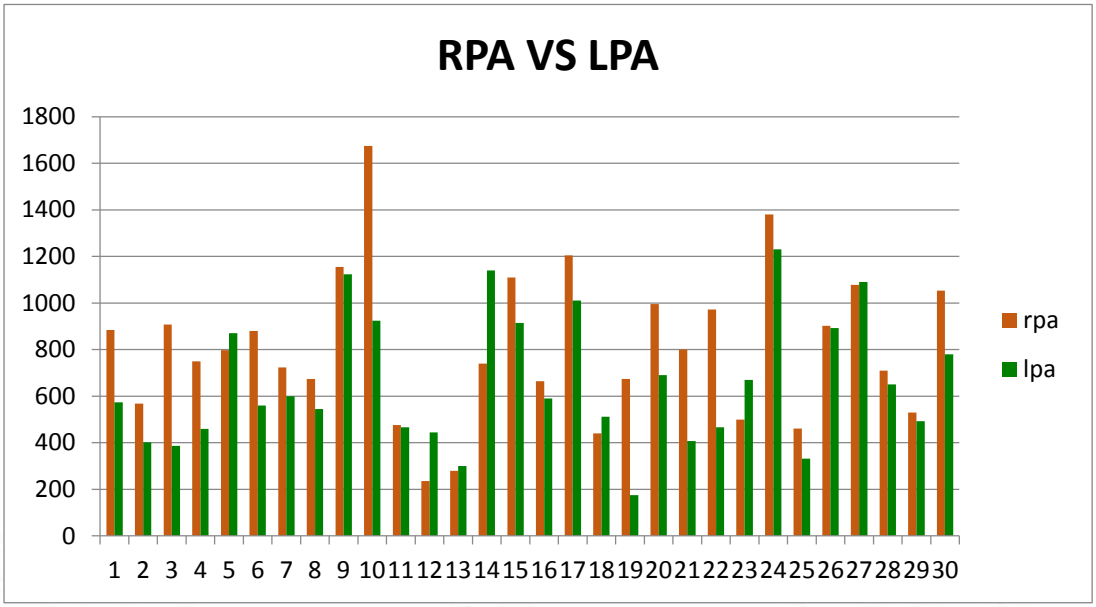


Figure 5.3. Bar chart comparing right & left pulmonary artery flows in the study population.

RPA- right pulmonary Artery, LPA- left pulmonary Artery

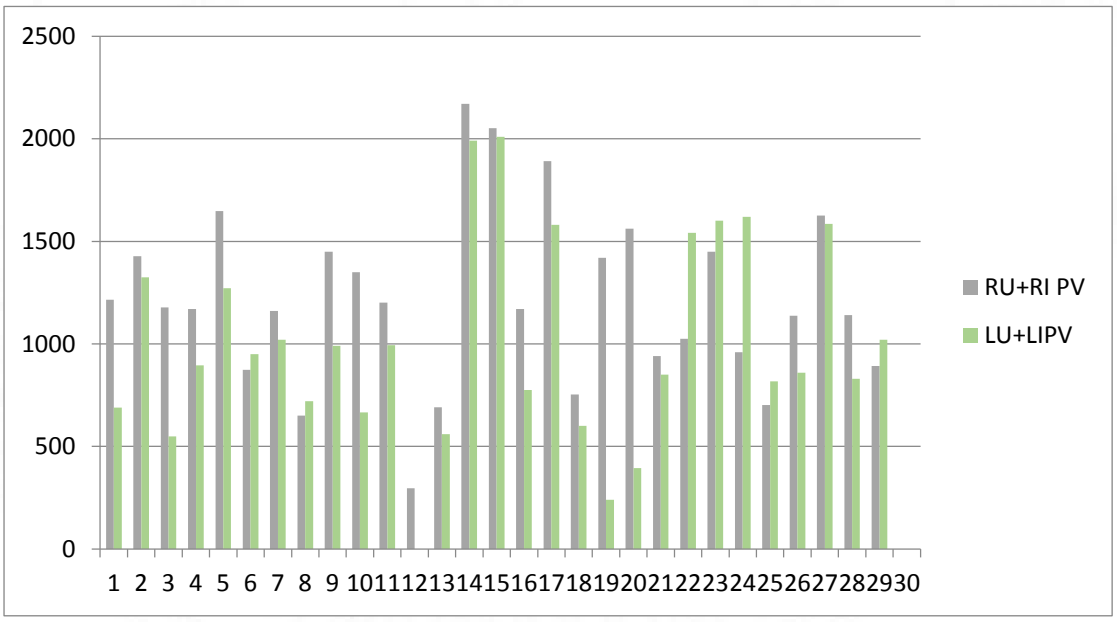


Figure 5.4. Bar chart comparing right & left pulmonary vein flows in the study population.

RU+RI PV- right upper & inferior pulmonary veins, LU+LI PV- left upper & inferior pulmonary veins. Pulmonary vein flow data was incomplete for 4 patients (Nos 8,12,19,30).

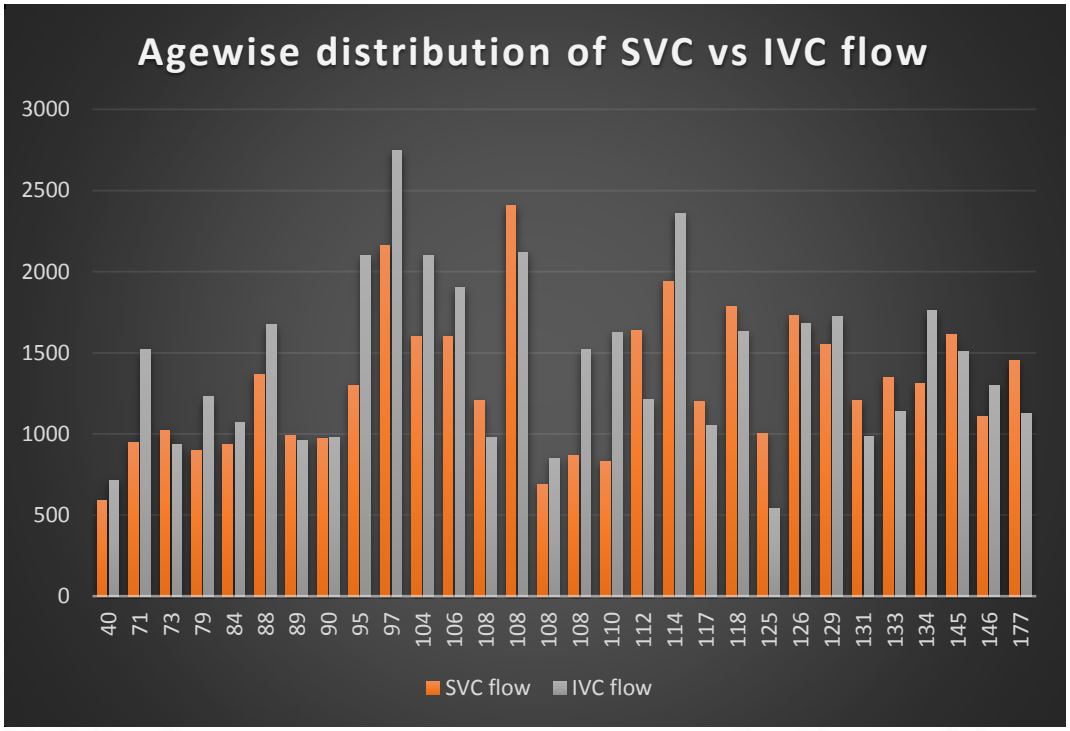


Figure 5.5. Bar chart depicting age-wise distribution of superior and inferior vena cavae flow.

SVC- Superior Vena Cava. IVC -Inferior Vena Cava. IVC flow was higher than SVC flow in all except 8 patients. No particular trend in the age-wise distribution of caval flows could be appreciated.

We assessed the correlation of pulmonary artery flows to the respective pulmonary vein flows. Pulmonary vein flows include collateral flow also and is expected to be higher than the respective pulmonary artery flows. This has been described in Table 5.9 and Figure 5.6. The mean difference (± SD) in pulmonary vein to pulmonary artery flows in the right & left lung were 490.58 (± 319.29)ml/min and 403.62 ± 363.30 ml/min respectively. There was a moderate correlation in the right-sided lung flows whereas there was a good correlation in the left-sided lung flows. Figure 5.7. depicts the Superior Vena Cava, total pulmonary artery and total pulmonary vein flows in each patient. Superior Vena Cava and total pulmonary artery flows are comparable. The magnitude of total pulmonary vein flows is higher as it includes collateral flows as well.

Table 5.8 Age-wise contribution of superior vena cava flow to the total caval flow. (n=30)

Age(months)	SVC/total caval flow
40	0.45
71	0.38
73	0.52
79	0.42
84	0.47
88	0.45
89	0.51
90	0.50
95	0.38
97	0.44
104	0.43
106	0.46
108	0.55
108	0.53
108	0.45
108	0.36
110	0.34
112	0.58
114	0.45
117	0.53
118	0.52
125	0.65
126	0.51
129	0.47
131	0.55
133	0.54
134	0.43
145	0.52
146	0.46
177	0.56
mean ± SD	0.48 ± 0.07

SVC- Superior Vena Cava

Table 5.9. Correlation of pulmonary artery flows to the respective pulmonary veins.

	Mean PA flow mean + SD (in ml/min)	Mean PV flow mean + SD (in ml/min)	Mean difference in flow per lung mean + SD (in ml/min)	Correlation coefficient	P value
Right sided	830.19 ± 317.57	1262.85 ± 391.25	490.58 ± 319.29	.388	0.05
Left sided	682.96 ± 277.93	1076.27 ± 449.18	403.62 ± 363.30	0.56	<0.01

PA- Pulmonary Artery. PV- pulmonary vein.

All variables expressed as Mean ± SD.

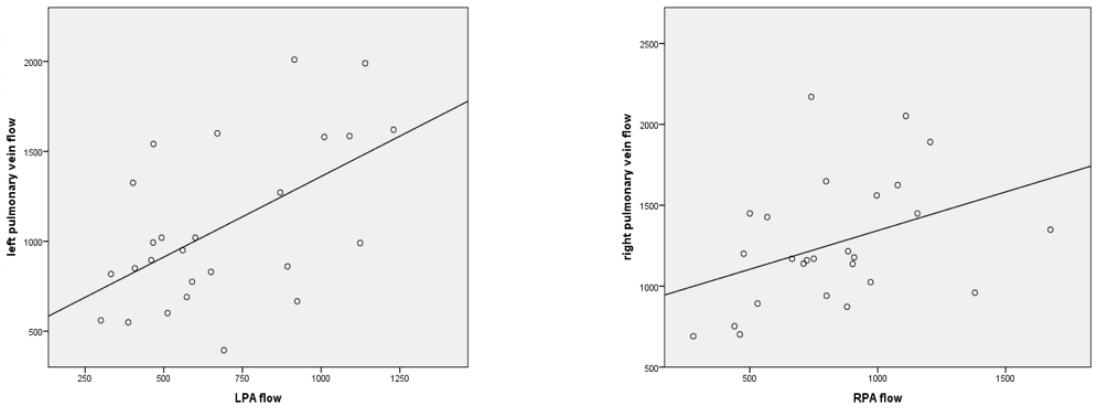


Figure 5.6. Scatter plot comparing pulmonary artery flows to the respective pulmonary vein flows in the study population. There was a moderate correlation in the right-sided lung flows whereas there was a good correlation in the left-sided lung flows.

