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Dyssynchrony and electromechanical delay are associated with focal fibrosis in the systemic right ventricle — Insights from echocardiography

Sonya V. Babu-Narayan [a,b,c,1,2], Daniele Prati [a,c,d,1,2], Riikka Rydman [a,b,c,e,1], Konstantinos Dimopoulos [a,c,1], Gerhard-Paul Diller [a,c,1], Anselm Uebing [a,1], Michael Y. Henein [c,1], Philip J. Kilner [b,c,1], Michael A. Gatzoulis [a,b,c,1], Wei Li [a,c,*,1]

[a] Adult Congenital Heart Unit, Royal Brompton Hospital, Sydney Street, London SW3 6NP, UK
[b] NIHR Cardiovascular Biomedical Research Unit, Royal Brompton Hospital, Sydney Street, London SW3 6NP, UK
[c] National Heart and Lung Institute, Imperial College, Dovehouse Street, London SW3 6LY, UK
[d] Department of Biomedical and Surgical Sciences, Section of Cardiology, Universita' degli Studi di Verona, Verona, Italy
[e] Department of Molecular Medicine and Surgery, Section of Clinical Physiology, Karolinska Institutet, Stockholm, Sweden

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ABSTRACT

Background: Systemic right ventricular (RV) dysfunction and sudden cardiac death remain problematic late after Mustard operation for transposition of the great arteries. The exact mechanism for that relationship is likely to be multifactorial including myocardial fibrosis. Doppler echocardiography gives further insights into the role of fibrosis shown by late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR) in late morbidity.
Methods and results: Twenty-two consecutive patients, mean age 28 ± 8 years, were studied with 2D echocardiography, and also assessed by LGE CMR. The presence of LGE in 13/22 patients (59%) was related to delayed septal shortening and lengthening ($P = 0.002$ & $P = 0.049$), prolonged systemic RV isovolumic contraction time ($P = 0.024$) and reduced systemic RV free wall and septal excursion ($P = 0.027$ & $P = 0.005$). The systemic RV total isovolumic time was prolonged but not related to extent of LGE. LGE extent was related to markers of electromechanical delay and dyssynchrony (delayed onset of RV free wall shortening and lengthening; $r = 0.73$ & $P = 0.004$ and $r = 0.62$ & $P = 0.041$, respectively, and QRS duration $r = 0.68$, $P < 0.01$) and was inversely related to systolic RV free wall shortening velocity ($r = -0.59$ & $P = 0.042$). The presence of LGE was also related to lower exercise capacity, ≥mild tricuspid regurgitation and more arrhythmia ($P = 0.008$, $P = 0.014$ and $P = 0.040$). RV free wall excursion and systolic tissue Doppler velocity were related to CMR derived RV ejection fraction ($r = 0.51$, $P = 0.015$, and $r = 0.77$, $P = <0.001$, respectively).
Conclusion: Post Mustard repair, myocardial fibrosis is related to dyssynchrony, RV long axis dysfunction and tricuspid regurgitation. Echocardiographic measurements of systemic RV function can be confidently used in serial follow-up following Mustard operation.

1. Introduction

Following the Mustard procedure [1] (atrial redirection surgery) for complete transposition of the great arteries, the right ventricle (RV) remains the systemic ventricle. Patients are at increasing risk of late ventricular dysfunction and sudden cardiac death [2–11]. The exact underlying pathophysiological mechanism is likely to be multifactorial. Myocardial ischaemia in the morphologically right systemic ventricle has been suggested based on the presence of perfusion defects [9], wall motion abnormalities and features suggestive of fibrosis on late gadolinium cardiovascular magnetic resonance (CMR) [12]. Ventricular long axis function is known for its sensitivity in detecting ischaemia as well as having characteristic features in non-ischaemic cardiomyopathies [13]. Patients post Mustard repair are also known to display RV dyssynchrony [14]. We sought to compare Doppler echocardiography variables and the presence of fibrosis detected by late gadolinium enhancement (LGE) CMR. Our objective was to determine the nature of the underlying ventricular disturbances that may explain the known deterioration of systemic ventricular function with age that occurs in these patients.

* Corresponding author: Adult Congenital Heart Program, Royal Brompton Hospital, Sydney Street, London SW3 6NP, UK.
E-mail address: w.li@rbht.uk (W. Li).

[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.
[2] The first and second author contributed equally to the work.

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2. Methods

All 22 adult patients (28 ± 8 years of age, 11 male) with transposition of the great arteries who had undergone the Mustard procedure and Doppler echocardiography, within 6 months of LGE CMR scan, were included. Age at Mustard repair was 1.8 ± 2 years. Length of follow-up after repair was 25.4 ± 4.6 years. All patients gave written informed consent to undergo CMR study with gadolinium. The study was conducted according to the declaration of Helsinki and approved by the local research ethics committee.

2.1. Patient characteristics

Fifteen of the 22 patients were in New York Heart Association class I and the remaining 6 were in class II and 1 in class III. Prior to the CMR study, eight patients had evidence for documented supraventricular arrhythmia (36%); atrial tachycardia in 7 and atrial fibrillation in 1. Twelve patients had reintervention for atrial pathway obstruction (5 surgical; 4 patients had transcatheter intervention). Only two patients had mild to moderate atrial pathway obstruction at the time of study. One patient had mild sub-pulmonary stenosis. Seven patients underwent patch closure of ventricular septal defect at the time of Mustard surgery. No patient had a history of, or electrocardiographic evidence of, coronary artery disease or systemic hypertension.

