Synergistic interaction between right ventricular mechanical dyssynchrony and pulmonary regurgitation determines early outcome following tetralogy of Fallot repair

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Abstract

Objective: The ability of the right ventricle to tolerate acute pulmonary regurgitation (PR) following tetralogy of Fallot (TOF) repair is variable and the mechanisms that underlie this are not completely understood. We hypothesise that dyssynchronous wall mechanics affects the RV tolerance to postoperative PR with adverse effect on early surgical outcome. Methods: Twenty-four TOFs (mean age 19.5 ± 15.5 months) undergoing elective repair were prospectively recruited. Ventricular wall mechanics was studied by tissue Doppler echocardiography following induction (preop) and postoperative day one (POD1) and compared with a control group (10 VSD/AVSD). Segmental dyssynchrony, defined as out-of-phase peak myocardial contraction, was determined at the base, mid, apical segments of the septum, RV and LV free walls and scored by the total number of affected segments. PR was graded from absent to severe and RV dimension was quantified by end-diastolic area index (RVEDAI). Cardiac index (CI) was measured by pulse contour cardiac output analysis. Outcome measures were CI, mixed venous oxygen saturation (SvO2), lactate, and duration of ventilation and critical care stay. Results: Preoperatively, biventricular free-wall motion was synchronous in both groups. Following surgery, TOF developed RV-septal dyssynchrony (>2 segments in 11 (46%) vs none in control, p = 0.01), while the LV free wall remained normal in both groups. RV-septal dyssynchrony correlated with the ventilation time (rho = 0.69, p = 0.003), critical care stay (rho = 0.58, p = 0.02) in the presence of PR (n = 16), but not with other outcome measures. The relationships between dyssynchrony and early outcome were not seen when PR was absent. In the presence of PR, median RVEDAI was greater with higher dyssynchrony score (>3 segments; p = 0.009). The degree of PR did not affect critical care/ventilation time or RVEDAI. The presence of transannular patch (p = 0.007) or at least moderate PR (p = 0.01) was associated with a more severe dyssynchrony. Conclusions: Dyssynchronous RV-septal wall mechanics occurs early after Fallot repair. The magnitude of dyssynchrony appears to interact synergistically with pulmonary regurgitation to influence RV dimension and early outcome.

Keywords: Tetralogy of Fallot; Right ventricular dysfunction; Pulmonary valve insufficiency; Cardiac surgery

1. Introduction

Pulmonary regurgitation (PR) following tetralogy of Fallot (TOF) repair is a consistent feature particularly when pulmonary valve-sparing procedure is not possible. While the consequences of chronic PR TOF repair are well studied, the relevance and clinical impact on the early postoperative phase is less clear. It appears that some children may cope well with acute PR while others less so and the mechanisms that underlie this variation are not fully understood. In order to avoid potential complications, consideration has been given to limit postoperative PR by the use of valve-sparing and monocusp procedures [1].

RV dysfunction following TOF repair has been well studied. The RV displays a pattern of reduced contractility and decreased chamber compliance in the early postoperative phase, resulting in diastolic dysfunction and longer ICU recovery [2]. This postoperative RV dysfunction and low cardiac output syndrome were associated with pressure overload and cyanosis induced ultrastructural changes at myocellular level [3]. In adult survivors, there appears to be a relationship between RV dimension and QRS duration describing a mechano-electrical interaction associated with adverse outcome [4]. The mechanism of this has been related to areas of myocardial fibrosis detected by late gadolinium enhancement cardiovascular magnetic resonance mainly at the surgical repair site in RV outflow tract (RVOT), but also distributed in other regions of the ventricular mass. [5] Such fibrosis may
interfere with the conduction and activation of myocardial contraction that contribute to disordered RV wall mechanics including RVOT aneurysm—akinesia and regional ventricular wall motion abnormalities at late Fallot follow-up [6—8].