RPA- right pulmonary Artery, LPA- left pulmonary Artery

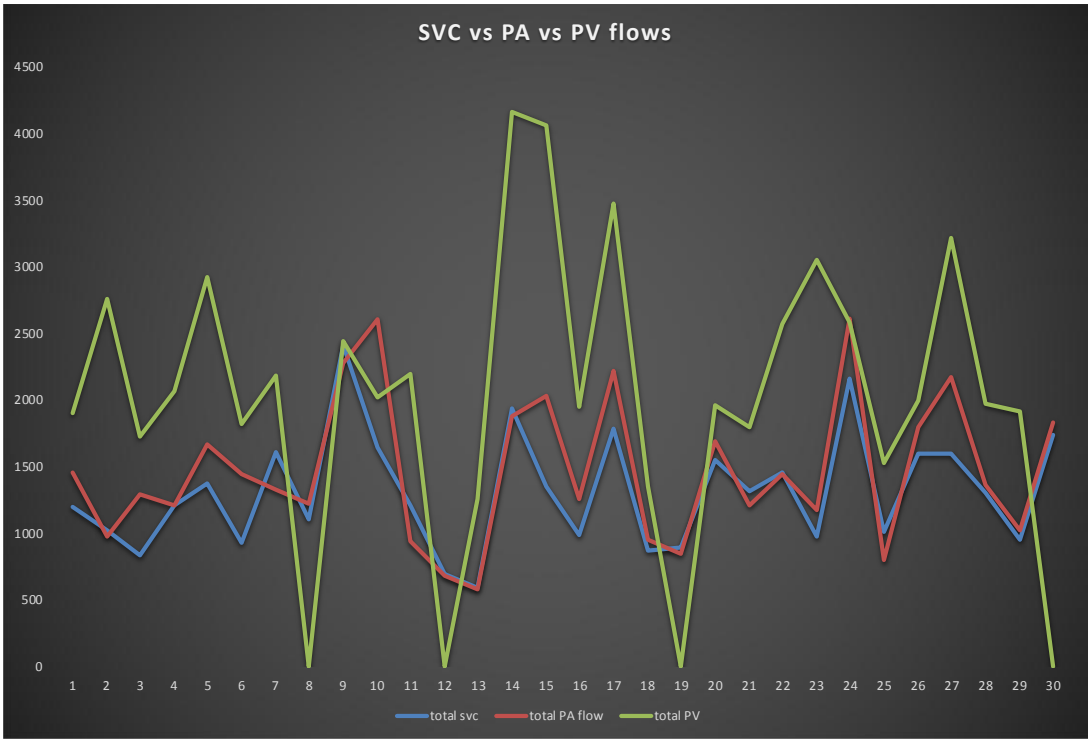


Figure 5.7. Line graph depicting the Superior Vena Cava, total pulmonary artery, and total pulmonary vein flows in the study population.

SVC- Superior Vena Cava. PV- Pulmonary vein, PA- Pulmonary Artery. Pulmonary vein flow data was incomplete for 4 patients (Nos 8,12,19,30).

Systemic and pulmonary blood flows were calculated using the formulae described before (See Materials & Methods). Tables 5.10 & 5.11 compares the values derived from catheterization and CMR and describes their correlation. CMR Qp was calculated using total SVC flows, total PA flows and as total PV flows. The first 2methods exclude the contribution of APC. CMR derived pulmonary flow, was numerically higher than catheterization derived values in most cases, especially when comparing using CMR derived total PV flows. Correlation between CMR & catheterization derived systemic and pulmonary flows were weak irrespective of formulae used (Figures 5.8, 5.9).

Table 5.10. Comparison of systemic and pulmonary blood flows measured from catheterization and CMR

Variable (ml/min)	Catheterisation Mean± SD		CMR Mean± SD		
Qp	conventional formula **Qp=** $\frac{\text{oxygen consumption}}{(\textbf{PVsat}-\textbf{PAsat})*\text{blood O2 content}}$	Alternate formula **Qp=** $\frac{\text{oxygen consumption}}{\textbf{2}(\textbf{PVsat}-\textbf{PAsat})*\text{blood O2 content}}$	total PV flow	Total SVC flows	Total PA flow
	1890.09 ± 599.10	945.04 ± 299.55	2339.12 ± 758.25	1309.50± 432.47	1513.15 ± 546.94
Qs	Salim et al. (22) **Qs=** $\frac{\text{oxygen consumption x } \textbf{PVsat} - \textbf{IVCsat}}{(\textbf{PVsat}-\textbf{PAsat})*(\textbf{Ao sat}-\textbf{IVCsat})*\text{blood O2 content}}$	conventional formula **Qs=** $\frac{\text{oxygen consumption}}{(\textbf{Aosat}-\textbf{MVsat})*\text{blood O2 content}}$	Total caval flow	total PV+IVC flow	Aortic flow
	4379.21 ± 1704.59	4192.21 ± 2198.92	2801.65 ± 903.06	3800.04 ± 1055.78	3097.62 ± 531.23

Qp-pulmonary flow, Qs-systemic flow. PA- Pulmonary Artery. PV- pulmonary vein. SVC- Superior Vena Cava. IVC -Inferior Vena Cava. CMR- cardiac magnetic resonance imaging.

All variables expressed as Mean ± SD.

Table 5.11. Correlation of systemic and pulmonary blood flows measured from catheterization and CMR

CMR derived Qp (total PV flow) n=26		
	cath Qp (conventional)	cath Qp **(**Alternate formula**)**
Pearson coefficient	-0.432	-0.432
P value	0.02	0.02
CMR derived Qp (total PA flow) n=30		
Pearson coefficient	-0.23	-0.23
P value	0.23	0.23
CMR derived Qp (total SVC flow) n=30		
Pearson coefficient	-0.23	-0.23
P value	0.23	0.23
CMR derived Qs (total caval flow) n=30		
	cath Qs (conventional)	cath Qs (Salim et al.) (22)
Pearson coefficient	-0.65	-0.18
P value	0.732	0.926
CMR derived Qs (aorta flow)) n=30		
Pearson coefficient	-0.05	-0.02
P value	0.80	0.93

Qp-pulmonary flow, Qs-systemic flow. PV- Pulmonary vein. CMR- cardiac magnetic resonance imaging. SVC- Superior Vena Cava. PA- Pulmonary Artery

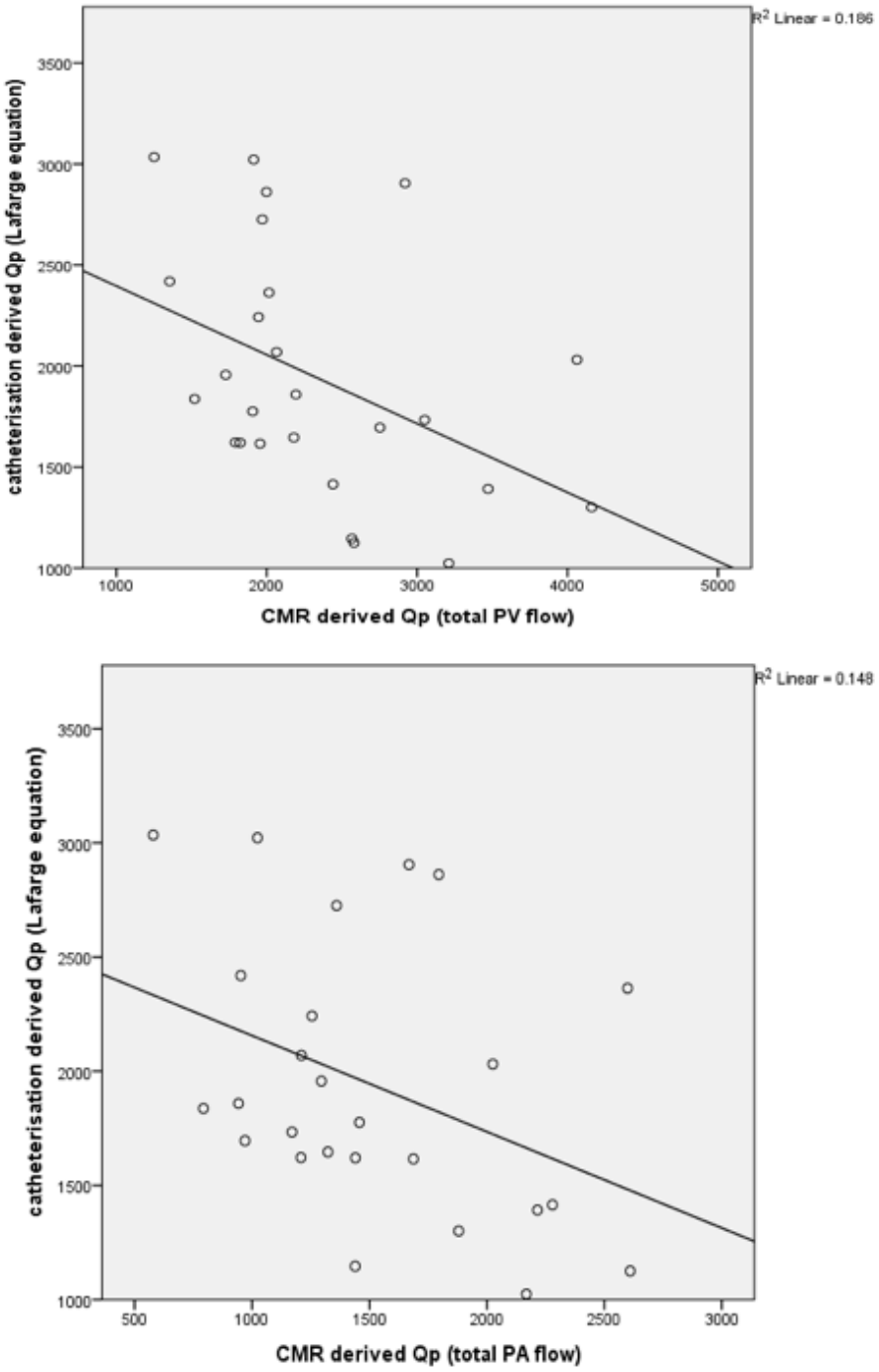


Figure 5.8. Scatter plot comparing pulmonary blood flows (Qp) measured from catheterization(conventional formula) and CMR (top-total PV flow, bottom – total PA flow) in the study population. There was a weak negative correlation between CMR derived Qp (total PV flow) and catheterization derived Qp.

