Ventripoint Diagnostics Ltd.

Use of VMS for Long-term Follow-up of TOF Patients Leading to Improved Outcomes

Case Study

Introduction

Tetralogy of Fallot (ToF) is the most common cyanotic congenital heart disease that is diagnosed when the patient is an infant or young child. These patients need close follow up and complicated management, including multiple surgical interventions.

It has been classically characterized by the combination of ventricular septal defect (VSD), right ventricular outflow tract obstruction (RVOTO), overriding aorta, and right ventricular hypertrophy. The presence of obstruction to the flow from the right ventricle to the pulmonary (lung) artery (RVOTO) along with the hole between the two sides of the heart (VSD) means that deoxygenated "blue" blood is shunted into the body circulation, resulting in characteristic generalized blue discoloration of the patient (best seen on the tongue and lips) - this is called "cyanosis". Surgical correction of the defect is usually performed at around six months of age, and is done by closing the hole in the heart with a patch and opening up the narrowing from the ventricle to the pulmonary artery. This is often done by putting a patch across the pulmonary valve - a "transannular patch" (TAP). This results in the pulmonary valve no longer functioning, which means blood is free to run back from the pulmonary artery to the right ventricle after the heart has finished contracting (pulmonary regurgitation). It is not possible to put an artificial valve in at this time, as a six month old baby would quickly outgrow it. This PR is well tolerated in children, but over time the right ventricle will become larger to compensate for this leak and can eventually lead to dysfunction of the right ventricle which may be irreversible.

The timing for a pulmonary valve replacement (PVR) for patients with Tetralogy of Fallot brings much debate from cardiologists because of varying outcomes that are dependent on the timing of intervention. PVR in younger children is associated with early dysfunction of the implanted valve; but if the right ventricle dilates too much and becomes dysfunctional then this may not reverse despite PVR.

The current management strategy for ToF with severe PR is to perform a PVR if the right ventricle dilates beyond a critical point or shows signs of dysfunction; or if the patient experiences symptoms or heart rhythm disturbances.

In this case study, we demonstrate the post-operative course of two patients who had undergone ToF repair with a subsequent PVR, using the VMS to monitor the short- and long-term effects and outcome on right ventricular size and function.

Case Presentation

Here, we present a case of two patients of Dr. Greg Skinner (a Consultant Pediatric Cardiologist) with ToF that have undergone PVR to analyze the patients' ventricular volume and function measurements before and after a pulmonary valve replacement. Although much progress has been made on deciding when to do a pulmonary valve replacement, the following patients highlight opportunities for progress and improving clinical outcomes.

1. Clinician was able to track the progression of the patient's pulmonary valve and RV remodeling using VMS.

2. Close correlation between VMS and cMRI for all cardiac measurements demonstrating the reliability of the VMS data.

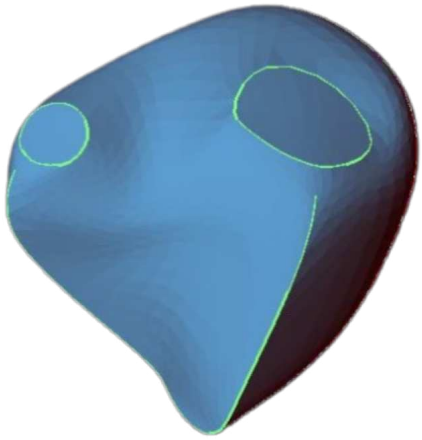


Figure 1: Illustrative Model of Tetralogy of Fallot Right Ventricle

Dr. Gregory Skinner MB BS MRCPCH

Dr. Skinner works as a Paediatric Cardiology Consultant, specializing in advanced echocardiography and cross-sectional imaging at the East Midlands Congenital Heart Centre (EMCHC) where he had previously competed his training. He is certified in Congenital Heart Disease Echocardiography by the European Society of Cardiovascular Imaging. Dr. Skinner runs a regular Advanced Echocardiography Imaging Clinic at Glenfield Hospital with his colleagues.