The mapping of regional myocardial velocity has been allowed by emerging new technology including tissue Doppler echocardiography and cardiovascular MRI. Tissue velocity mapping allows a direct measurement of myocardial contractility and comparison of velocities between various myocardial segments at isochronal time points [6,9]. This imaging technique has the ability to identify any dyssynchronous ventricular wall motion by detecting any temporal variation between myocardial segmental contractions. The shift in contraction and relaxation phase of different ventricular regions has been termed as mechanical dyssynchrony [10]. This phenomenon has been well studied in adult LV dysfunction and supports the benefits of cardiac resynchronisation therapy (CRT) in improving functional outcome [9,11]. Ventricular dyssynchrony exerts various deleterious effects on the heart which include suboptimal ventricular filling, increased wall stress, and may contribute to cellular damage and regional apoptosis [12].

In the perioperative period, Fallot patients are subjected to various insults including preoperative hypoxaemia, abnormal loading physiology, surgical trauma, myocardial resection, ischaemia reperfusion injury, and postoperative conduction anomalies, all of which have the potential to contribute to regional myocardial dysfunction. We therefore hypothesise that Fallot patients develop dysynchronous wall mechanics early after surgery. In this study, we explored the extent and distribution of ventricular dyssynchrony pre- and post-Fallot repair. We further examined if a subset of patients with PR and poorer outcome may be explained by coexisting ventricular dyssynchrony, which renders the RV less tolerant of the acute volume overload.

2. Materials and methods

This single institutional study was undertaken prospectively in the Scottish National Paediatric Cardiac Service based in Royal Hospital for Sick Children, Yorkhill, Glasgow. The study was approved by Glasgow West research ethics committee.

2.1. Study protocol

Preoperative tissue Doppler imaging (TDI) with concurrent ECG was performed on-table following induction of general anaesthesia. A standard apical 4-chamber view in colour tissue Doppler mode was obtained using a transducer probe (2.5—7.5 MHz) with an optimal setting for depth, sector size and velocity range. Three or more loops were stored for subsequent offline analysis. A repeat of TDI was obtained on postoperative day one (POD1) in the intensive care unit (ICU). Postoperative epicardial pacing was withheld temporarily for TDI recordings in stable patients who tolerated haemodynamically (n = 3); pacing-dependent patients were otherwise excluded. A 12-lead ECG was obtained preoperatively and POD1.

All patients have standard postoperative invasive monitoring. Lactate level and mixed venous oxygen saturation (%) \((S(O_2))\) were measured routinely. In 15 patients, cardiac index (CI) was measured using pulse contour cardiac output technology as part of the study protocol. A size 3F PULSIOMATIC arterial thermodilution catheter was inserted perioperatively into the femoral artery. Continuous cardiac output monitoring was started immediately after surgery in the ICU and calibrated every 8 h.

2.2. Patients

Twenty-four tetralogy of Fallot patients (5 with DORV variant) undergoing elective surgical repair were studied (Table 1). TOF repair was undertaken via a transpulmonary and transatrial approach. When a transannular incision was required to enlarge the annulus, a monocusp patch was routinely used. A ventriculotomy was reserved for severe infundibular hypoplasia in the presence of adequate annular dimension, thereby avoiding a transannular patch (TAP). Epicardial echo was routinely performed to exclude any residual lesion at the end of the procedure.

Ten patients (mean age 6.6 months ± 4.5 SD) who had open heart surgery for VSD closure without infundibular resection were recruited in control group (5 complete AVSD, 4 VSD, 1 VSD/PA band removal) to compare the ventricular wall mechanics with TOF before and after surgery.

2.3. Ventricular wall mechanics assessment

Offline analysis was performed using quantitative analysis (Q-Analyse), EchoPac 4.0.1 GE-Vingmed USS software package. A total of 9 segments were analysed from the apical 4-chamber view (Fig. 1).

The systolic and diastolic phases in a cardiac cycle are identified by timing the opening and closure of the tricuspid and pulmonary valves. The timing of (1) TV opening and closure