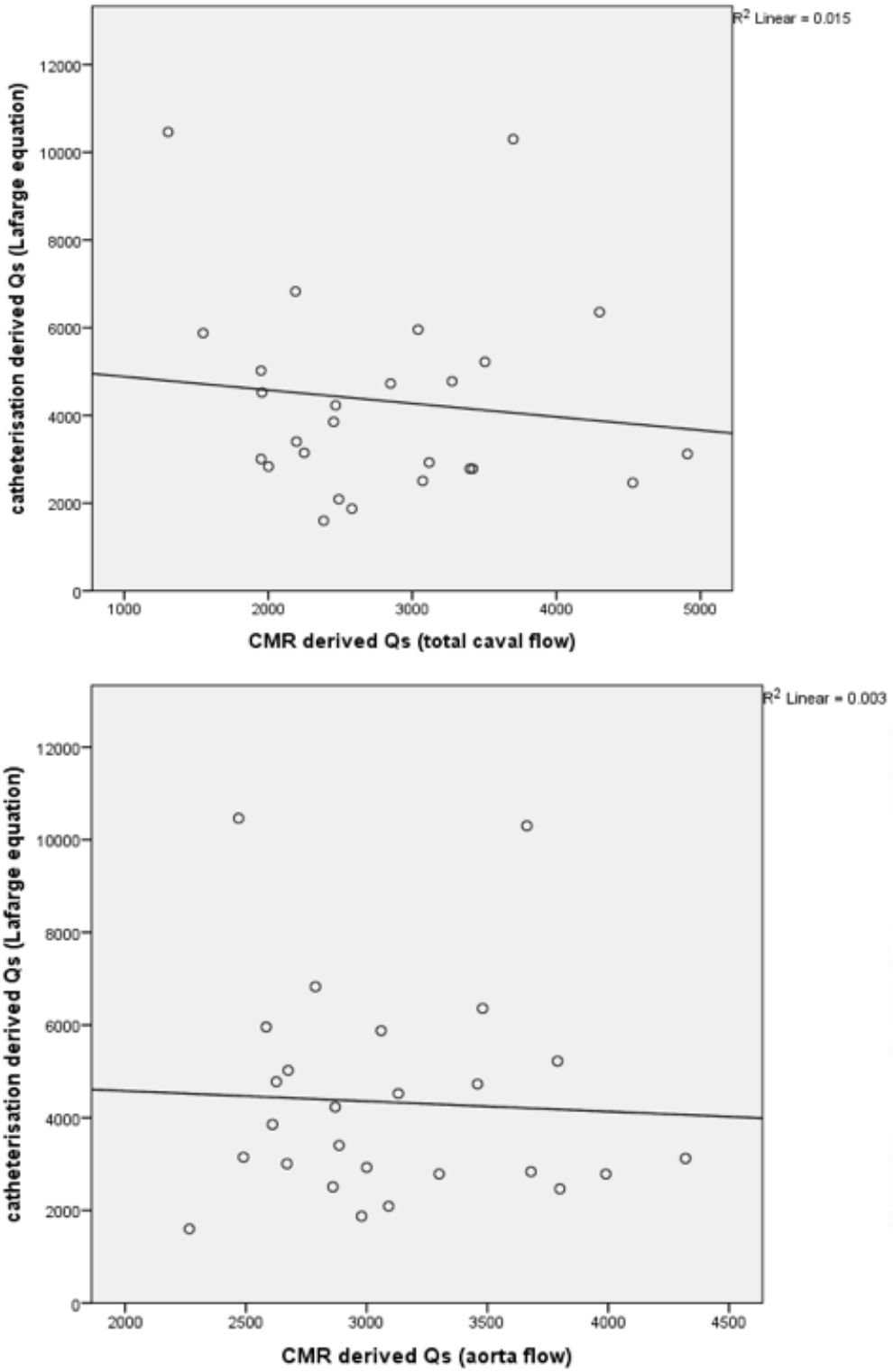


Figure 5.9. Scatter plot comparing systemic blood flows (Qs) measured from catheterization (conventional formula) and CMR (top-total caval flow, bottom – aortic flow) in the study population. There was no correlation between CMR derived Qs and catheterization derived Qs.

Qp/Qs derived from catheterization and CMR were compared using the different formulae described earlier. Tables 5.12 & 5.13 compares the values derived from catheterization and CMR and describes their correlation. CMR derived Qp/Qs was numerically higher than catheterization derived values when Qp was taken as total PV flow (which accounts for collateral flow as well) and their correlation is at best weak (that is when catheterization Qp/Qs is derived using Salim et al. formula). (Figure 5.10). When the other 2 formulae for CMR derived Qp/Qs (doesn't account for APC flow) was used the catheterization derived Qp/Qs & CMR derived Qp/Qs had numerically comparable means. However, there was no correlation between catheterization derived & CMR derived Qp/Qs.

Table 5.12. Comparison of Qp/Qs measured from catheterization and CMR

	Qp/Qs							
	Salim (22) $\frac{Qp}{Qs} = \frac{AO-IVC}{PV-IVC}$	Fang (52) $= \frac{AO-SVC}{PV-SVC}$	Downing (3) $= \frac{AO-SVC}{PV-PA}$	Conventional formula $= \frac{AO-MV}{(PV-PA)}$	Alternate formula $= \frac{AO-MV}{2(PV-PA)}$	MRI Qp/Qs = $\frac{PV\ flow}{SVC+IVC}$	MRI Qp/Qs = $\frac{RPA+LPA}{SVC+IVC}$	MRI Qp/Qs = $\frac{SVC}{SVC+IVC}$
Mean ± SD	0.47 ±0.13	0.48 ±0.17	0.63 ±0.18	0.54 ±0.28	0.31 ±0.09	0.88 ±0.30	0.54 ±0.12	0.48 ±0.07

Qp-pulmonary flow, Qs-systemic flow. SVC- Superior Vena Cava saturation, IVC- Inferior Vena Cava saturation, PV- Pulmonary vein saturation. PA- pulmonary Artery saturation, Ao- aorta saturation. All variables expressed as Mean ± SD.

Table 5.13. Correlation of Qp/Qs measured from catheterization and CMR

Cath Qp/QS		CMR Qp/Qs		
		$\frac{Total\ PV\ flow}{SVC+IVC}$	$\frac{RPA+LPA}{SVC+IVC}$	$\frac{Total\ SVC\ flow}{SVC+IVC}$
Salim et al.(22)	Pearson coefficient	0.229	0.138	0.149
	P value	0.260	0.468	0.432
Fang et al. (52)	Pearson coefficient	0.022	0.119	-0.175
	P value	0.915	0.532	0.355
Downing et al. (3)	Pearson coefficient	-0.055	0.107	-0.231
	P value	0.791	0.573	0.219
Alternate formula	Pearson coefficient	-0.055	0.107	-0.231
	P value	0.791	0.573	0.219
Conventional formula	Pearson coefficient	-0.059	-0.53	-0.282
	P value	0.775	0.782	0.131

Qp-pulmonary flow, Qs-systemic flow. SVC- Superior Vena Cava flow, IVC- Inferior Vena Cava flow, PV- Pulmonary vein flow. RPA- right pulmonary Artery flow. LPA- left pulmonary Artery flow

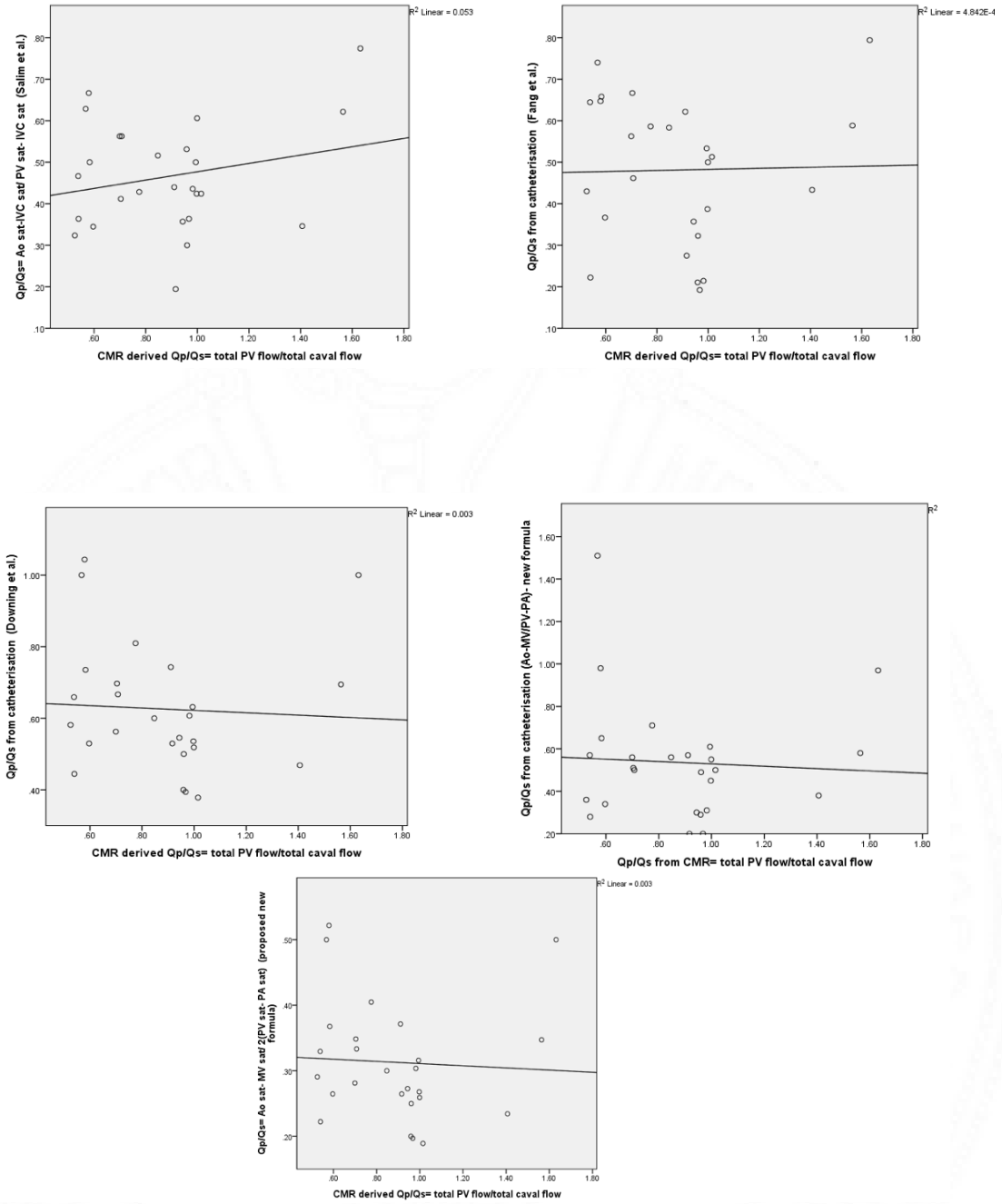


Figure 5.10. Scatter plot comparing Qp/Qs measured from catheterization (different formulae) and CMR derived Qp/Qs in the study population. There was no correlation between CMR-derived Qp/Qs and catheterization-derived Qp/Qs

The correlation of systemic saturation with other variables was studied (Table 5.13.). There was a good correlation of systemic saturation with catheterization-derived Qp/Qs (strongest correlation when Qp/Qs was calculated with Salim et al. formula). There was no correlation of systemic saturation with CMR derived Qp/Qs, SVC flow, or collateral flow. Systemic saturation also correlated moderately with IVC and Mean PA saturations.

