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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Factors associated with biventricular dysfunction in patients with repaired tetralogy of Fallot

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Abstract

Background: Impaired right ventricular (RV) mechanics is a common problem in patients after repair of tetralogy of Fallot (TOF). Moreover, impaired left ventricular (LV) systolic function has also been demonstrated in this population. There are no studies evaluating patients after TOF repair with impaired both RV and LV ejection fractions (RVEF, LVEF).

Aim: We hypothesised that a considerable group of patients with repaired TOF would demonstrate both RV and LV systolic function impairment. Accordingly, the purpose of our study was to characterise patients with biventricular dysfunction after TOF repair.

Methods: Consecutive patients with repaired TOF undergoing cardiac magnetic resonance (n = 146, mean age 26.4 ± 8.2 years, age range 13.6–51.3 years, 60.3% males, 54 patients [37.0%] with early correction and 92 [63.0%] with late correction).

Results: There were 31 patients (21.2% of the study population; 90.3% males) with biventricular dysfunction. Normal both RVEF and LVEF were observed in 65 (44.5%) individuals. Neither the presence nor the extent of late gadolinium enhancement differed between patients with normal both RVEF and LVEF vs. low both RVEF and LVEF. There were no differences in pulmonary regurgitation (PR) fraction, peak RV outflow tract (RVOT) gradient, and the incidences of significant PR and RVOT obstruction between these groups (p = NS for all comparisons). Multivariate logistic regression revealed that male sex and RVOT aneurysm/akinesia (only in patients repaired early) were associated with the presence of biventricular dysfunction.

Conclusions: In patients with repaired TOF, male sex and RVOT aneurysm/akinesia were independently associated with biventricular dysfunction. Impaired both RVEF and LVEF were common in patients with repaired TOF, with the vast majority being males.

Key words: tetralogy of Fallot, late gadolinium enhancement, systolic heart failure, magnetic resonance imaging

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INTRODUCTION

Impaired right ventricular (RV) mechanics is a common problem in patients after repair of tetralogy of Fallot (TOF) [1]. Moreover, impaired left ventricular (LV) systolic function has been demonstrated in this population as well [2–6].

There is a growing body of evidence that lower RV ejection fraction (RVEF) and/or lower LV ejection fraction (LVEF) in this population are associated with an increased risk for sustained ventricular tachycardia, death and progression of heart failure [2–4]. To date, there have been no studies focus-

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ing particularly on evaluating patients with impaired both RV and LV systolic functions after TOF repair.

It can be speculated that patients with biventricular dysfunction are at the highest risk for adverse outcomes. On the other hand, patients with normal RV and LV systolic functions are perceived as having favourable clinical outcomes [4]. The care for patients with congenital heart diseases is challenging, and the continuously growing number of patients and follow-up visits are among the main problems. It would be prudent to estimate how many TOF patients require close follow-up, including those with biventricular dysfunction.

We hypothesised that a considerable group of patients with repaired TOF would demonstrate both RV and LV systolic function impairment. However, detailed analyses on the prevalence of this condition as well as demographic characteristics of this population are lacking. Therefore, we decided to perform the current study in a large cohort of patients with repaired TOF to characterise patients in whom both low RVEF and low LVEF were present.

METHODS

Patient population

The study population comprised consecutive patients after TOF repair being referred for a cardiac magnetic resonance (CMR) as a part of a routine clinical assessment from June 2008 until the end of January 2012. Exclusion criteria encompassed pulmonary atresia, poor CMR image quality, incomplete CMR data set, incomplete echocardiographic study, known coronary artery disease (CAD), and age at TOF repair ≥ 18 years. Patients were further stratified into subgroups with early correction (< three years of age) or with late correction (≥ three years). Clinical and demographic variables were extracted from patients' medical records. The approval for analysis was granted by the local Ethics Committee. Each patient and/or their parents/guardians gave written informed consent for CMR study.

CMR

All CMR images were acquired with a 1.5 T scanner (Avanto, Siemens, Germany). Retrospectively ECG gated breath-hold steady-state free precession cine images were acquired in LV short axis and analysed with the dedicated software (MASS 6.2.1, Medis, Leiden, the Netherlands). LV and RV endocardial and epicardial contours were outlined manually in end-systolic and end-diastolic frames, and thence LV end-systolic volume (LVESV), LV end-diastolic volume (LVEDV), LVEF, RV end-systolic volume (RVESV), RV end-diastolic volume (RVEDV), RVEF were calculated. Impaired LV systolic function was defined as LVEF < 55%, and impaired RV systolic function as RVEF < 45% [1, 4]. Combined LVEF < 55% plus RVEF < 45% was defined as biventricular dysfunction, and combined LVEF ≥ 55% plus RVEF ≥ 45% as normal systolic ventricular performance. All volume and mass parameters were indexed for body surface area. The RV/LV volume ratio was calculated by dividing RVEDV by LVEDV.