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of TOF patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD, range) months</td>
<td>19.5, 15.5, 3.7—78.2</td>
</tr>
<tr>
<td>Gender (n, %)</td>
<td>13 males (54%)</td>
</tr>
<tr>
<td>Weight (mean, SD, range) kg</td>
<td>10.2, 3.0, 4.4—19.2</td>
</tr>
<tr>
<td>Haematocrit level % (median, Q1—Q3)</td>
<td>41.7, 37.2—48.6</td>
</tr>
<tr>
<td>O2 saturation ≥85% (n, %)</td>
<td>9 (38%)</td>
</tr>
<tr>
<td>Modified BT shunt (n, %)</td>
<td>11 (46%)</td>
</tr>
<tr>
<td>Cross-clamp time (median, Q1—Q3, min)</td>
<td>75.0, 65.5—106.3</td>
</tr>
<tr>
<td>Bypass time (median, Q1—Q3, min)</td>
<td>143.5, 108.5—221.3</td>
</tr>
<tr>
<td>Transannular patch use (n, %)</td>
<td>11 (46%)</td>
</tr>
<tr>
<td>Pulmonary monocusp (n, %)</td>
<td>10 (42%)</td>
</tr>
<tr>
<td>Subvalvar patch (n, %)</td>
<td>7 (29%)</td>
</tr>
<tr>
<td>Branch PA patch (n, %)</td>
<td>5 (21%)</td>
</tr>
<tr>
<td>Critical care stay (median, Q1—Q3, days)</td>
<td>5.39, 2.62—8.89</td>
</tr>
<tr>
<td>Ventilation time (median, Q1—Q3, h)</td>
<td>92.8, 22.6—156.9</td>
</tr>
<tr>
<td>Mixed venous oxygen saturation POD1 (median, Q1—Q3)</td>
<td>66.5, 60.0—71.0</td>
</tr>
<tr>
<td>Lactate POD1 (median, Q1—Q3)</td>
<td>1.3, 0.93—1.65</td>
</tr>
<tr>
<td>Inotrope Score POD1 (median, Q1—Q3)</td>
<td>10.0, 3.5—14.8</td>
</tr>
<tr>
<td>Cardiac index POD1 (median, Q1—Q3)</td>
<td>3.1, 2.7—3.4</td>
</tr>
<tr>
<td>RV end-diastolic area index (median, Q1—Q3)</td>
<td>7.63, 6.45—9.08</td>
</tr>
<tr>
<td>PR severity (absent:mild:moderate:severe)</td>
<td>8:8:5:3</td>
</tr>
<tr>
<td>Restrictive physiology (n, %)</td>
<td>9, 38%</td>
</tr>
</tbody>
</table>

* Defined as antegrade flow across pulmonary artery coincident with atrial systole.
is identified from tricuspid inflow velocity at the apical 4-chamber view and (2) systolic ejection phase from the RVOT outflow velocity at the parasternal short axis RVOT view. Isovolumetric contraction (IVC) is defined as the phase between tricuspid valve closure and pulmonary valve opening. The mid-points of the basal, mid and apical segments of interventricular septum, RV and LV free wall were sampled (sample area 6 mm x 6 mm) between the endocardial and epicardial border to obtain the myocardial tissue velocity wave profile. Myocardial tissue velocity representing contraction and relaxation of each myocardial segment along longitudinal axis was recorded from the apical 4-chamber view. Smoothing of the curves was set to a maximum of 30 ms in Q-analysis software. The LV basal segment was used as a reference point during analysis. Peak myocardial contraction is defined as the maximum positive, i.e. apically directed velocity wave occurring after the isovolumetric contraction phase. Three or more cardiac cycles were studied.

2.3.1. Definition of segmental dyssynchrony

Segmental dyssynchrony was defined as out of phase peak myocardial contraction. In a normal ventricle contracting synchronously, all segments will contract in the same phase with all the velocity waves in alignment (Fig. 2a). By contrast, in a dysynchronous ventricle, there will be a temporal variation between these segments and their velocity waves will be out of phase (Fig. 2b).

2.4. RV loading assessment

Pulmonary regurgitation severity (PR) was graded from being absent to mild, moderate, and severe. PR severity was assessed qualitatively by two investigators (one (SL) blinded to the type of surgical repair) based on width of the regurgitant jet and level of the diastolic retrograde flow seen in the parasternal short axis RVOT view: branch PA (severe PR), main pulmonary trunk (moderate) and RVOT (mild) [13]. RV dimension was quantified by RV end-diastolic area index (RVEDAI, cm²). RVEDAI was measured by tracing the endocardial borders of the RV in the apical 4-chamber view at the time of tricuspid valve closure and indexed to body surface area (BSA). Papillary muscles and the moderator band were excluded from the tracing.