Table 5.14. Correlation of systemic saturation (Aortic saturation) with other variables

Variables	Correlation coefficient Pearson r	P-value
SVC saturation	0.33	0.07
IVC saturation	0.55	<0.01
Mean PA saturation	0.51	<0.01
BDG pressures	-0.16	0.41
TPG	-0.13	0.50
SVC flow	-0.242	0.23
Cath Qp	0.27	0.182
MRI Qp(total PV flow)	-0.11	0.588
Average APCA flow (CMR derived)	-0.080	0.70
Qp/Qs		
Salim et al.(22)	0.70	<0.01
Fang et al.(52)	0.62	<0.01
Downing et al. (3)	0.47	<0.01
conventional MV formula	0.48	0.014
Alternate formula	0.47	0.015
CMR derived Qp/Qs	0.097	0.64

Qp-pulmonary flow, Qs-systemic flow. SVC-Superior Vena Cava, IVC- Inferior Vena Cava. BDG- bidirectional Glenn, PA- Pulmonary Artery. TPG- transpulmonary gradient. CMR/MRI- cardiac magnetic resonance imaging. APCA- aortopulmonary collateral.

The study population was divided into 2 based on an arbitrary cut-off value of Qp/Qs = 0.7 and the 2 groups, namely Qp/Qs ≥ 0.7 and Qp/Qs <0.7 were compared. Patients with CMRI derived Qp/Qs ≥ 0.7 had significantly higher systemic to pulmonary artery collateral flow when compared with those with Qp/Qs <0.7, but did not differ significantly in terms of other parameters (Table 5.15 - 5.17).

Table 5.15. Comparison of patients with CMRI derived Qp/Qs <0.7 with Qp/Qs ≥ 0.7

Variables	Qp/Qs <0.7 (n=7)	Qp/Qs ≥ 0.7 (n=19)	P VALUE
Age	111±15	107±30	0.75
BSA	0.96± 0.14	0.83± 0.18	0.11
HB	18.94 ±2.7	18.64±2.57	0.80
PCV	58.43 ±9.54	57.27± 8.85	0.77
CTR	49.86 ± 5.55	48.5 ±6.4	0.63
Aorta sat	82.71± 4.11	80.84± 5.05	0.35
SVC SAT	66.43± 5.53	65.79± 5.99	0.18
RPA SAT	66.14±11.18	65.47 ± 7.49	0.86
LPA SAT	70.86±11.05	66.8±5.89	0.24
IVC SAT	61.29± 10.64	66.32±5.71	0.96
Salim et al (22)	0.47 ± 0.14	0.46±0.13	0.23
Fang et al (52)	0.53±0.19	0.46±0.17	0.40
Downing et al (3)	0.71±0.23	0.59±0.15	0.14
Conventional formula	0.67±0.44	0.48±0.18	0.14
Alternate formula	0.36±0.11	0.30±0.07	0.138
Cath Qp	1969.16±687.41	1929.19±582.36	0.88
CMR Qp(total PV flow)	2012.57±406.78	2459.42±828.63	0.19
APCA flow	335.36± 118.53	878.03± 357.48	0.001

Qp-pulmonary flow, Qs-systemic flow. SVC- Superior Vena Cava, IVC- Inferior Vena Cava. BSA-body surface area. Hb- Hemoglobin. PCV- Packed cell volume. CTR- cardiothoracic ratio. RPA- right pulmonary Artery, LPA- left pulmonary Artery. Sat- saturation. BDG- bidirectional Glenn, PA-pulmonary Artery. TPG- transpulmonary gradient. CMR- cardiac magnetic resonance imaging. APCA-aortopulmonary collateral. .

Table 5.16. Characteristics of patients with CMRI derived Qp/Qs < 0.7 (n=7)

Sl no	age	BSA	HB	PCV	IVC sat	SVC sat	aorta sat	Salim et al (22)	Qp/Qs (Alternate formula)	CTR	CMR Qp/Qs	collateral comments	APCA flow CMR
1	97	1.12	23.1	71	57	63	74	0.32	0.36	56	0.53	no MAPCA /PAVM	310
2	108	0.89	16.3	50	54	69	83	0.47	0.57	58	0.54	multiple small, one 2.2mm APCA	445.5
3	104	0.79	21.7	70	79	75	83	0.36	0.28	44	0.54	no PAVM/ no APCA, trickle of APBF	120
4	108	1.16	18.1	54	46	61	83	0.63	1.51	45	0.57	no PAVM/collaterals, trickle of APBF	260.5
5	134	0.96	18.8	57	60	72	85	0.50	0.98	46	0.58	no MAPCA /PAVM	397.5
6	95	0.84	15.6	46	65	63	87	0.67	0.65	48	0.58	no PAVM/collaterals, trickle of APBF	355
7	129	0.95	19	61	68	62	84	0.34	0.34	52	0.60	small PAVM,	459
Mean ± SD	111 ± 15	0.96 ± 0.14	18.94 ± 2.7	58.43 ± 9.54	61.29 ± 10.64	66.43 ± 5.53	82.71 ± 4.11	0.47 ± 0.14	0.67 ± 0.44	49.86 ± 5.55	0.56 ± 0.03		335.36 ± 118.53

Qp-pulmonary flow, Qs-systemic flow. SVC- Superior Vena Cava, IVC- Inferior Vena Cava. BSA- body surface area. Hb- Hemoglobin. PCV- Packed cell volume. CTR- cardiothoracic ratio.. Sat- saturation. CMR- cardiac magnetic resonance imaging. APCA- aortopulmonary collateral. MAPCA-major aortopulmonary collateral. PAVM- pulmonary arteriovenous malformation. APBF- antegrade pulmonary blood flow

Table 5.17. Characteristics of patients with CMRI derived Qp/Qs ≥ 0.7 (n=19)

Sl no	age	BSA	HB	PCV	aorta sat	SVC sat	IVC sat	Salim et al (22)	Qp/Qs (Alternate formula)	CTR	CMR	collateral comments	APCA flow CMR(ml/min)
1	110	0.79	15.6	51	89	69	82	0.41	0.56	51	0.70	B/L- diffuse small PAVM	294
2	145	1.24	18.7	57	82	64	64	0.56	0.51	59	0.70	3-4 APCA	487
3	112	0.9	17.4	55.6	82	70	64	0.56	0.5	47	0.71	small PAVM,	597
4	71	0.6	16.8	47	78	61	69	0.43	0.71	50	0.78	multiple PAVM	646
5	117	0.75	16.8	51	83	62	67	0.52	0.56	43	0.85	multiple small collateral from DTA, no PAVM	344.5
6	84	0.8	17.5	53	83	60	72	0.44	0.57	47	0.91	no MAPCA /PAVM	1030.5
7	106	0.85	21.4	68	70	59	63	0.19	0.2	43	0.92	no MAPCA /PAVM	664
8	108	0.76	15.4	46	80	70	70	0.36	0.3	48	0.94	no MAPCA/PAVM	727
9	88	0.79	18.1	55	77	67	68	0.30	0.29	44	0.96	no MAPCA, small PAVM	853.5
10	40	0.54	15.8	48	82	78	65	0.53	0.49	53	0.96	no MAPCA, small PAVM	918.5
11	114	0.64	24.5	75	78	73	66	0.36	0.2	43	0.97	1 collateral (2.5mm)	1550
12	125	0.88	21.3	70	74	68	57	0.44	0.31	62	0.98	small collateral, trickle of apbf	1119.5
13	177	1.18	23.3	71	77	53	56	0.50	0.61	40	0.99	small PAVM,	762.5
14	131	0.98	20.8	66.5	86	73	66	0.61	0.45	57	1.00	small collaterals, trickle of APBF	971
15	89	0.72	17.1	52	79	67	65	0.42	0.55	54	1.00	no PAVM/collaterals, trickle of APBF	707.5
16	118	0.8	19.7	63	79	59	65	0.42	0.5	50	1.01	no MAPCA /PAVM	913
17	73	0.76	18.7	55	81	68	72	0.35	0.38	50	1.41	multiple APCA. no PAVM	1478
18	90	0.78	17.2	52	84	64	61	0.62	0.58	40	1.56	no MAPCA /PAVM	1300
19	133	1.07	18.1	52	92	65	68	0.77	0.97	41	1.63	small collaterals	1319
Mean ± SD	107 ± 30	0.83 ± 0.18	18.64 ± 2.57	57.27 ± 8.85	80.84 ± 5.05	65.79 ± 5.99	66.32 ± 5.71	0.46 ± 0.13	0.49 ± 0.18	48.5 ± 6.4	1.00 ± 0.26		878.03 ± 357.48

Qp-pulmonary flow, Qs-systemic flow. SVC- Superior Vena Cava, IVC- Inferior Vena Cava. BSA- body surface area. Hb- Hemoglobin. PCV- Packed cell volume. CTR- cardiothoracic ratio.. Sat- saturation. CMR- cardiac magnetic resonance imaging. APCA- aortopulmonary collateral. MAPCA-major aortopulmonary collateral. PAVM- pulmonary arteriovenous malformation. APBF- antegrade pulmonary blood flow

Indexed Pulmonary vascular resistance was calculated from isolated catheterisation data and combined CMR-cath data. It was seen that catheterisation derived PVRI was numerically higher than combined CMR-cath calculated PVRI (Table 5.18). PVRI greater than 3WUm^2 was seen in 3 when calculated from catheterisation data alone; while through combined CMR-cath data only 1 patient had a PVRI > 3WUm^2. There was a moderate correlation between PVRI derived through catheterisation and from combined CMR-cath data. (Table 5.19, figure 5.11). Table 5.20 lists out Qp, Qs and PVRI characteristics of the study population.

Table 5.18. Comparison of patients with CMRI derived PVRI with combined CMR-cath calculated PVRI

PVRI (WUm^2) from Oximetry (n=26)		**PVRI (WUm^2) combined CMR-cath formula (n=26)**
Conventional formula	**Alternate formula**	
1.88± 1.34 (Range- 0.53- 5.81)	3.77±2.51	1.44 (± 0.90) (Range- 0.27- 3.72)

All variables expressed as Mean± SD

PVRI -Indexed Pulmonary vascular resistance. CMR- cardiac magnetic resonance imaging.Cath- catheterisation.

Table 5.19. Correlation of catheterisation derived PVRI with combined cath-CMR derived PVRI

	Cath PVRI (Conventional)	**Cath PVRI (Alternate formula)**
Pearson coefficient	0.532	0.532
P value	<0.01	<0.01

PVRI -Indexed Pulmonary vascular resistance. CMR- cardiac magnetic resonance imaging. Cath- catheterisation.

