VALIDATION OF A NEW METHOD FOR NON INVASIVE ESTIMATION OF PULMONARY VASCULAR RESISTANCE USING DOPPLER ECHOCARDIOGRAPHY IN PATIENTS WITH VSD & PULMONARY HYPERTENSION

Thesis

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LIST OF ABBREVIATIONS

a **p**	Trans pulmonary pressure gradient
3D	Three dimentional
ASD	Atrial septal defect
AT	Acceleration time
BMI	Body mass index
BSA	Body surface area
CHD	Congenital heart disease
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
CTA	CT angiography
CTD	Connective tissue disease
CXR	Chest radiograph
DE	**Doppler echocardiography**
DT	Deceleration time
ES	Eisenmenger syndrome
Hb	**Haemoglobin**
IVS	Inter ventricular septum
LV	Left ventricle
PA	Pulmonary artery
PADP	Pulmonary artery diastolic pressure
PAH	Pulmonary arterial hypertension
PASP	Pulmonary artery systolic pressure
PE	Pulmonary embolism
PH	Pulmonary hypertension

LIST OF ABBREVIATIONS (Cont...)

PPH	Primary Pulmonary hypertension
P V	**Pulmonary vein**
PVR	Pulmonary vascular resistance
PVRI	Pulmonary vascular resistance index
Qp	Trans pulmonary flow
RA	Right atrium
Ram	Right atrium mean pressure
RAP	Right atrium pressure
RV	Right ventricle
RVET	Right ventricular ejection time
RVOT	Right ventricular output tract
RVSP	Right ventricular systolic pressure
SPAP	Systolic Pulmonary artery pressure
TR	Tricuspid valve regurgitation
TRV	Tricuspid regurgitation velocity
TVI_{index}	Time velocity integral/ Body surface area
TVI_{RVOT}	Right ventricular outflow tract time velocity integral
VSDs	Ventricular septal defects
WHO	The World Health Organization
WU	Wood units

INTRODUCTION

Ventricular septal defect (VSD) is the most common congenital defect and closure of VSD is the most common open heart procedure performed in pediatric cardiac surgery[1].

A large VSD with considerable left-to-right shunt commonly presents in infancy with respiratory symptom and failure to thrive[2]. The closure of such VSD is performed in developed countries at early age before the onset of pulmonary hypertension with excellent long term results [3].

Approximately one third of all patients with congenital heart disease (CHD) who have not undergone corrective procedure will die from pulmonary vascular disease. However the frequency of pulmonary hypertension and the subsequent development of reversed shunt vary depending on the specific heart defect and operative interventions[4].

About fifty percent of infants with a large nonrestrictive (VSD) or (PDA) develop pulmonary arterial hypertension (PAH) by early childhood, forty percent of patient with (VSD) or (PDA) and transposition of great arteries (TGA) develop PAH in 1st year of life[5].

PAH is characterized by progressive vascular remodeling and obliteration of peripheral pulmonary arterial vasculature associated with marked elevation of pulmonary vascular resistance (PVR)[6]. The prognosis for patients with PAH is poor and closely related to hemodynamic variables reflecting right heart function[7].

The emergence of pulmonary hypertension surely represents a limiting factor in the care of infants and children with these defects. The presence of pulmonary hypertension means that the pulmonary vascular resistance (PVR) will be maintained at a high level with medial muscular hypertrophy of the pulmonary arterioles and occlusion of many smaller branches[8]. This may be the result of increased flow across the pulmonary vascular bed causing peripheral extension of muscle from differentiating pericytes and intermediate cells in pre capillary vessels. In addition, damage to the pulmonary vascular endothelium from a mechanical stretch injury sets a series of events in motion at the cellular level (implicated in the pathogenesis of pulmonary vascular disease)[9].

As PVR approaches and equals systemic vascular resistance, left-to-right shunting is decreased, and right-to-left shunting leads to systemic desaturation and visible cyanosis. Persistent and increasing right-to-left shunting

leads to increasing peripheral hypoxemia and increasing polycythemia. Oxygen carrying capacity is increased, but at higher levels, increased viscosity leads to decreasing oxygen delivery to the tissues[10].

Surgery is usually contraindicated when calculated PVR is > 1/2 the calculated systemic vascular resistance. Repair must be evaluated carefully if PVR is at all above normal. The long-term outlook for patients with elevated PVR who undergo closure of their defect(s) is worse than for un repaired patients with the same lesion(s). This may be related to the absence of a communication between the right and left circulations, which may serve as a "pop-off valve" in patients who are at risk for pulmonary hypertensive crises[10].

Complication from pulmonary hypertension arise both preoperatively and postoperatively, and they can severely limit surgical repair or long term survival. The accurate evaluation of pulmonary vascular resistance is a key component in evaluating the operability of congenital cardiac lesions[11,12].

The current standard for measuring the PVR is by invasive measurement of flow and pressure in the pulmonary artery. Although this technique is well established, its

invasive nature precludes it from being used in the routine follow up. A noninvasive method of evaluating PVR would (1) allow more frequent assessment of PVR. (2) Facilitate the monitoring of individual patient responses, and (3) provide remote-site assessment of PVR [12].

AIM OF THE STUDY

The aim of this study is:

1- To study the correlation between the ratio of the tricuspid regurgitation velocity in cm/sec (TRV) to the velocity time integral of the RVOT with invasive measurements of pulmonary pressure and PVR in patients with VSD .

2- Validate previously postulated equations to measure the PVR non invasively using this ratio in patients with VSD & pulmonary hypertension compared to the gold standard invasive measurement of PVR using Fick's method.

SCALE OF THE PROBLEM

Incidence and Prevalence of Congenital Heart Disease:

Congenital heart disease (CHD) is one of the commonest congenital defect with an incidence of 1/120 live birth. The risk is estimated at 2 to 3 % in children with an affected first- degree relative (higher if the relative is a parent)[(1)]. Among CHD, ventricular septal defect (VSD) is the most common in both children and adults, and closure of the VSD is the most common open heart procedure performed in pediatric surgery[(3)].

A VSD is a hole or a defect in the septum that divides the 2 lower chambers of the heart and that results in a communication between the ventricular cavities. The defect may occur as a primary anomaly without additional major associated cardiac defects or it may occur as a single component of a wide variety of intracardiac anomalies, including tetralogy of Fallot (TOF), complete atrioventricular (AV) canal defects, transposition of great arteries, and corrected transpositions.

Although the true incidence is difficult to determine due to tendency for spontaneous closure in some cases[(13)], incidence of VSD is about 2/1000 live birth accounting for

more than 20% of all CHD. VSDs are the most common congenital heart defects encountered after bicuspid aortic valve[14].

Credit for the first clinical description is generally given to Roger's article published in 1879[14]. The phrase maladie de Roger is still used to refer to a small asymptomatic VSD. In 1898, Eisenmenger described a patient with VSD, cyanosis, and pulmonary hypetension.

This combination of a VSD, pulmonary vascular disease, and cyanosis has been termed the Eisenmenger complex. Pulmonary vascular disease and cyanosis in combination with any other systemic-to-pulmonary connection has been called the Eisenmenger syndrome[15].

Smaller VSDs usually close spontaneously before the age of 2 years, in general nearly 35% of perimembranous defects close spontaneously and 75% to 80% of all VSDs close spontaneously by 10 year of age[16]. The defect close by two mechanisms: 1-muscular septum growth, or 2-aneurysmal tissue from a septal leaflet of the tricuspid valve in the case of perimembranous defects[17]. For large and non restrictive defects, spontaneous closure are much lower, roughly 10% to15%; for malalignment defects spontaneous closure is rare.