2.5. Outcome measures

Outcome measures were postoperative day one cardiac index, lactate level, mixed venous oxygen saturation (S\textsubscript{v}O\textsubscript{2}), inotrope score, and length of ventilation and critical care (intensive and high dependency unit) stay. Inotrope score was calculated based on Wernovsky et al. [14]:

\[ \text{Inotrope score} = \frac{1}{2} (\text{dopamine} + \text{dobutamine} + \text{amrinone}) \times 1 \times (\text{milrinone} \times 20) + \frac{1}{100} (\text{epinephrine} + \text{norepinephrine} + \text{isoproterenol}) \times 100 \]

(dosage is expressed in µg/kg/min)

2.6. Statistical analysis

Statistical analysis was performed using MINITAB release 14.2. The continuous variables were analysed with Mann—Whitney or Kruskal—Wallis test and Fisher’s exact test was used for categorical variables. The strength of relationship between two variables was tested using Spearman’s rank correlation (rho). A \( p \) value (two-tailed) of <0.05 was considered as statistically significant.

3. Results

3.1. Pre- and postoperative RV dyssynchrony

Preoperatively, the right and left ventricular free-wall motions were synchronous before surgery in both groups. In the septum, one (10%) control and six (25%) TOF patients had a single dysynchronous segment consistently located at the apical segment (\( p = 0.6 \)).

Postoperatively, in the TOF group, one or more dysynchronous segments were identified in the RV free wall (24 patients, 100%) and septum (15, 63%) (vs 8, 80% and 7, 70% in control group, \( p = NS \)). The LV free wall was spared in both groups. The extent of segmental involvement was greater in TOF: \( \geq 2 \) segments in RV [13 (54%) TOF vs 1 (10%) control; \( p = 0.02 \)] and septum [8 (33%) TOF vs none control; \( p = 0.07 \)]. TOF patients had a more severe total RV-septal dyssynchrony (\( p = 0.01 \) (Fig. 3).

3.2. Relationship between postoperative PR and early outcome

PR was observed in 16 patients (67%) postoperatively (8 mild, 5 moderate and 3 severe PR). The degree of PR did not correlate with the critical care stay or ventilation time (Fig. 4). There was no significant relationship between the

Fig. 1. Apical 4-chamber view was divided into nine segments (1: RV basal, 2: RV mid, 3: RV apex, 4: IVS basal, 5: IVS mid, 6: IVS apex, 7: LV basal, 8: LV mid, 9: LV apex) for wall motion analysis.
degree of PR and RVEDAI (median RVEDAI in mild PR 7.04 vs moderate PR 11.23 vs free PR 7.44; \( p = 0.21 \)).

In the transannular patch group (\( n = 11 \)), PR was present in 10 (91%) of patients (2 mild, 5 moderate, 3 severe) versus 6 (46%) patients (all mild) in the absence of transannular patch (\( p = 0.03 \)). Seven patients had bovine monocusp (4 moderate, 3 free PR) and 3 patients had autologous pericardial monocusp (2 mild, 1 moderate).

3.3. Relationship between RV dyssynchrony, PR and early outcome

The degree of total RV-septal dyssynchrony (\( n = 24 \)) correlated with the ventilation time (rho = 0.58, 95% CI: 0.23–0.80; \( p = 0.003 \)), and critical care stay (rho = 0.50, 95% CI: 0.12–0.75; \( p = 0.01 \)), but not with CI (rho = 0.10, 95% CI: −0.43 to 0.58; \( p = 0.70 \)), lactate (rho = 0.17, 95% CI: −0.25 to 0.54; \( p = 0.41 \)), \( S_O_2 \) (rho = 0.17, 95% CI: −0.27 to 0.55; \( p = 0.43 \)) or inotrope score (rho = 0.28, 95% CI: −0.15 to 0.61; \( p = 0.19 \)).