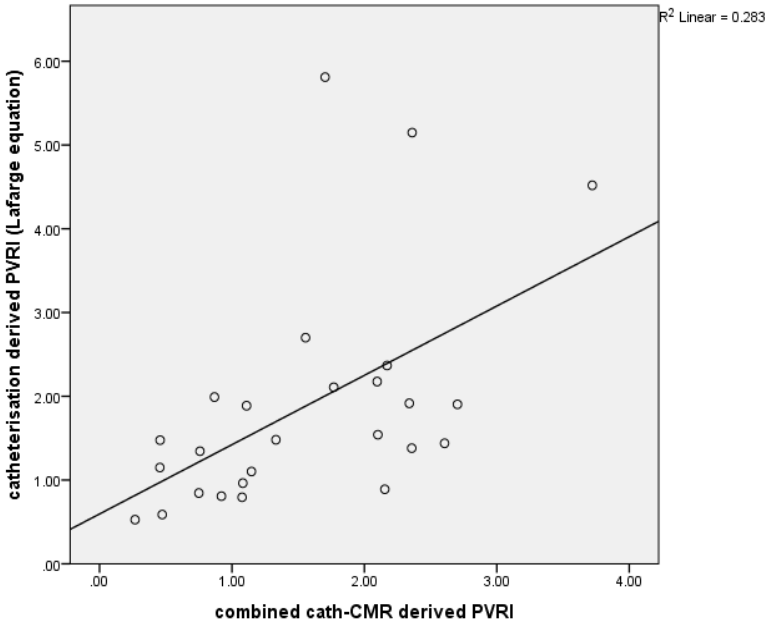


Figure 5.11. Scatter plot comparing catheterization calculated PVRI with combined CMR-cath calculated PVRI in the study population. There was a moderate correlation between the two. (Pearson r = 0.532, p value<0.01)

Table 5.19. Comparison of Qp, Qs and PVRI in the study population using different formulae (catheterisation & CMR)

sl no	Qp					Qs					PVRI	
	catheterisation		CMR			catheterisation		CMR				
	Qp conventional	Qp alternate formula	Qp= total PV flow	Qp= SVC flow	Qp= PA flows	Qs Salim et al. (22)	Qs conventional	Qs= SVC+IVC	Qs= total PV+IVC	aorta	cath	combined CMR-cath
1	1776	888	1906	1200	1457	3492	3147	2250	2956	2490	0.84	0.75
2	1696	848	2752	1024	970	4972	4522	1957	3685	3131	1.34	0.76
3	1957	978	1727	831	1295	4823	3855	2454	3350	2610	0.81	0.92
4	2069	1035	2065	1209	1210	5880	6828	2189	3045	2788	1.10	1.15
5	2905	1452	2919	1368	1668	9827	5958	3040	4591	2584	2.18	2.10
6	1621	810	1823	932	1440	3738	2836	2002	2893	3680	1.48	1.33
7	1647	823	2180	1612	1323	2971	2927	3117	3685	3000	4.52	3.72
8	947	474		1109	1219	2441	1619	2409		3100	2.41	
9	1415	707	2440	2410	2279	3077	2465	4530	4560	3800	1.89	1.11
10	2363	1182	2015	1639	2599	4264	4727	2849	3225	3459	1.90	2.70
11	1859	930	2194	1209	942	3113	3403	2196	3181	2886	2.11	1.77
12	1504	752		690	680	2963	2632	1539		2477	1.76	
13	3034	1517	1251	590	579	5797	10463	1305	1966	2470	0.89	2.15
14	1301	650	4160	1940	1880	3630	6358	4300	6520	3480	1.48	0.46
15	2031	1016	4062	1350	2025	2663	2089	2490	5202	3091	0.53	0.27
16	2242	1121	1945	990	1255	5364	5022	1950	2905	2675	0.96	1.08
17	1392	696	3471	1786	2215	3330	2784	3420	5105	3990	1.15	0.46
18	2419	1209	1354	867	952	3906	1601	2385	2872	2266	1.44	2.61
19	1483	742		896	849	5475	4747	2126		2800	1.35	
20	1616	808	1955	1553	1687	4757	4779	3276	3678	2626	0.59	0.47
21	1622	811	1791	1310	1208	3292	2507	3072	3553	2860	2.37	2.17
22	1146	573	2566	1454	1439	2326	1873	2581	3693	2979	5.15	2.36
23	1734	867	3050	970	1170	2831	3008	1950	4030	2670	2.70	1.56
24	1125	563	2580	2160	2610	3530	3121	4910	5330	4320	1.99	0.87
25	1837	919	1520	1005	793	4277	5878	1548	2063	3060	1.92	2.34
26	2861	1431	1998	1600	1795	7986	10301	3700	4098	3663	1.38	2.36
27	1024	512	3210	1600	2168	5345	5223	3504	5114	3790	5.81	1.70
28	2726	1363	1970	1300	1360	4149	2786	3400	4070	3300	1.54	2.10
29	3022	1511	1913	950	1023	7157	4231	2468	3431	2870	0.79	1.08
30	2329	1165		1731	1833	4000	4076	3409		2950	2.19	

Qp-pulmonary flow, Qs-systemic flow. SVC- Superior Vena Cava, IVC- Inferior Vena Cava. PV- pulmonary vein. CMR- cardiac magnetic resonance imaging. APCA- aortopulmonary collateral. PVRI -Indexed Pulmonary vascular resistance. Cath- catheterisation.

DISCUSSION

We compared Qp, Qs, and Qp/Qs calculated from Fick-principle based cardiac catheterization to phase-contrast CMR derived measurements of the same in 30 BDGS patients using different formulae. Fick's principle assumes a steady state, representative of the patient's baseline level of activity, throughout the study. This is not true of a patient under sedation & general anesthesia. Oxygen consumption, the numerator in Fick's formula, is cumbersome to quantify & hence is often adopted from weight & age-based charts. This too, introduces a certain quantum of error in the calculations.(35,36) Hence often, Qp/Qs is calculated eliminating the need for calculating oxygen consumption. Additionally, applying Fick's principle in BDGS physiology is wrought with innate difficulties of imprecise knowledge about the best site for obtaining a mixed venous sample. This is because the superior and inferior vena caval circuits are separate; additional sources of pulmonary blood flow, that is APC are not adequately accounted for. Saturations measured are also vulnerable to streaming effects of blood. Fick's principle reflects the effective pulmonary blood flow, thereby resulting in an underestimation of true Qp in patients with APC. However, cardiac catheterisation allows measurement of pressures in different chambers directly, thereby having good accuracy. It also allows for interventions like APC coiling in the same sitting. (3,21,41,74). It also has the twin risks of being invasive and of radiation exposure. PC MRI for flow estimation is limited by spatial resolution, especially in vessels with low-frequency flows and small calibre like pulmonary veins. Accuracy of flow data also depends on operator expertise as it is heavily dependent on selecting a plane perpendicular to the vessel of interest & selecting an optimal encoding velocity. (5)

The mean (± SD) age of the study population was 108.83 (± 26.72) months with a mean (± SD) age at BDGS surgery of 21.43 (± 19.08) months. The majority of the population was comprised of Tricuspid atresia with Ventricular septal defect with pulmonary stenosis (43.33%). They had undergone cardiac catheterization and CMR as part of evaluation to determine candidacy for Fontan surgery. The baseline aortic saturation was 81 (± 5)% with a mean SVC saturation of 64 (± 8)%. The mean BDG pressure, LV end-diastolic pressure & transpulmonary gradient were 11.93 ± 2.77

mmHg, 9.9 ± 2.54 mmHg and 3.77± 1.74 mmHg respectively. Antegrade pulmonary blood flow was preserved in 20% and 40% had evidence of aortopulmonary collateral on angiography. Eight patients had PAVM.

Internal validation of CMRI flow data was carried out by comparing aortic flow to the total caval flow, which showed a good correlation of r= 0.681 ($p<0.01$). A previous unpublished study from our centre which compared Qp/Qs from oximetry to PC MRI in simple shunt lesions had found a good correlation between the two modalities(r= 0.77) ($p<0.01$).(75) The mean (± SD) superior vena cava flow to the total caval flow in our study population was 0.48 (± 0.07) with no particular trend in the age-wise contribution of superior vena cava flow to the total caval flow. Houlind et al.(24) had studied 7 TCPC patients with a mean age of 9 years, they had concluded that SVC & IVC flows are similar in this population as estimated by non sedated CMR studies. Similar results were obtained by Hjortdal et al.(76) in their CMR based study estimating flows in rest & exercise in 11 TCPC patients. However, Whitehead et al.(25) found the IVC fraction to be a function of age & BSA in his study of 105 Fontan patients. This was in agreement with the findings of Pederson et al. (77). This apparent discrepancy in the available data may be attributable to the baseline state of the study subjects. General anesthesia and sedation are known to lower cerebral oxygen consumption while hypercarbia, acid-base imbalance, supplemental oxygen, etc alter pulmonary resistance. Downing et al. found that SVC flow is usually in excess of the upper body oxygen demand. (3). Bilateral lung flows were compared and it was seen that the right lung has relatively higher flows. Similar findings were obtained by Whitehead et al.(25). In our study, it was seen that superior vena caval flows were comparable to total pulmonary artery flows. Intuitively, ipsilateral pulmonary vein flows were much higher in magnitude, as they include collateral flow as well. Similarly, CMR derived Qp, was significantly higher than catheterization derived Qp when CMR Qp was calculated as total PV flows. It was seen that estimation of Qp by the formula put forward by Salim et al.(22) was numerically closer to CMR derived Qp by total PA flows than the alternate formula. Qs was calculated from both oximetry & cardiac catheterisation using different formulae previously described. With regard to estimation of Qs, conventional formula (which uses calculated mixed venous saturation) was much more closer to CMR derived values of Qs, especially when Qs was calculated as a sum of total PV & IVC flow. It

was seen that correlation between CMR & catheterization-derived systemic and pulmonary flows was weak irrespective of the formulae used. The findings of our study are consistent with previous studies, in that the cath derived Qs is an overestimation when compared with CMR derived Qs, irrespective of the formula used. It is also important to note that Downing et al. (3) had calculated a median total oxygen consumption of 173 mL/min per m^2 using data from CMR and oximetry in their study population as opposed to the assumed MVO_2 values of 160 (130–190) mL/min per m^2 which was used in catheterisation derived flow calculations. This suggests that the error in assumed MVO2 may be significant and may lead to underestimation of flows by Fick principle-based formulae. Table 6.1 & 6.2 compares similar previous studies in the BDGS population comparing CMR and cardiac catheterisation derived Qp & Qs.

Table 6.1 Comparison of pulmonary blood flows measured from catheterization and CMR

Author	No of subjects	Age	Qp cath	Qp CMR	Pearson r	P-value
Our Study	26	108.83 (± 26.72) mo	1890.09±599.10 (ml/min)	2339.12±758.25 (ml/min)	-0.432	0.02
Downing et al. (3)	30	2.6 y (11 mo–7 y)	2.3 ± 0.6 (L/min/m^2)	3.4±0.8 (L/min/m^2)	0.57	0.22
Hart et al. (74)	(N=16 pre BDG & 10 post BDG)	0.6 (0.4-1.7) years			0.04	0.86

Qp- pulmonary blood flow, Qs- systemic blood flow, BDG- Bidirectional Glenn

Table 6.2 Comparison of systemic blood flows measured from catheterization and CMR

Author	No	age	Qs cath	Qs CMR	Pearson r	P value
Our Study	26	108.83 (± 26.72) mo	4192.21±2198.92 (ml/min)	2801.65±903.06 (ml/min)	-0.12	0.55
Downing et al. (3)	30	2.6 y (11 mo–7 y)	3.8 ± 1.0 ($L/min/m^2$)	3.3 ±0.8 ($L/min/m^2$)	0.29	0.24
Hart et al. (74)	16 pre BDG 10 post BDG)	0.6 (0.4-1.7) years			0.44	0.02

Qp- pulmonary blood flow, Qs- systemic blood flow, BDG- Bidirectional Glenn , CMR-cardiac magnetic resonance imaging

Qp/Qs was calculated from CMR and catheterisation data separately using previously described formulae & using various combinations of Qp & Qs. These were then assessed for correlation. As discussed above, catheterisation derived Qp and Qs varied from CMR derived corresponding values in opposite direction. None of the Qp/Qs values was ≥1 when calculated by catheterisation. In contrast, CMR derived Qp/Qs often exceeded 1. It was seen that Qp/Qs calculated from all the 4 established Fick-principle-based formulae had comparable values. The exception was the Alternate formula which had a Mean(± SD) Qp/Qs of 0.31 ±0.09 with few values as low as 0.20. Such low values of Qp/Qs are non-physiological and unlikely to support survival in the BDGS circuit. Hence, it appears that assuming a separate oxygen consumption for the upper body circulation traversed by SVC flows to estimate Qp & Qp/Qs may not be prudent or relevant. Table 6.3 & 6.4 compares Qp/Qs derived by the 2 modalities across previous similar studies in BDGS population comparing CMR and cardiac catheterisation derived Qp & Qs. No correlation was seen between Qp/Qs by cardiac catheterisation with that derived from PC MRI in post-BDGS patients.