East Midlands Congenital Heart Centre, Leicester, England

The East Midlands Congenital Heart Centre is located close to the Leicester City Centre, in Leicester, UK. It is part of the University Hospitals of Leicester NHS Trust. The hospital is nationally recognized for its medical care for heart disease, lung cancer, and breast care and and is one of the largest Extra-corporeal Membrane Oxygenation (ECMO) centres in the UK. The heart centre at Glenfield Hospital provides patients with advanced research and techniques including surgery with a Robotic Arm, TAVI (Trans-Catheter Aortic Valve Insertion) and the use of suture-less valve in heart surgery.

History

Patient 1 is a 17-year-old male with ToF. He initially had trans-annular patch (TAP) repair at the age of 9 months resulting in significant pulmonary regurgitation and right ventricular dilatation.

At age 13, the patient was accepted for surgical PVR based on the VMS RV volumes and Cardiopulmonary exercise test (CPEX) and symptoms (breathlessness on exertion):

- RV indexed end diastolic volume of 129 ml/m2
- RV indexed end systolic volume of 56ml/m2;
- EF 57%
- VO2 max 23ml/kg/min
- LV:RV diastolic volume ratio 2:1 (good indicator of a significantly dilated RV)

The patient proceeded to have PVR at age 13 (25 mm Trifecta bioprosthesis).

Patient 2 is a 19-year old male with ToF. The patient had TAP (transannular patch repair) at the age of 11 months.

When the patient reached 15 years of age, they had a valve replacement on the basis of the VMS data and symptoms (breathlessness on exertion):

- RV indexed end diastolic volume of 167 ml/m2
- RV indexed end systolic volume of 92 ml/m2
- VO2 max 32 ml/kg/min

Discussion

Cardiac imaging plays a pivotal role in the diagnosis and surveillance of patients with severe pulmonary regurgitation following ToF repair by identifying and measuring anatomic and functional abnormalities (i.e., RV volume overload, pulmonary regurgitation, tricuspid regurgitation, residual interatrial or interventricular shunts, RV pressure overload, RV systolic or diastolic dysfunction, LV systolic or diastolic dysfunction, arrhythmias, etc.) to inform clinical decisions on optimal time of pulmonary valve replacement (PVR). It is important to depict the size, morphology and function of the RV and pulmonary valve prior to repair. Additionally, after repair, surveillance of cardiac remodeling or continued dilatation due to tricuspid and pulmonary regurgitation or RV systolic and diastolic dysfunction, needs to be evaluated.

Cardiac MRI (cMRI) is considered the gold standard modality for quantification of ventricular size/volume and function. CMR is poorly tolerated by younger patients, usually requiring general anaesthesia. For this reason, it is not suitable for regular surveillance of younger patients. Thus, echocardiography is the preferred modality, at least until around 10 years old to monitor patients because it provides good functional assessment of the RV, pulmonary and tricuspid valves.

For both of Dr. Skinner's patients, the pulmonary valve replacement (PVR) was done at a relatively young age and required close long-term follow-up to monitor RV remodeling and for structural degeneration of the bioprosthesis. The following are the results for the cardiac measurements related to size and function of the RV pre-PVR and post-PVR for the first patient:

	cMRI	VMS	PVR	VMS	VMS	cMRI	VMS
	May 2013	Aug 2016	Jan 2017	Nov 2017	Nov 2018	Feb 2019	Sep 2019
BSA	1.3	1.5		1.6	1.8	1.8	1.9
RV							
EDV	185	199		237	282	296	275
EDVi	144	129		144	160	166	148
ESV	111	86		138	194	191	180
ESVi	85	56		84	110	107	97
SV	57	113		99	88	105	95
EF	40	57		42	31	36	34
LV							
EDV	70	95			166	165	169
EDVi	54	62			94	93	91
ESV	35	41			90	82	84
ESVi	27	27			51	46	46
SV	36	54			76	83	85
EF	51	57			46	50	50

Pre-operatively Patient 1 had a CMR scan three years prior to the operation. After the PVR in 2017, there were follow-ups with standard 2D transthoracic echocardiography once every 12 to 18 months as part of the long-term sequential follow-up of the patient because it provides information on RV size and qualitative function and was more readily available compared to cMRI.