In the subset of patients with PR (\( n = 16 \)), total dyssynchrony (RV-septal) correlated with ventilation time (rho = 0.003), critical care stay (rho = 0.02) (Fig. 5), but not with CI (rho = −0.26, 95% CI: −0.76 to 0.44; \( p = 0.44 \)), lactate (rho = 0.50, 95% CI: 0.01–0.80; \( p = 0.05 \)), \( S_O_2 \) (rho = 0.04, 95% CI: −0.46 to 0.53; \( p = 0.87 \)) or inotrope score (rho = 0.41, 95% CI: −0.10 to 0.80; \( p = 0.11 \)). There were no relationships between the extent of dyssynchrony and early outcome measures in the absence of PR (\( n = 8 \)). In the presence of PR (\( n = 16 \)), the median RVEDAI was greater in the ventricles with higher dyssynchrony scores (rho = 0.009) (Fig. 6).
In addition, TOF patients who developed significant effusion requiring new pleural or pericardial drain \((n = 10)\) postoperatively had a more extensive RV-septal dyssynchrony than those without \((n = 14)\) any significant effusion (median 3 vs 2 dyssynchronous segments; \(p = 0.04\)). There was no relationship seen between cross-clamp time (and CPB time) and early outcome measures \((p = \text{NS})\).

### 3.4. ECG findings

There was a significant widening the duration (median, Q1–Q3) of QRS complex 69.0 ms (60.5–77.0) preoperatively compared to 99.0 ms (85.5–106.0) postoperatively (day 1) \((95\% \text{ CI median difference: } -36.01, -20.00; \ p = 0.0000)\). Four (17%; 3 partial, 1 complete) patients had right bundle branch block preoperatively compared to 23 (96%; 19 complete, 4 partial) postoperatively \((p = 0.0000)\).

### 3.5. Perioperative variables and the extent of postoperative RV-septal dyssynchrony

A greater extent of RV septal dyssynchrony was associated with the use of transannular patch (median 3 vs 2.0; 95% CI median difference: \(-3.0 \text{ to } 0.0; \ p = 0.07\)) and the presence of moderate-severe PR (median 2.0 when PR absent vs 2.0 when PR mild vs 3.0 when PR at least moderate; \(p = 0.01\)) (Fig. 7).

No correlation was seen between the extent of postoperative RV-septal dyssynchrony and age \((\text{rho} = -0.08, 95\% \text{ CI: } -0.47 \text{ to } 0.33; \ p = 0.70)\), weight \((\text{rho} = 0.05, 95\% \text{ CI: } -0.36 \text{ to } 0.44; \ p = 0.81)\), haematocrit \((\text{rho} = 0.14, 95\% \text{ CI: } -0.28 \text{ to } 0.51; \ p = 0.5)\), preoperative oxygen saturations \((\text{rho} = -0.25, 95\% \text{ CI: } -0.59 \text{ to } 0.17; \ p = 0.23)\), cardiopulmonary bypass time \((\text{rho} = 0.27, 95\% \text{ CI: } -0.15 \text{ to } 0.61; \ p = 0.19)\), aortic cross-clamp time \((\text{rho} = 0.13, 95\% \text{ CI: } -0.29 \text{ to } 0.50; \ p = 0.55)\), and QRS duration \((\text{rho} = -0.15, 95\% \text{ CI: } -0.52 \text{ to } 0.27; \ p = 0.48)\). The extent of postop dyssynchrony was not associated with the presence of preoperative dyssynchrony (median 2.0 preop vs
3.0 postop; 95% CI median difference: −1.0 to 1.0; p = 0.64) or the presence of restrictive RV physiology (median 2.0 in restrictive vs 2.0 in non-restrictive, 95% CI median difference: −1.0 to 1.0; p = 1.00). As only one patient did not have RBBB, the association between dyssynchrony and presence of RBBB could not be tested.

4. Discussion

This principal findings of this study were that in TOF patients undergoing repair: (1) an essentially normal biventricular free-wall motion preoperatively, (2) all patients develop RV-septal dyssynchrony to a variable extent early after repair, (3) dysynchronous wall mechanics and pulmonary regurgitation interact synergistically to influence early clinical outcome and (4) the use of transannular patch or presence of at least moderate PR is a risk factor of greater degree of dyssynchrony.