Table 6.3 Comparison of Qp/Qs measured from catheterization and CMR

Author	N	age	Formula used	Qp/Qs from cath	Qp/Qs from CMR	Collateral flow from CMR
Our Study	26	108.83 (± 26.72) mo	Salim et al. (22) Qp= AO-IVC / Qs PV-IVC	0.47±0.13	0.88±0.30	411.11± 169.03 ml/min (IQR 409.5-957.9) ml/min
			Fang et al. (52) Qp= AO-SVC / Qs PV-SVC	0.48±0.17		
			Downing et al. (3) Qp= AO-SVC / Qs PV-PA	0.63±0.18		
			Conventional Qp= AO-MV / Qs (PV-PA)	0.54±0.28		
			Alternate formula Qp= AO-MV / Qs 2(PV-PA)	0.31±0.09		
Downing et al. (3)	30	2.6 y (11 mo–7 y)	Qp= Ao-MV / Qs PV-PA	0.6 (0.4-0.8)	1.1 (0.5-1.6)	
Grosse-Wortmann et al. (56)	16	44.4 (14.2-154.9) months	$Q_{APC}=Q_P-Q_{PA}$		0.93±0.26	1.42(0.58- 3.83) L/min/m^2
Hart et al. (74)	(N=16 pre BDG & 10 post BDG)	0.6 (0.4-1.7) years				1.81 ± 0.59 L/min/m^2 in post BDG pts

Qp/Qs-Ratio of pulmonary blood flow to systemic blood flow, BDG- Bidirectional Glenn. SVC-Superior Vena Cava saturation, IVC- Inferior Vena Cava saturation, PV- Pulmonary vein saturation. PA- pulmonary Artery saturation, Ao- aorta saturation. Q_{APC}- collateral flow. Q_{PA}-flow in pulmonary artery. IQR- interquartile range

Table 6.4 Correlation of Qp/Qs measured from catheterization and CMR

Correlation coefficient	Salim et al. (22)	Fang et al. (52)	Downing et al. (3)	Alternate formula	Conventional formula
	Current study (n=26)				
Pearson r	0.229	0.022	-0.055	-0.055	-0.059
P VALUE	.260	.915	.791	.791	.775
	Downing et al. study (n=30) (3)		Hart et al.(74) (N=16 pre BDG & 10 post BDG)		
Pearson r	0.08		0.48		
Pc	0.01		0.02		

Qp/Qs-Ratio of pulmonary blood flow to systemic blood flow, BDG- Bidirectional Glenn.

On comparison of patients with CMR derived Qp/Qs ≥ 0.7 with Qp/Qs <0.7, they had a mean (± SD) APC flow of 878.03 (± 357.48)ml/min vs 335.36 (± 118.53)ml/min ($p<0.01$). However the 2 subgroups did not differ significantly in terms of other parameters including age, BSA, Hb, PCV, CTR, saturations in Aorta, SVC, RPA, LPA and IVC, and cath derived Qp/Qs, cath Qp, CMR Qp.

We looked at different variables affecting systemic saturation. Aortic saturation correlated moderately with Mean PA and IVC saturation and correlated best with catheterisation derived Qp/Qs (particularly when Salim et al. (22) formula was; a correlation coefficient of 0.70 $p <0.01$). However, this is not true of MRI-derived Qp/Qs. This may be explained by the fact that catheterization Qp/Qs looked at effective pulmonary blood flow whereas MRI gave total pulmonary blood flow with is inclusive of collateral flow (which is wasted circulation & represents left to right shunt). There was no correlation between BDG pressures or transpulmonary gradient with aortic saturation. Neither did SVC flows, APC flows or catheterisation derived Qp dictate systemic saturation. Poor correlation with SVC flows & catheterization-derived Qp may be due to the dependence of systemic saturation on a multitude of other parameters like BSA, PVR, effective PBF, etc. The presence of a venovenous collateral shunting blood away from lungs into the systemic venous circulation (IVC) or cardiac chamber(atria); serves as a right to left shunt. It doesn't take part in oxygenation. Errors in estimated body oxygen consumption may also be contributory.

Comparison of PVRI estimated from oximetry with combined CMR-cath formula resulted in higher PVRI values when determined from catheterisation data alone. Catheterisation derived PVRI from conventional formula recorded a PVRI> 3 WUm^2 in 3 patients with highest PVRI recorded being 5.81 WUm^2. On the other hand, only one patient had a PVRI> 3 WUm^2 (3.72 WUm^2) in the combined CMR-cath group. This was consistent with the findings of previous authors (3,74). This is illustrated in Table 6.5. The clinical implication of this finding is that patients may be precluded from Fontan surgery if catheterisation data is the sole determinant for surgery. Hence, we are in agreement with the previous investigators and support a combined cath- CMR based approach for the best physiological characterisation of this patient cohort.

Table 6.5. Correlation of Qp/Qs measured from catheterization and CMR

Author	**PVRI (WUm^2)* Oximetry**	**PVRI (WUm^2)* combined CMR-cath formula (n=26)**
	conventional	
Current study (n=26)	1.88 ± 1.34	1.44 (± 0.90) (IQR- 0.84-2.21)
Downing et al. (n=30) (3)	2.0 (0.8-5.6)	1.1 (0.6 –3.7)

PVRI -Indexed Pulmonary vascular resistance. CMR- cardiac magnetic resonance imaging.
Cath- catheterisation. Qp/Qs-Ratio of pulmonary blood flow to systemic blood flow. IQR- interquartile range

LIMITATIONS

This study was limited by its small sample size and single-center study design. Given the COVID 19 pandemic & lockdown, elective admissions were reduced and deferred, resulting in fewer case enrollments and a longer delay between CMRI & cardiac catheterization.

Antegrade PBF was preserved in 20% of our patients; in the presence of antegrade PBF (Qp in this subset is PV flow + a fraction of IVC flow); values may not be reliable as factors such as streaming, degree of mixing come into play. Bilateral Glenn shunt was present in 30% of our patients- here also oximetry may be coloured by streaming & degree of mixing.

Mean time elapsed between CMR & cardiac catheterisation was 130 days. Sources of PBF may have changed over time secondary to collateral vessel formation.

All patients received general anesthesia during cardiac catheterization but only 43.33% received general anesthesia during CMR. Hence SVC, IVC, saturations might have been altered. Eight patients received supplemental oxygen during general anesthesia which also might have altered the flows & saturation.

PC MRI for flow estimation is limited by spatial resolution, especially in low-frequency flow vessels with small calibre like pulmonary veins. Motion artefacts and respiratory flow variations may also interfere with CMR readings.

Oximetry is limited by multiple assumptions involved & potential sources of error.

Intra-observer and inter-observer variability in the quantification of flow by PC MRI was not performed thereby raising concerns about the reproducibility of the measurements.

CONCLUSIONS

- Qp from PC MRI is consistently higher than Qp by cardiac catheterization while the opposite is true for Qs
- Qp/Qs derived from PC MRI is consistently higher than Qp/Qs by cardiac catheterization
- In this study, there was no correlation between Qp, Qs, Qp/Qs and PVRI by cardiac catheterisation with that derived from PC MRI
- Amongst different Fick-principle-based formulae for estimating catheterisation derived Qp/Qs, the best correlation (though weak) with CMR Qp/Qs was with Salim et al. formula. Qp/Qs using other formulae were comparable in magnitude with each other. This suggests that conventional mixed venous formula might also be used in this population for estimating Qp/Qs. However, it appears that assuming a separate oxygen consumption for the upper body circulation traversed by SVC flows to estimate Qp & Qp/Qs may not be prudent or relevant. Hence we abandon the alternate formula to calculate Qp & Qp/Qs.
- PVRI calculated from catheterisation data alone is an overestimate when compared to PVRI calculated from the combined CMR-cath formula. This is due to the numerically lower values of Qp derived from oximetry when compared to CMR values. This is especially true when CMR-derived Qp (total PV flow) is higher which might be indicative of higher collateral flows.
- Patients with CMRI derived Qp/Qs ≥ 0.7 had significantly higher systemic to pulmonary artery collateral flow when compared with those with Qp/Qs <0.7, but did not differ significantly in terms of other parameters
- In our study, aortic saturation reflects Qp/Qs (as derived by catheterisation) and not SVC or collateral flow. Mean PA and IVC saturation also moderately correlated with aortic saturation.

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श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
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Institutional Ethics Committee
(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1337/FEBRUARY-2019 11.11.2020

Dr. Gayathri Bhuvaneswaran Kartha
Resident
Department of Cardiology
SCTIMST, Thiruvananthapuram

Dear Dr. Gayathri Bhuvaneswaran Kartha,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "COMPARISON OF OXIMETRY WITH CARDIAC MAGNETIC RESONANCE IMAGING FOR ESTIMATION OF FLOW IN BIDIRECTIONAL GLENN SHUNT (IEC/1337)" on 16th February, 2019.

The following documents were reviewed:

Original submission

1. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 27.01.2019 with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Patient Information Sheet and Consent Form in English and Malayalam*
7. *CV of Principal Investigator and Co- Principal Investigators*

Revised submission

1. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 06.11.2020 with checklist*
2. *TAC Approval Letter*
3. *Revised IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Patient Information Sheet in England*
7. *Patient Information Sheet in Malayalam*
8. *Consent Form in English*
9. *Consent Form in Malayalam*
10. *CV of Principal Investigator and Co- Principal Investigators*
11. *Declaration Form*

The following members of the Ethics Committee were present at the meeting held on 16th February, 2019 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. Rema M. N	MD	Female	Basic Medical Scientist	No
3.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
4.	Dr. Harikrishna Varma PR	Ph.D(Materials Science)	Male	Medical Technology	Yes
5.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
6.	Dr. S S Giri Sankar	LL.M. Ph.D.	Male	Legal Expert	No
7.	Dr. Aneesh V Pillai	BA. LLB (Hons.), LLM, Ph. D, SET (Law)	Male	Legal Expert	No
8.	Dr. P. Manickam	BSMS, MSc (Epid).,PhD	Male	Health Science Expert/ Social Scientist	No
9.	Mr. Satheesh Chandran	MSW, PGDPM	Male	Lay person/ NGO/ Social Scientist	No
10.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
11.	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

STUDY PROFORMA

Name	Hospital number	Age
Gender	Weight	Height
BSA		
Diagnosis		

Age at BDGS YEAR OF BDG

Type of BDG(BDG, B/L, Hemifontan)

Systemic ventricle(right, left, both)

Time from BDGS to cardiac catheterization

Time from BDGS to CMRI

Hemoglobin

GA during CMRI

CARDIAC CATHETERIZATION

Angiography

Variable	n
Aortopulmonary collateral	
PAVM	
Preserved antegrade pulmonary blood flow	
Veno venous collateral	

oximetry:

Sample	spO2
SVC	
IVC	
RPA	
LPA	
RUPV	
LUPV	
AORTA	

PRESSURES

CHAMBER	PRESSURES
SVC	
RPA	
LPA	
LA	
RA	
LV	
AORTA	

CMRI:

FLOW ESTIMATION:

PAs, PVs, SVC, IVC and aorta to measure flows

CHAMBER	FLOW
SVC	
IVC	
RPA	
LPA MPA	
RIGHT 1)UPV 2)MPV 3)LPV	
Left 1)UPV 2)MPV 3)LPV	
AORTA	

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY, THIRUVANANATHAPURAM, KERALA 695011

Patient information sheet

Title Of The Study:

Comparison of oximetry with Cardiac Magnetic resonance imaging for estimation of flow in bidirectional Glenn shunt

Name Of The Investigators:

Dr Gayathri Bhuvaneswaran Kartha, Dr Ajit Kumar V.K., Dr Abhilash S.P., Dr Anoop A.