Pulmonary regurgitation (PR) and aortic regurgitation (AR) were quantified in terms of PR fraction (PRF) and AR fraction (ARF) on the basis of a flow sensitive gradient echo sequence. PRF ≥ 20% was defined as significant PR.

All imaging studies (echocardiography and CMR) were screened for the presence of residual ventricular septal defect (VSD). Significant VSD was defined as a shunt > 1.5:1 (Qp:Qs) measured on the basis of effective stroke volumes (forward flow minus regurgitant flow) in the aorta and pulmonary trunk [7, 8]. We assessed the presence of aneurysmal or akinetic regions in RV outflow tract (RVOT) as described previously [6].

We evaluated the presence and extent of late gadolinium enhancement (LGE) using the previously described methods [9]. In brief, for LV-LGE we used a standard 17-segment model: segments were scored on a five-point scale describing the percentage of the myocardium occupied by LGE (0 = no LGE, 1 = 1–24%, 2 = 25–49%, 3 = 50–74%, and 4 = 75–100% of the myocardium in the segment that showed LGE). For RV-LGE, we adopted the following grading system in each of seven RV regions (Fig. 1): 0 = no LGE, 1 = up to 2 cm of linear LGE extent, 2 = 2–3 cm, 3 = greater than 3 cm [9]. LGE in trabeculations was scored as follows: 0 = no LGE, 1 = LGE in 1 trabeculation, 2 = LGE in 2–4 trabeculations, and 3 = LGE in > 4 trabeculations. The inferior and superior RV-LV hinge points were each scored as either 0 for the absence of LGE or 1 for the presence of LGE, and were encountered only in RV-LGE scores. The maximum LV-LGE and RV-LGE scores were 68 and 20, respectively. Total-LGE score was calculated as the sum of RV-LGE score and LV-LGE score. Images were acquired in LV short axis, LV long axis and RVOT view (a breath-hold segmented inversion recovery sequence, a single-shot inversion recovery sequence, and/or a phase sensitive inversion recovery sequence were used). Additional images were acquired in selected cases in the plane cutting the area occupied by LGE and we swapped the phase-encode direction to exclude artifacts. All images were acquired 10–15 min after intravenous administration of 0.2 mmol/kg gadobutrol (Gadovist, Bayer Pharma AG, Berlin, Germany).

Echocardiography

Standard transthoracic echocardiography was performed in all patients with systems available commercially. Peak instantaneous RVOT gradient was calculated with the use of the Bernoulli equation on the basis of the maximal velocity across RVOT. Peak gradient ≥ 30 mm Hg was considered significant [8].

Statistical analysis

Data are presented as numbers and percentages, means ± standard deviations or medians with interquartile ranges (IQR). Categorical variables were compared with the use of either the χ^2 test or the Fisher exact test. Continuous variables were