4.1. Extent and distribution of ventricular dyssynchrony in Fallot patients

The use of tissue Doppler analysis has enabled characterisation of regional myocardial contraction, allowing useful functional assessment including tissue velocity, strain, and isovolumetric acceleration and simultaneous comparison of different myocardial regions at various isochronal time points. Put simply, in normal ventricular contraction the direction of myocardial movement during systole–diastole remains consistent throughout the ventricular mass. However with dysynchronous pattern, certain regions of myocardium move in a paradoxical or out-of-phase fashion which compromises overall ventricular efficiency.

In both study groups, TOF and VSD control, dysynchronous segments were evident to a variable extent in the RV free wall and septum with sparing of the LV free wall. However, when we considered the extent of dyssynchrony, the ventricle in the Fallot group was more severely affected. The majority of patients in the VSD group had only single segment dyssynchrony in the RV or septum, predominantly confined to the apical region. In contrast, dyssynchronous segments were distributed from apical to basal region with a more extensive involvement in the Fallot group. We believe this study is the first to describe perioperative changes in regional wall motion, delineating both the wall motion pre- and post-repair.

It appears that a substantial number of patients, although to a lesser extent than we identified in the early post-operative phase, also demonstrated dysynchronous RV wall mechanics at late Fallot follow-up. Vogel et al. examined 74 Fallot patients at a mean of 15 years following surgical repair [6]. Regional wall motion abnormality was evident in 68% (50) of the follow-up cohort: 43% (32/74) isolated RV free wall abnormality, 22% (16/74) both RV-septal wall, 3% (2/74) isolated septal wall involvement. A lesser degree of involvement, up to 55% of the free-wall length was also seen at late follow-up, unlike involvement of up to the basal segment in our study. These observations suggest that some of the abnormal segments may recover with time due to potentially reversible perioperative factors, whilst in the majority of affected segments, the disordered wall mechanics persists into adulthood, presumably due to permanent damage to the mechanical activation pathway. The LV free wall was also spared in the late follow-up cohort and mirrored the findings in the early postoperative patients.

In other late follow-up studies, abnormal wall mechanics was also found at the surgical repair site associated with RVOT aneurysm—akinesia [7,8].

The high incidence of dyssynchrony early after Fallot repair suggests that while this may not be detrimental to all patients, especially in those with a single affected segment, in some, this may be physiologically significant with a more extensive segmental involvement.

4.2. Pathogenesis of RV dyssynchrony in Fallot repair

This study established a crucial fact that ventricular free-wall motion is largely normal in the RV prior to surgical repair. The development of dysynchronous mechanics post-Fallot repair suggests that it is not inherent to the condition and is induced by the consequences of surgery. Furthermore we have a comparison with control group who underwent VSD closure without RVOTO relief as in the Fallot group and appear to be less affected. So, what renders TOF group more susceptible? It could result from conduction abnormalities caused by myocardial resection.
or perhaps due to the altered RV loading conditions, where preoperatively the RV is pressure loaded and postoperatively it becomes volume loaded to a varying degree because of PR. Chronic RV pressure overloading prior to surgery did not seem to be causally related to incidence of dyssynchrony as very few Fallot patients were affected preoperatively and this was confined to a single segment located in the septum.

A loss of synchronous ventricular contraction can result from disruption of the conduction pathway or diseased myocardial segment. Studies in adult patients with LV dyssynchrony suggest that this may be due to conduction abnormalities resulting from dilated cardiomyopathy or ischaemic myocardial segment related to regional vascularisation. In patients with LV failure, left bundle branch block is the most common cause of ventricular conduction delay [10,15]. Approximately one-third of adults with LV dysfunction also have widened QRS suggesting intraventricular conduction abnormality. The delay in electro-mechanical activation is probably caused by intercellular fibrotic tissue growth involving the conduction system [16].

It is likely that the pathogenesis of RV dyssynchrony in Fallot is also mediated by conduction abnormalities, although the hypothesis will remain conjectural as a direct cause and effect relationship is difficult to demonstrate. A significantly widened QRS complex and the presence of RBBB is almost invariably in most Fallot patients after surgery which may account for the high prevalence of dyssynchronous segments post-repair. This study however did not show any relationship between duration of QRS and RBBB and the degree of dyssynchrony. The relationship between ECG abnormalities and mechanical dyssynchrony may be complex and will not be explained by simple correlation. The prolonged QRS duration suggests an abnormal intraventricular conduction although it may not be sensitive enough to detect the extent of dyssynchrony. This is supported by adult studies which showed that QRS duration is not a sensitive marker to select responders to CRT [9].