Dear Patient/Parent,

You/your child is being invited to participate in our study on Comparison of oximetry with Cardiac Magnetic resonance imaging for estimation of flow in patients with bidirectional Glenn shunt. Before you agree to participate in this study, you should take some time to read this sheet carefully and understand it completely. Ask any questions that you have about the study and the content of this sheet to your doctor without any hesitation. You can discuss this with your family members also. Take sufficient time to decide whether or not to take part in this study. Disagreeing to participate in this study will not result in apying any fine or losing any benefits which you are otherwise entitled to. Your decisin to participate or not to participate will not make any change in your relation with your study doctor or any other doctor.

What will be done in this study?

As per the current clinical practice, patients with bidirectional Glenn shunt undergo evaluation by cardiac catheterization and cardiac MRI (CMRI) for delineation of cardiac anatomy, oximetry and hemodynamics before the next stage of treatment. You/your child will undergo CMRI & cardiac catheterisation through which operabililty can be determined. Accordingly if deemed operable, patient will be referred for surgery. If assessment reveals in-operability, patient will be prescribed appropriate medications and reassessed on follow up as per hospital protocol. We will be recording data from each of the above steps for analysis.

Any additional test will be conducted?

This study doesnot involve any additional pricks, blood tests or invasive procedures.

Will you have to pay for the study?

You will not have any added expenses for participating in this study

Will the participation in the study delay your treatment?

Participation in this study would not delay your treatment including intervention/surgery

Is there any adverse events in participating in this study.

Adverse events are those associated with cardiac catheterization and CMRI like access site hematoma, allergic reaction to the contrast agent & hypovolemia. There is no added side effect incurred through participating in this study.

Can you withdraw from this study after it starts?

Your participation 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 treatment at this hospital, including intervention/surgery in any way.

Will your personal details be kept confidential?

The results of this study will be used for thesis submission as a part of academic research and will be submitted to a medical journal for publication. You will not be identified by name in any publication or presentation of results.

What happens after the study is over?

You may or may not benefit from the study that you are participating. Once the study is over, in future it may be of help in deciding management of similar patients.

If you have any further questions, please contact :**Dr Gayathri Bhuvaneswaran Kartha (Principal Investigator), Senior Resident, Department of Cardiology, SCTIMST (Email:drgayathri@sctimst.ac.in, mobile number:8870069729)**

For any technical clarifictions, please contact **Dr Mala Ramanathan, Member secretary, IEC, SCTIMST & Additional Professor, AMCHSS, SCTIMST (email: iec.mem.sec@sctimst.ac.in, Phone no:0471-2524-234)**

CONSENT FORM

Title of the study:

Comparison of Oximetry with Cardiac Magnetic resonance imaging for estimation of flow in bidirectional Glenn shunt

Participant's name:

Age (in years):

I_____, father/mother/legal guardian of _____ declare that (Please tick boxes)

• I have read the above information provided to me regarding the study. **[ ]**

• I have clarified any doubts that I had. [ ]

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

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

• I understand that my identity will not be revealed in any information released to third parties or in publication of study results. [ ]

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

- I understand that participation in the study means that I am willing to undergo the said procedure as already explained and my health records shall be accessed by the investigators for the purpose of the study. [ ]
- I understand that I do not have to bear any extra expense for the purpose of this study. No financial support will be provided to me for participation in the study. []
- I have been provided with the contact numbers of the principle investigator, in case I want to know more about the study and participants rights [ ].

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

Name:

Signature:

Relation to participant:

Name of witness:

Signature:

Relation to participant:

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 all questions asked were answered.

Name:

Signature:

Date:

Place: SCTIMST, Thiruvananthapuram

Principal investigator

Dr. Gayathri Bhuvaneswaran Kartha

SreeChitra Quarters, Kumarapuram

Trivandrum

Mobile. 08870069729

Date -

Study Independent Contact Person

Dr. K Shivakumar

0471-2524593

MASTER CHART

sl no	gender 1.f 2.m	age cath	lafarge mvo2	weight	height	bsa	hb	pcv	diagnosis	diagnosis types	PA PLASTY 1Y 2N	YEAR OF BDG	age at bdgs months	type of bdg 1. left 2. right 3. b/l	systemic ventricle 1. right 2.left 3. bicentricular	number of sorces of pbf	sorces of pbf COMMENTS	cath date
1	2	117	142	17	119	0.75	16.8	51	TA VSD PS p/bdg 2009	1		12.10.09	5	1	2			21.3.19
2	1	73	138	19.9	104	0.76	18.7	55	UNBAL AVCD PULM ATRESIA PDA MAPCA TO LPA P/BDG 2016	2		27.5.2016	20	2	1			14.10.2020
3	1	110	137	18.2	123	0.79	15.6	51	UNBAL AVCD SEV PSP/BTS+PDA INTER 2009P/B/L BDG 2012	2		22.2.2012	29	3	1			2.1.2019
4	2	108	143	18	117	0.76	15.4	46	TA REST VSD PS P/BDG	1		20.10.2010	3	2	2	BDG		4.7.2019
5	2	88	143	19.6	113.5	0.79	18.1	55	TA REST VSD PS P/BDG	1		23.4.2012	12	2	2		APCA ?PAVM(CT NO PAVM) BDG	29.8.2018
6	1	84	135	19.9	115.5	0.80	17.5	53	TA VSD PS P/BDG 2012	1	2	11.12.2012	68	2	2		RBDG	18.7.2019
7	1	145	134	39	142	1.24	18.7	57	MITRAL ATRESIA, DOLV, PS SV(LV) B/L BDG 2009	9	2	6.10.2009	33	3	2		B/BDG APCA	13.2.2019
8	1	146	127	33.3	140	1.14	22.4	73	TA TGA VSD PS P/B/L BDG MPA INTERR	9	2	24.2.2009	25	3	2			7.3.2019
9	1	108	138	22	129	0.89	16.3	50	hypoplastic MV & TV multiple VSD pah NRGA pab(2mo)	1		5.9.2013	26	3	1		B/L BDG, SMALL APCA	9.7.2020
10	2	112	151	22.3	131	0.90	17.4	55.6	cctga vsd PA	4		19.8.2010	16	2	1		rbdg	13.9.18
11	2	131	142	25	139	0.98	20.8	66.5	TA nrga no antegrade pbf 2015	1		20.2.15	88	2	2		rbdg	19.9.18
12	1	108	131	22.3	126	0.88	18.3	62	TA PA NRGA p/bdg	1		22.1.10	7	2	2			27.9.18
13	2	40	163	12	87	0.54	15.8	48	vsd PULM ATRESIA d malposed aorta from rv rbdg +CONF PLASTY2011	3	conf plasyt	25.4.2016	11	2	1		rbdg	17.10.18
14	2	114	143	12	123	0.64	24.5	75	complete unbal avcd vsd sev ps p rbdg+pda interr 2010	2		10.2.2010	9	2	2		rbdg	7.11.18
15	2	133	135	29.3	141	1.07	18.1	52	dilv vsd ps p/bdg+pda lig 2008	4		1.2.08	5	2	2		rbdg	8.11.2008
16	2	89	146	16.8	111.5	0.72	17.1	52	dlga vsd sev ps p/bas+ bdg 2012	5		4.1.12	7	2	1		rbdg trickle of antegrade	14.11.18
17	1	118	138	18.7	122.5	0.80	19.7	63	TA VSD ps bdg 2013	1		16.8.13	52	2	2		rbdg	28.2.19
18	1	108	131	34	142	1.16	18.1	54	tga vsd sev pa bl bdg2011	5		20.3.19	9	3	2		b/l bdg trickle of apbf	20.3.19
19	1	79	138	15.7	104	0.67	17.1	51	ta vsd ps bas+bdg 2013	1		28.5.2013	8	1	2			3.4.19
20	2	129	142	25.6	126	0.95	19	61	PA IVS P BDG /CONFL PLASTY/CC FISTULA LIGN 2010. P/ MAPCA COILING 27/7/20	6	1	3.1.2012	26	2	2		BDG. COILED MAPCA, RESIDUAL CORON CAMERAL FISTULA	28.7.20
21	2	134	141	25.3	132.5	0.96	18.8	57	dilv ps bdg2009	4		3.12.2009	18	2	2		bdg	28.8.19
22	1	177	138	34	147.5	1.18	23.3	71	sv p b/l bdg2007	9		17.7.2007	32	3	1			28.8.19
23	2	90	146	18	121	0.78	17.2	52	TA small vsd nrga sev PS	1		3.2.14	22	3	2	b/l bdg		16.10.19
24	2	97	152	32	140	1.12	23.1	71	sv(rv) p/pab2011p/b/l bdg with mpa interr 2013	9		3.5.2013	20	3	1		b/l bdg	17.10.19
25	1	125	149	20.7	133.8	0.88	21.3	70	TA VSD PS tga p/bdg pab2010	1		31.5.2010	11	1	2		bdg small apca	26.11.19
26	2	104	152	19.5	114	0.79	21.7	70	ta vsd ps nrga p/bdg2011	1		26.11.2011	10	1	2			18.12.19
27	1	106	152	21.4	122	0.85	21.4	68	DILV PULM ATRESIA TRANSPOSED GA P/BTS + CORTRIATRIATUM REPAIR + PDA LIGATN 2010 P/BDG RMBT TAKEDOWN 2013	4	BTS 2010, BTS TAKEDOWN 2013	21.2.2013	31	2	2			20.3.2019
28	2	95	133	20.6	123.5	0.84	15.6	46	DORV VSD PS LPA STENOSIS P/BDG LPA PLASTY, TRANSPOSED GV	7	PAB	11.6.2012	16	2	3			2.1.2019
29	1	71	145	13	99	0.60	16.8	47	DORV VSD PS	7		21.10.09	5	2	1			11.7.19
30	2	126	149	20.3	129.5	0.85	16.8	48	TOF PS HYPOPLAST RV, CORONARY CROSSING RVOT P/ B/L BDG, PAB, LPA PLASTY	8	1	24.7.2010	19	3	1		B/L BDG MAPCA COILED DURING THIS CATH	30.5.19