2.2. Two-dimensional, M-mode and Doppler echocardiography

Transthoracic echocardiography was performed using a Phillips Sonos 5500 echocardiograph (Philips Medical Systems, Eindhoven, The Netherlands) interfaced with a multifrequency MHz transducer. An ECG (lead II) and a phonocardiogram were superimposed on each echocardiographic recording. Pulmonary, septal and systemic ventricular long-axis recordings were obtained from the apical 4-chamber view with the M-mode cursor positioned at the left and septal angles of the left atrioventricular (AV) ring and the right angle of the right AV ring (Fig. 1a). The probe and cursor were positioned to guarantee the beam direction as parallel as possible to the direction of ring motion. Parameters of electromechanical delay and dyssynchrony (QRS complex to onset of shortening; Q-OS, and second heart sound to onset of lengthening; S2-OL) were also measured as shown in Fig. 1b.

Basal ventricular myocardial tissue Doppler velocities were acquired at the AV ring level, with the sample volume positioned at the angles described above. Peak systolic, early- and late-diastolic velocities were measured from tissue Doppler recordings of the pulmonary and systemic ventricular free wall and septum. Systemic RV and sub-pulmonary ventricular systolic function were assessed semiquantitatively by an experienced echocardiographer who performed all studies and graded them according to the following grades: 1 = normal, 2 = mildly impaired, 3 = moderately impaired and 4 = severely impaired systolic function. Tricuspid regurgitation was graded as: 0 = absent or trivial, 1 = mild, 2 = moderate and 3 = severe. Diastolic filling parameters including peak velocities of E and A wave, E wave deceleration time and ventricular filling times, were measured. Systemic RV isovolumic relaxation time was measured as the interval between the closure of the semilunar valves (at the time of the second heart sound on the phonocardiogram) and the onset of the ventricular filling on the tricuspid valve pulsed wave Doppler velocities. RV myocardial performance index was calculated as the sum of isovolumic contraction time (ICT) and isovolumic relaxation time (IRT), divided by ejection time. Total RV ejection and filling times were derived as the product of the corresponding time interval and heart rate and were expressed as seconds per minute (s/min) using the following equation:

$$\textit{Total isovolumic time } (T\text{-}IVT) \textit{ was calculated as } 60\text{–}(\textit{total ejection time} + \textit{total filling time}).$$

Inflow tract diameters of the pulmonary and systemic ventricles were obtained from the 2D apical 4-chamber view as described in Fig. 1a.

An experienced researcher measured most of the echocardiographic and Doppler parameters, another measured the dyssynchrony data; both were blinded to the patient's clinical status and other data, including CMR. Intra- and inter-observer reproducibility of echocardiographic long-axis function parameters and CMR measurements was reassuring as previously reported measured [12,15].

2.3. Cardiovascular magnetic resonance with late gadolinium enhancement

Late gadolinium imaging was performed as previously described in detail [12] by a single operator with the use of a 2-dimensional segmented fast low-angle shot inversion recovery sequence, the acquisition optimized for imaging non-ischaemic myocardial fibrosis and the RV using a 1.5-Tesla Siemens Sonata scanner [12]. All atrial pathways were formally assessed with specifically piloted cines and phase velocity mapping. Briefly, imaging was performed from 5 min after injection of 0.1 mmol/kg–0.2 mmol IV gadolinium-DTPA with active effort taken to exclude or recognize artefacts during acquisition including off-null effects and with phase swapping, systolic images and cross cuts to define sometimes subtle RV LGE. The inversion time was meticulously adjusted to maintain nulling

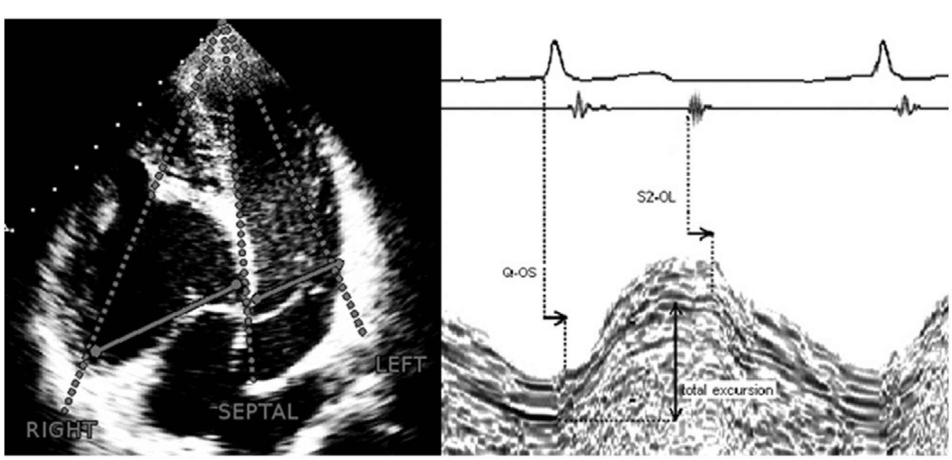

Fig. 1. The left panel shows M-mode recording of pulmonary, septal and systemic ventricular long-axis excursion and 2D-measurement of the inflow tract diameters of the pulmonary and systemic ventricle from the apical 4-chamber view. The right panel shows M-mode recording of long-axis motion. Q-OS, time from q to onset of shortening; S2-OL, time from second heart sound to onset of lengthening.