The degree of pulmonary regurgitation, RV EDD, and the use of transannular patch were shown to be associated with a more extensive dyssynchrony in univariate analysis. However, the occurrence of dyssynchrony even in their absence suggests that these factors are not causative but their presence predisposes to a higher risk of acquiring a more extensive dyssynchrony. The use of TAP will result in a more severe PR, but is also suggestive of a higher degree of RVOT resection required in a more severe spectrum of Fallot patients. The resection of obstructing muscle bundles as well as placement of stitches to close VSD may potentially incorporate tissues which contain conduction fibres and lead to disruption of electromechanical co-ordination.

### 4.3. Postoperative pulmonary regurgitation and relationship with RV septal dyssynchrony

An adequate surgical relief of RVOTO to unload the RV is typically achieved by accepting variable degrees of pulmonary regurgitation postoperatively. Pulmonary valve incompetence subjects the RV to adverse chronic volume loading contributing to RV dilatation, dysfunction and risk of ventricular arrhythmia [17]. This is especially true for patients who required transannular patch who had a more severe pulmonary regurgitation, dilated RV, and poorer right and left ventricular ejection fraction as measured by MR study [18]. Chronic RV overload has also been linked to prolonged QRS duration and increased risk of ventricular arrhythmia late after Fallot repair describing a mechano-electrical interaction [4,19].

It is conventionally accepted that pulmonary regurgitation is well tolerated over an extended period of time, and chronic volume dilatation and right dysfunction will not ensue until later in life. While the consequences of chronic PR on late Fallot survivors are well studied, RV tolerance to acute PR in the very early postoperative period is less clear. Surgical procedure to maintain pulmonary competency in patients who required transannular incision is associated with a better early surgical outcome in terms of shorter inotropic, ventilation and ICU recovery time [1].

Although pulmonary regurgitation is also associated with other congenital heart conditions such as isolated congenital pulmonary valve incompetence and following pulmonary valvuloplasty or valvotomy, the deleterious effects on RV function appear more pronounced with the Fallot group with an increased requirement for surgical re-intervention and risk of cardiac death [20,21]. MRI studies had shown that PR was not solely involved in the mechanism of RV dysfunction [8,22]. This study supported previous observations and in addition, demonstrated the potential role RV wall mechanical dyssynchrony in the pathogenesis of RV dysfunction and its related morbidity following Fallot repair.

### 4.4. RV dyssynchrony and outcome

Dyssynchronous ventricular contraction is now a recognised mechanism for impaired cardiac function in adult patients with heart failure. Ventricular dyssynchrony exacerbates symptoms of left heart failure and cardiac resynchronisation therapy is now an established treatment modality to improve ventricular function and reverse LV remodelling in the adult population [11]. Experience in resynchronisation therapy is much more limited in the paediatric population [23].

As a congenital heart patient is more prone to right heart dysfunction the extent and distribution of RV dyssynchrony and its impact on outcome following repair will be of special interest in the paediatric population. Dyssynchrony may represent a modifiable risk factor to improve early surgical outcome. In fact, multi-site ventricular pacing has been shown to provide acute haemodynamic benefits in the early postoperative period following congenital heart surgery [24]. The role of RV resynchronisation in failing RV is still preliminary but promising and its indication and role in TOF patients need further exploration [25].

We have shown here that RV dyssynchrony may represent a novel mechanism of right heart dysfunction in the early postoperative period yet to be described in previous studies. This study serves to identify the high-risk group and provides a new knowledge that there may be a window of opportunity to improve early postoperative outcome in a subset of Fallot patients. The magnitude of RV dyssynchrony interacts with pulmonary regurgitation to influence RV dimension and early outcome. It indicates that some patients may not tolerate
the effect of PR well in the immediate postoperative period due to dysynchronous wall mechanics, suggesting that PR can be deleterious even in the very early period after surgery. It is our current institutional policy to avoid PR by not using transannular patch where possible, if not, then this is limited by using monocusp patch.