antegrade pbf 1. Y 2 N	pa anatomy 1. continent good 2. non confluent 3. stenotic	pa anatomy comments	rsvc/bdg sat	lsvc/bdg sat (in case of b/l)	svc	ivc	rpa	lpa	rupv	rlpv	lupv	llpv	aorta	svc	rpa pr	lpa	la mean	ra mean	lved	aorta sys	aorta diast	rpa size cath	lpa size cath	SMALL COLLATERALS IY 2N	collateral comments	pavm 1. Y 2 N	fio2
2	1		62		62	67	63	63	98				83	9	9	9	7	7	8	90	60	10	9.5	1	multiple smll collatral from DTA	2	60
2			68		68	72	66	66	99		98		81	13	13	13	10	10	10	78	42	8.4	7.4	1	MULTIPLE APCA FROM RSCA, RIMA. MAPCA FROM BASE OF SCA TO RIGHT LOWER & MID LOBE	2	21
2	1		69		69	82	66	67	99				89	11	11	11	9	9	13	83	53	8	10.5	2	MILD BLOTCHINESS B/L- DIFFUSE SMALL PAVM	1	40
2	1		70		70	70	68	62	98		99		80	10	8	8	5	5	8	99	62	10.8	11	2		2	21
2	1		67		67	68	78	78					77	15	15	15	7	7	16	109	68	10	10	1		1	21
2	1		60		60	72	57	67	95		99		83	7	7	7	4	4	8	90	53	9.2	5.3	2		2	21
2	1		64		64	64	64	64			96		82	16	16	16	10	12	10	90	56			1	3-4 APCA FROM SCA LIMA	2	21
2	1		56	46	46	63	57	48	97			96	76	9	9	9	7	7	8	82				1	2.5MM COLL TO LEFT LUNG	2	21
2	1		54		54	69	55	55		99			83	10	10	10	7	7	8	86	46	12.7	11.1	1	both lungs	2	
2	1	lpa smaller	70		70	64	69	69	96		97		82	16	16	15	10	10	12	76	53	10	6.5	2	small pavm,	1	21
3	1		73		73	66	72	72	99		99		86	12	11	11	7	7	8	92	61			1	small collaterals	2	
2			62		62	66	64	64	99		99		83	15	15	15	12	12	8					2	small pavm,	1	70
2	1	lpa origin stenosis	78		78	65	72	73	97			97	82	14	14	14	9	9	10	73	40	8	7.5	2		1	21
2	1		73		73	66	69	65	99	99			78	12	11	11	8	7	10	100	76			1	1 collateral 2.5mm from DT	2	21
2			65		65	68	72	72	99				92	8	8	8	7	8	8	98	50			1	small collaterals	2	21
1	1		67		67	65	64	76	97		99		79	8	9	9	6	6	11	90	54			2		2	21
2	1		59		59	65	58	65	98				79	7	7	7	5	5	8	108	54			2		2	25
1	1		46		46	61	76	73	94		99		83	13	13	13	10	10	15	140				2		2	21
2			57		57	59	59	59	99				70	10	10	10	7	7	5	78	36			2		2	70
2	3	lpa origin stenosis	70	68	68	62	76	76	99		80		84	12	12	12	11	11	12	90	56	10.2	7.1	2		1	21
2	1		60		60	72	61	67			98		85	11	11	11	7	7	11	80	45	9.9	95	2		2	50
2	1		53		53	56	60	61	98		98		77	13	13	13	8	8	8	108	60	11.17	8.54	2		1	50
2	1	segment between lpa & rpa small	64		64	61	66	59	98				84	15	14	14	8	8	8	98	66	8.8	11	2		2	
2	1		57	59	57	63	49	59	99		96		74	15	14	14	12	12	14	90	68	10	10	2		2	50
3	1		68		68	57	68	68	95		97		74	15	15	15	11	11	9	150	80	10.5	8.8	1	small coll trickle of apbf	2	21
3			79		79	75	76	83		97	97		83	14	14	13	8	9	12	100	50	11	8.5	2		2	
2	1		59		59	63	43	54	99				70	15	14	14	7	7	10	74	42	13.8	8	2		2	21
3	1		65		65	63	70	83	99		99		87	11	11	11	6	6	8	63	35	11	10.5	2		2	50
2	2	small lpa	61		61	69	69	69	84			97	78	9	9	10	6	6	8	67	41	8.5	4.5	1	multiple diffuse pavm	1	21
2	1		73		73	77	75	68	99			99	90	13	15	15	9	10	13	90	56	10	10	2	SMALL PAVM, NOT MAJOR MAPCA DISTALLY SMALL CALIBRE	2	21

pcep	type of bdg 1. left 2. right 3. b/l	time	ga during cmr 1. V 2 N	aorta	ivc	SVC flow	PV flow	PA flows	qp (coventional)	qp alternate	qs(conventional)	sallm qs	qs=total caval flow	sallm et al	fang et al	downing	alternate	qp/qs= total pv flow/total caval flow	qp/qs (pa/caval)	qp/qs (svc/caval)	pvri (alternate)	pvri cath conventional	total pvri CMR
	1	88	2	2490	1050	1200	1906	1457	1775.71	887.86	3146.83	3491.79	2250	0.52	0.58	0.60	0.30	0.85	0.65	0.53	1.69	0.84	0.75
	1	44	1	3131	933	1024	2752	970	1695.70	847.85	4521.86	4971.80	1957	0.35	0.43	0.47	0.23	1.41	0.50	0.52	2.69	1.34	0.76
	1	62	2	2610	1623	831	1727	1295	1956.79	978.39	3855.16	4823.12	2454	0.41	0.67	0.70	0.35	0.70	0.53	0.34	1.61	0.81	0.92
	1	320	2	2788	980	1209	2065	1210	2069.01	1034.50	6827.73	5879.69	2189	0.36	0.36	0.55	0.27	0.94	0.55	0.55	2.20	1.10	1.15
	2	5	2	2584	1672	1368	2919	1668	2904.61	1452.31	5958.18	9826.56	3040	0.30	0.32	0.50	0.25	0.96	0.55	0.45	4.35	2.18	2.10
	2	18	1	3680	1070	932	1823	1440	1620.65	810.32	2836.13	3738.27	2002	0.44	0.62	0.74	0.37	0.91	0.72	0.47	2.96	1.48	1.33
0	2	257	1	3000	1505	1612	2180	1323	1646.55	823.27	2927.20	2970.89	3117	0.56	0.56	0.56	0.28	0.70	0.42	0.52	9.04	4.52	3.72
	2	158	2	3100	1300	1109	1370	1219	947.47	473.73	1618.97	2441.01	2409	0.39	0.60	0.68	0.34	0.57	0.51	0.46	4.81	2.41	1.71
	2	480	2	3800	2120	2410	2440	2279	1414.82	707.41	2465.42	3077.00	4530	0.47	0.64	0.66	0.33	0.54	0.50	0.53	3.77	1.89	1.11
0	2	747	2	3459	1210	1639	2015	2599	2363.33	1181.67	4726.67	4264.19	2849	0.56	0.46	0.67	0.33	0.71	0.91	0.58	3.81	1.90	2.70
	2	725	2	2886	987	1209	2194	942	1859.18	929.59	3403.25	3113.44	2196	0.61	0.50	0.52	0.26	1.00	0.43	0.55	4.22	2.11	1.77
4	2	481	2	2477	849	690	296	680	1503.88	751.94	2631.79	2962.87	1539	0.52	0.57	0.60	0.30	0.19	0.44	0.45	3.51	1.76	0.00
4	2	462	1	2470	715	590	1251	579	3034.25	1517.13	10462.94	5796.78	1305	0.53	0.21	0.40	0.20	0.96	0.44	0.45	1.78	0.89	2.15
	2	480	2	3480	2360	1940	4160	1880	1300.52	650.26	6358.10	3629.81	4300	0.36	0.19	0.39	0.20	0.97	0.44	0.45	2.95	1.48	0.46
	2	82	2	3091	1140	1350	4062	2025	2031.20	1015.60	2089.23	2662.79	2490	0.77	0.79	1.00	0.50	1.63	0.81	0.54	1.05	0.53	0.27
0	2	66	1	2675	960	990	1945	1255	2242.12	1121.06	5022.36	5363.89	1950	0.42	0.39	0.54	0.27	1.00	0.64	0.51	1.93	0.96	1.08
0	2	132	2	3990	1634	1786	3471	2215	1392.11	696.05	2784.21	3330.37	3420	0.42	0.51	0.38	0.19	1.01	0.65	0.52	2.30	1.15	0.46
0	2	289	2	2266	1518	867	1354	952	2418.97	1209.49	1600.52	3905.81	2385	0.63	0.74	1.00	0.50	0.57	0.40	0.36	2.88	1.44	2.61
0	2	138	1	2800	1230	896	1660	849	1483.49	741.74	4747.16	5475.02	2126	0.28	0.31	0.33	0.16	0.78	0.40	0.42	2.71	1.35	1.21
	2	40	2	2626	1723	1553	1955	1687	1616.28	808.14	4778.57	4757.17	3276	0.34	0.37	0.53	0.26	0.60	0.51	0.47	1.18	0.59	0.47
5	2	73	1	2860	1762	1310	1791	1208	1621.97	810.99	2506.68	3292.36	3072	0.50	0.66	0.74	0.37	0.58	0.39	0.43	4.73	2.37	2.17
5	3	40	1	2979	1127	1454	2566	1439	1146.04	573.02	1873.10	2326.29	2581	0.50	0.53	0.63	0.32	0.99	0.56	0.56	10.30	5.15	2.36
	3	68	1	2670	980	970	3050	1170	1733.74	866.87	3007.93	2830.68	1950	0.62	0.59	0.69	0.35	1.56	0.60	0.50	5.40	2.70	1.56
	3	578	1	4320	2750	2160	2580	2610	1125.19	562.59	3121.48	3529.76	4910	0.32	0.43	0.58	0.29	0.53	0.53	0.44	3.98	1.99	0.87
0	3	3	2	3060	543	1005	1520	793	1837.00	918.50	5878.41	4277.20	1548	0.44	0.21	0.61	0.30	0.98	0.51	0.65	3.83	1.92	2.34
	3	96	1	3663	2100	1600	1998	1795	2861.36	1430.68	10300.89	7986.18	3700	0.36	0.22	0.44	0.22	0.54	0.49	0.43	2.76	1.38	2.36
	3	131	2	3790	1904	1600	3210	2168	1024.05	512.02	5222.65	5345.14	3504	0.19	0.28	0.53	0.26	0.92	0.62	0.46	11.62	5.81	1.70
	3	124	1	3300	2100	1300	1970	1360	2725.59	1362.79	2786.16	4149.40	3400	0.67	0.65	1.04	0.52	0.58	0.40	0.38	3.08	1.54	2.10
	3	130	1	2870	1518	950	1913	1023	3022.04	1511.02	4230.86	7156.68	2468	0.43	0.59	0.81	0.40	0.78	0.41	0.38	1.59	0.79	1.08
	3	473	2950	1678	1731	0	1833		2329.06	1164.53	4075.85	4000.31	3409	0.59	0.65	0.61	0.30	0.00	0.54	0.51	4.38	2.19	0.00

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