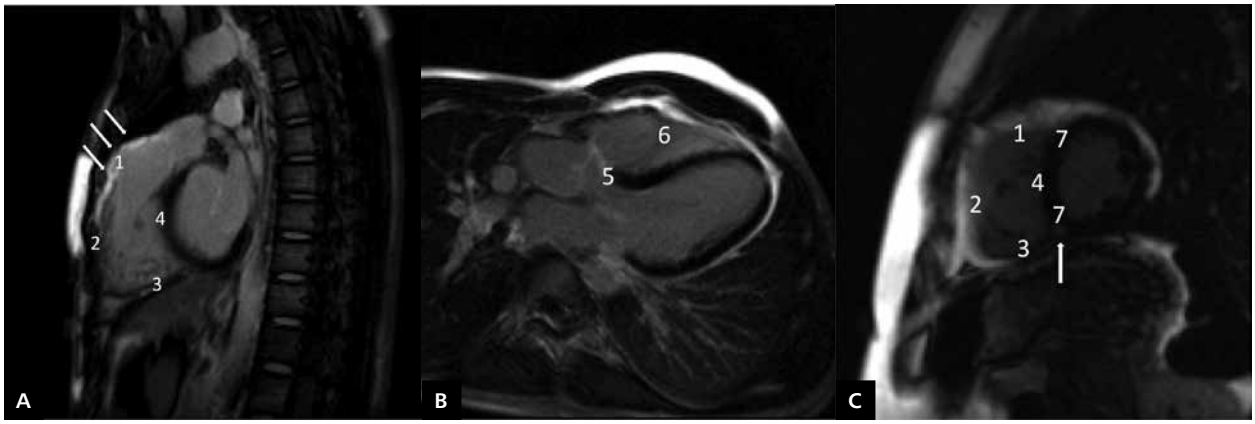

Figure 1. Representative images demonstrating late gadolinium enhancement (arrows) in right ventricular outflow tract (RVOT) (**A**), ventricular septal defect (VSD) patch region (**B**), and inferior right ventricle (RV)-left ventricle (LV) insertion region (**C**). The numbers indicate seven regions of the RV: (1) anterior wall of RVOT, (2) RV anterior wall, (3) RV inferior wall, (4) RV surface of septum, (5) VSD patch region, (6) trabecular bands, and (7) inferior and superior RV/LV hinge points

tested for normal distribution with the use of the Kolmogorov-Smirnov test, and were compared by either the Student t-test or the Mann-Whitney test, where appropriate. Logistic regression with its accompanying c-statistic, which is equivalent to the area under the receiver operating characteristic curve, were used to determine the performance of the models in identifying impaired systolic ventricular performance. The following variables were considered as candidate predictors and were entered into the multivariable model: age at TOF repair, palliative shunt in the history, time remained palliated, age at CMR study, time since initial correction, number of previous cardiothoracic surgeries, sex, arrhythmias in the history, RVOT aneurysm/akinesia, PRF, peak RVOT gradient, presence of any VSD, more than mild mitral regurgitation/AR, more than mild tricuspid regurgitation, RV-LGE score, total-LGE score. Subsequently, the variables which showed the least significant associations were excluded one by one until all variables remained significant ($p < 0.05$). Statistical analyses were performed with the use of MedCalc 12.1.4.0 software (MedCalc, Mariakerke, Belgium). All tests were two-sided, and a level of $p < 0.05$ was considered statistically significant.

RESULTS

Patient population

A CMR study was performed in 182 patients with repaired TOF in the analysed period. Thirty-six patients were excluded due to the following causes: incomplete CMR study (n = 4), artifacts precluding analysis (n = 7), incomplete echocardiographic study (n = 3), known CAD (n = 1), and old age at TOF repair (n = 21). The final analysis included 146 patients (age range 13.6–51.3 years; see Table 1 for further details) who were divided into two subgroups according to their age at TOF repair: the early correction group (n = 54, 37%) and the late correction group (n = 92, 63%).

Baseline characteristics and findings of imaging studies

Baseline characteristics and findings of imaging studies are summarised in Tables 1 and 2. All patients were in sinus rhythm during CMR study. Biventricular dysfunction was present in 31 patients (21.2% of the study population), and normal both RVEF and LVEF in 65 (44.5%) individuals. The remaining 50 patients had either RV systolic dysfunction with normal LVEF (n = 30, 20.6%) or LV systolic dysfunction with normal RVEF (n = 20, 13.8%). The lowest value of RVEF was 23% and of LVEF was 41%. Individuals with biventricular dysfunction were more often male ($p < 0.0001$), had larger RVEDV, RVESV, RV mass, LVEDV, LVESV, and LV mass compared to patients with normal RV and LV systolic functions (Tables 1, 2). There were no differences in PRF, peak RVOT gradient, and the incidences of significant PR and RVOT obstruction between these groups. The presence of VSD was not associated with impaired systolic ventricular performance. The small number of patients with significant VSD precluded reliable analyses. Patients with biventricular dysfunction were more likely to have RVOT aneurysm/akinesia compared to patients with normal ventricular ejection fractions ($p = 0.02$, Table 2). In the entire study cohort, there were 25 (17.1%) patients with more than mild tricuspid regurgitation, and five (3.4%) patients with significant mitral regurgitation or AR. We found no differences in the prevalence of these regurgitations among patients with biventricular dysfunction vs. those with normal ventricular systolic functions (Table 2), nor did these variables prove to be independent predictors of biventricular dysfunction (Table 3).

LGE

There were no differences in the presence and the extent of LV-LGE or RV-LGE between the groups analysed (Table 2).