4.5. Study limitations

In the current study we investigated early postoperative ventricular mechanics and therefore did not know to what extent dysynchrony persisted beyond this point. Our study is limited by not being able to use MRI in early postoperative patients and an accurate RV function could not be assessed objectively with 2D echocardiography. Future studies are required to assess evolution of RV dysynchrony, its effect on late outcome, and the role of multi-site pacing in Fallot patients.

Acknowledgement

We will like to thank Dr David Young from Department of Statistics and Modeling Science, University of Strathclyde for reviewing the statistical method and analysis in this study.

References


Appendix A. Conference discussion

**Dr L.H. Edmunds** (Philadelphia, Pennsylvania, USA): I’m going to start with a question. Did you do any transtrial repairs for the TOP? Did you do any without making an incision in the right ventricular outflow tract in the repair operation?

**Mr Peng**: Yes, we did.

**Dr Edmunds**: And did you find any difference in the dysynchrony?

**Mr Peng**: Yes, these patients tend to have a lesser degree of dysynchrony. I mean, these are the patients who also actually didn’t require transannular patch or RYOT patch, and therefore, they are the patients who also are less likely to have a significant degree of dysynchrony after surgery.

**Dr Edmunds**: So you had less with the transtrial repair?
Mr Peng: Yes, they tend to have less than the subgroup who required transannular.

Dr G. Sarris (Athens, Greece): I have one question. Did you correlate the electrocardiographic situation with the echocardiographic data of dyssynchrony. In other words, was there any correlation with the presence of right bundle branch block with the extent or degree of asynchrony, and did you consider utilising resynchronisation therapy to see if these changes were reversible and if there would be a positive effect on postoperative haemodynamics by re-establishing synchrony or moving contraction towards a more synchronous pattern?

Mr Peng: For the first part of the questions, yes, we did attempt to try to see whether right bundle branch block is a predictive risk factor. The majority of our patients have right bundle branch block postoperatively, but however, from univariate analysis we did not identify any relationship.

For the second question, the study will open a window of opportunity to determine whether biventricular pacing or multi-site ventricular pacing might be a potential therapy for this group of patients in terms of outcomes.

Dr Sarris: This would be an interesting addition, because we have found out clinically, without having done such a careful study, that in situations of haemodynamic compromise resynchronisation is of significant clinical benefit, but certainly a carefully designed study can look into this in a more scientific way.

Mr W. Brown (Birmingham, United Kingdom): Did any of these patients exhibit or correlate with restrictive right ventricular diastolic function?

Mr Peng: As part of our univariate and multivariate analyses, we evaluated the relationship with restrictive physiology. We did not find any correlation between restrictive physiology and the degree of dyssynchrony.

Mr Tsang (London, United Kingdom): May I also ask a question? Why did you restrict your analysis to preop and day 1 postop? Why didn’t you do some more at the time of discharge or 6 months later?

Mr Peng: At the moment, we’re gathering more data. In a subgroup of these patients, we have performed echo on postop day 7. Our initial data, which was not presented here, showed that approximately 90% or more remains in dyssynchrony, at the same level of dyssynchrony on postop day 1.

Dr Edmunds: Do you think that dyssynchrony will last, or do you think it will improve and become less with time? What was the mean duration between operation and your last assessment?

Mr Peng: There are one or two studies in the late follow-up, many years after repair, showed that about 60% of patients have some evidence of dyssynchrony. Some patients will improve, but a large number of them remain in some degree of dyssynchrony at late follow-up. This will have an impact for us to understand the relationship between pulmonary regurgitation and dyssynchrony and late outcome.

Mr A. Lotto (London, United Kingdom): How do you explain the septal wall dyssynchrony if the transannular patch is the reason for your dyssynchrony in the right ventricle?

Mr Peng: We didn’t actually look at dyssynchrony at the transannular area, but we only identified the transannular patch as a risk factor. Did I get your question right?

Dr Lotto: I was just wondering how the transannular patch affects the intraventricular septum in the dyssynchrony?

Mr Peng: I think the answer to this question would be quite speculative. I believe that transannular incision site might interrupt the conduction pathway, and also led to a greater degree of pulmonary regurgitation. So as such, this will lead to a greater dyssynchrony whether in the RV free wall or the septum.