2D echocardiography has limitations in that it does not allow for an accurate quantitative analysis of the RV due to difficulties in imaging the entire RV due to its crescentic nongeometric shape and its retrosternal position. Assessment of right ventricular size is performed subjectively, and determining whether the ventricle is dilated or has reduced function is unreliable. Therefore, VMS was used in conjunction with the 2D echocardiography to follow the patient post-PVR. The VMS adopts the scanning protocol in transthoracic echocardiography which includes all the standard echocardiographic views and has a good correlation of measured RV volumes with the cMRI data.

An MRI scan was done within 3 months of a VMS scan at the same body surface area and there was a close correlation between VMS and MRI for all the cardiac measurements, thereby demonstrating the reliability of the VMS data. With the VMS, the clinician was able to track the progression of the patient's prosthetic valve and RV remodeling. The data obtained was consistent and correlated well with the MRI data.

Furthermore, this data provided information on the long-term outcome of surgical correction and allowed the clinician to determine timing of re-intervention or re-operation. With the VMS, some useful information regarding RV modelling was obtained, namely showed that RV remodeling did not occur and the patient had a relatively dilated right ventricle (as evidenced by the 2:1 RV:LV ratio and reduced ejection fraction).

The following are the results for the cardiac measurements related to size and function of the RV pre-PVR and post-PVR for Patient 2:

	cMRI	VMS	PVR	VMS	VMS	VMS
	Oct 2013	Apr 2016	Nov 2016	Apr 2017	May 2018	Mar 2020
BSA	1.5	1.8		1.9	2.1	2.2
RV						
EDV	188	309		253	299	292
EDVi	129	170		135	145	136
ESV	111	167		164	159	178
ESVi	76	92		87	77	83
SV	77	142		90	140	114
EF	41%	46%		35%	47%	39%
LV					145	
EDV	118			163	191	171
EDVi	81			87	93	79
ESV	54			69	91	85
ESVi	37			37	44	40
SV	64			94	101	86
EF	54%			58%	53%	50%

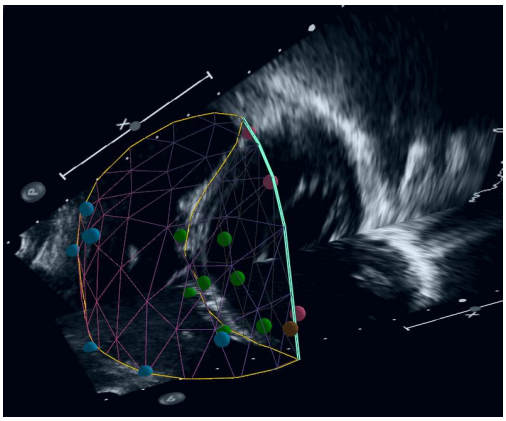
Pre-operatively the second patient had a CMR scan three years prior to the operation. After the PVR in 2016, there were follow-ups with standard 2D transthoracic echocardiography once every 12 to 18 months as part of the long-term sequential follow-up of the patient and showed that there was a significant improvement initially with the valve replacement and a reasonable degree of RV remodeling.

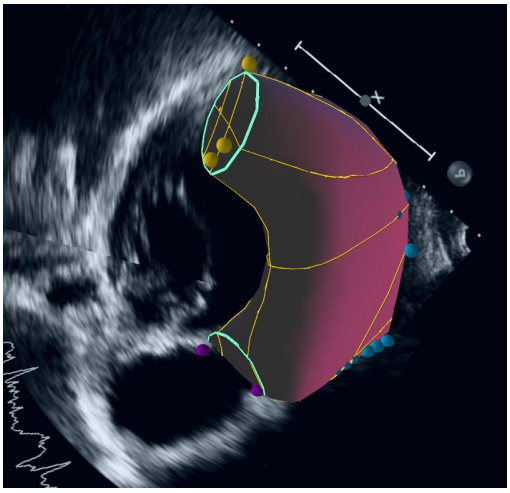
"We have a lot of patients referred to us with severe pulmonary regurgitation following ToF repair. We follow them up on a regular basis both before and after PVR with VMS. This longitudinal data gives far greater insight into both the indication for PVR, as well as the outcomes. This is invaluable both for the individual patient, but also informs our practice to ensure the best outcomes for our patients."