Table 1. Baseline characteristics

Variable	All patients (n = 146)	Biventricular dysfunction (RVEF < 45% and LVEF < 55%) (n = 31, 21.2%)	Normal ventricular systolic performance (RVEF ≥ 45% and LVEF ≥ 55%) (n = 65, 44.5%)	P*
Age at CMR study [years]	26.4 ± 8.2	25.6 ± 7.3	25.8 ± 8.4	0.90
Males	88 (60.3%)	28 (90.3%)	31 (47.7%)	< 0.0001
Age at initial correction [years]†	3.8 (2.3–5.9)	3.2 (1.9–5.6)	3.5 (2.2–5.3)	0.66
Time since initial correction [years]	21.6 ± 6.4	21.4 ± 6.0	21.2 ± 6.4	0.90
Prior palliative shunt	38 (26.0%)	9 (29.0%)	18 (27.7%)	0.91
Time from first palliative shunt to TOF repair [years]†	0 (0–7.3)	0 (0–5.5)	0 (0–19.3)	0.70
Type of TOF repair:				
Patch	82 (56.2%)	17 (54.8%)	38 (58.5%)	0.81
Conduit	14 (9.6%)	3 (9.7%)	4 (6.1%)	
Details unknown	50 (34.2%)	11 (35.5%)	23 (35.4%)	
Number of previous cardiothoracic surgeries†	1 (1–2)	2 (1–2)	1 (1–2)	0.36
NYHA class†	1 (1–2)	1 (1–2)	1 (1–2)	0.71
NYHA class ≥ 2	41 (28.1%)	9 (29.0%)	17 (37.7%)	0.96
Arrhythmias in the history	30 (20.5%)	3 (9.7%)	4 (6.2%)	0.68

Data are presented as mean values ± standard deviation or medians (interquartile ranges) as appropriate, unless stated otherwise; *Patients with biventricular dysfunction vs. patients with normal ventricular systolic performance; †Data are medians with interquartile ranges in parentheses; CMR — cardiac magnetic resonance; LVEF — left ventricular ejection fraction; NYHA — New York Heart Association; RVEF — right ventricular ejection fraction; TOF — tetralogy of Fallot

Only four patients showed LV-LGE outside the RV-LV insertion regions (Fig. 1) with LGE localised in LV apex (segment 17).

In patients with normal both LVEF and RVEF, RV-LGE scores were higher among patients with RVOT aneurysm/akinesia compared to the remaining ones (median: 4.0, IQR: 3.0–4.5 vs. median: 2.0, IQR: 1.0–4.0, p = 0.003). Among patients with biventricular dysfunction, the difference did not reach statistical significance (median: 3.0, IQR: 2.3–4.0 vs. median: 2.0, IQR: 1.0–3.8, p = 0.16).

Impact of age at TOF repair

Age at TOF repair did not differ between patients with biventricular dysfunction and those with normal both LVEF and RVEF. Mean LVEF and RVEF in patients with early correction (< three years of age) were 56.7 ± 7.2% and 46.7 ± 8.7%, and in patients with late correction (3–18 years of age) 57.2 ± 6.5% and 45.8 ± 7.8%, respectively (p = 0.68 for LVEF, p = 0.52 for RVEF).

The comparison of patients with biventricular dysfunction and those with normal systolic function in subgroups with early and late correction mirrored the results in the entire study population. The exceptions were: (1) higher incidence of RVOT aneurysm/akinesia was observed in patients with biventricular dysfunction but only in a subgroup with early correction (in patients with late correction, the incidence of RVOT aneurysm/akinesia was similar irrespective of ventricular systolic functions); (2) in patients with late correction and normal systolic functions, higher median peak RVOT gradient was observed, and they were more likely to have significant RVOT gradient compared to patients with late correction and biventricular dysfunction; these differences were not present in patients corrected early in life.

Multivariate analysis

Multivariate logistic regression revealed that male sex was significantly associated with biventricular dysfunction (Table 3). Additionally, in patients with early TOF correction, but not in those corrected later in life, the presence of RVOT aneurysm/akinesia proved to be an independent predictor of biventricular dysfunction.

DISCUSSION

There are several findings in our study. First, male sex was an independent predictor of impaired ventricular systolic performance. This is in agreement with studies in healthy volunteers reporting higher LVEF and/or RVEF in women [10, 11]. Some investigations, however, have revealed no differences in either LVEF or RVEF between the sexes [12, 13]. Large population-based studies in individuals free of clinical cardiovascular diseases have confirmed that women