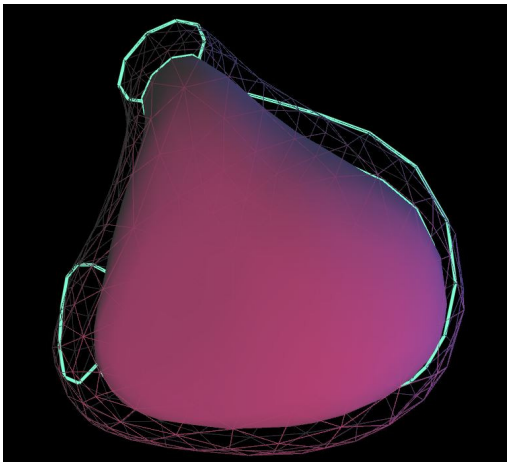
-Dr. Gregory Skinner

Clinical VMS Images

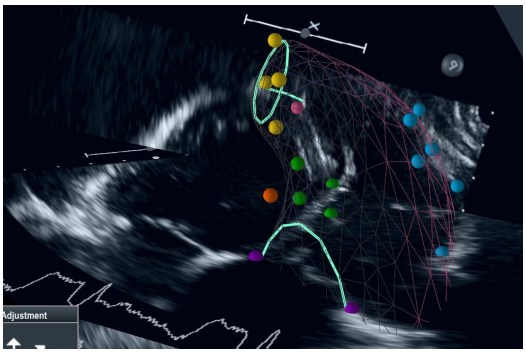
Patient 1

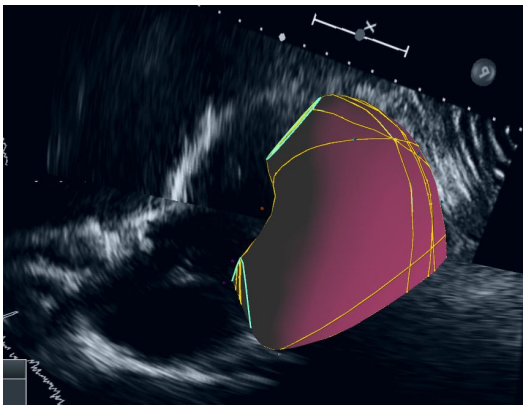


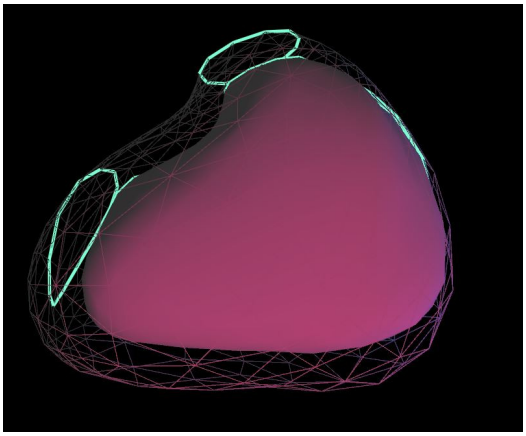




Patient 2







Conclusion

Benefits of the VMS:

Greater diagnostic confidence with an accuracy equivalent to MRI.

VMS EDV and ESV measurements correlate well with cMRI. The measurements are within +-10% to those obtained from cMRI.

Consistent volume and function measurements

VMS provides 3D models of the patient's heart with consistent volume and function information for patients with less-than-optimal imaging windows.

VMS is a valid alternative to cMRI for children

Due to the limited accessibility of cMRI and the need for sedation or general anesthesia, the clinician has an alternative tool with which to track the progression of the patient's prosthetic valve and RV remodeling. VMS can be used with patients in whom cMRI is contraindicated due to pacemakers, a lot of image artefact due to large metallic implants, claustrophobia, Intellectual Disability or Developmental Delay who may tolerate echo but not cMRI.

VMS

The VMS is a diagnostic aid that provides a point of care solution to better communicate the heart's structure and function without the need for MRI. The VMS+ marries the ingenuity of the cardiac MRI and Echo with the power of Ventripoint's KBR technology. KBR enables you to construct a 3D model of the heart and calculates volumes and ejection fractions for all chambers with an accuracy comparable to the MRI.

Learn more about the newest generation, VMS+: **www.ventripoint.com**

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