Table 2. Findings of imaging studies

	All patients (n = 146)	Biventricular dysfunction (n = 31, 21.2%)	Normal ventricular systolic performance (n = 65, 44.5%)	P*
RVEDV [mL/m^2]	160.4 ± 47.4	187.1 ± 59.5	143.7 ± 36.8	0.0006
RVESV [mL/m^2]	88.1 ± 35.8	118.0 ± 44.5	68.8 ± 20.2	< 0.0001
RVSV [mL/m^2]	72.3 ±19.2	69.1 ± 19.7	74.9 ± 19.6	0.19
RVEF [%]	46.1 ± 8.1	37.6 ± 5.0	52.2 ± 4.8	< 0.0001
Right ventricular mass [g/m^2]	31.3 ± 9.4	34.3 ± 11.1	28.8 ± 7.2	0.01
RV mass-to-volume ratio [g/mL]	0.2 ± 0.05	0.19 ± 0.05	0.21 ± 0.06	0.11
LVEDV [mL/m^2]	88.8 ± 20.2	98.2 ± 19.0	84.2 ± 17.8	0.0006
LVESV [mL/m^2]	38.7 ± 12.5	49.8 ± 11.6	32.8 ± 9.2	< 0.0001
LVSV [mL/m^2]	50.1 ± 10.6	48.4 ± 8.7	51.4 ± 9.8	0.13
LVEF [%]	57.0 ± 6.8	49.4 ± 3.8	61.4 ± 5.0	< 0.0001
Left ventricular mass [g/m^2]	56.0 ± 13.9	60.7 ± 11.8	53.3 ± 12.8	0.007
LV mass-to-volume ratio [g/mL]	0.64 ± 0.14	0.63 ± 0.13	0.65 ± 0.14	0.68
RV/LV ratio	1.86 ± 0.65	1.94 ± 0.60	1.74 ± 0.41	0.09
PR fraction [%]	27.7 ± 16.3	27.8 ± 15.5	27.0 ± 16.1	0.81
Significant PR (PR fraction ≥ 20%)	102 (69.9%)	22 (71.0%)	45 (69.2%)	0.94
Median AR fraction [%]	1 (0–2)	1 (0–3)	1 (0–2)	0.36
More than mild MR/AR	5 (3.4%)	1 (3.2%)	2 (3.1%)	1.0
More than mild tricuspid regurgitation	25 (17.1%)	6 (19.4%)	11 (16.9%)	0.99
Median peak RVOT gradient [mm Hg]	20 (9–35)	16 (6–24)	20 (8–35)	0.32
Significant RVOT gradient (≥ 30 mm Hg)	48 (32.9%)	7 (22.6)	23 (35.4%)	0.30
Residual VSD	26 (17.8%)	9 (29.0%)	10 (15.4%)	0.22
Significant residual VSD (Qp:Qs > 1.5)	4 (2.7%)	1 (3.2%)	2 (3.1%)	1.0
RVOT aneurysm/akinesia	70 (47.9%)	18 (58.1%)	21 (32.3%)	0.02
LGE data:†				
RV-LGE	115/122 (94.3%)	25/26 (96.2%)	50/54 (92.6%)	1.0
Median RV-LGE score	3 (1–4)	3 (1–4)	3 (1–4)	0.84
LV-LGE‡	4 (3.2%)	0 (0%)	3/54 (5.6%)	0.55
Median LV-LGE score	0 (0–0)	0 (0–0)	0 (0–0)	0.29
Median total-LGE score§	3 (1–4)	3 (1–4)	3 (1–4)	0.79

Data are presented as mean values ± standard deviation or medians (interquartile ranges) as appropriate, unless stated otherwise; *Patients with biventricular dysfunction vs. patients with normal ventricular systolic performance; †Data available for 122 patients; ‡All patients with LV-LGE had RV-LGE; §Total-LGE score was calculated as the sum of RV-LGE score and LV-LGE score. All parameters, except peak RVOT gradient, were derived from cardiac magnetic resonance imaging. Peak RVOT gradient was derived from echocardiographic studies based on the maximal velocity across RVOT determined with the use of continuous wave Doppler; AR — aortic regurgitation; LVEDV — left ventricular end-diastolic volume; LVEF — left ventricular ejection fraction; LVESV — left ventricular end-systolic volume; LV-LGE — left ventricular late gadolinium enhancement; MR — mitral regurgitation; PR — pulmonary regurgitation; RVEDV — right ventricular end-diastolic volume; RVEF — right ventricular ejection fraction; RVESV — right ventricular end-systolic volume; RV-LGE — right ventricular late gadolinium enhancement; RVOT — right ventricular outflow tract; RV/LV ratio — right-to-left ventricular end-diastolic volume ratio; total-LGE — total late gadolinium enhancement; VSD — ventricular septal defect

have higher RVEF and LVEF than men [14, 15]. In patients with repaired TOF, it has been shown that male sex is associated with LV dysfunction [5, 16]. Additionally, Sarikouch et al. [17] demonstrated that male TOF patients had lower LVEF as well as RVEF compared to female ones. Previous investigations showed that there were sex-based differences in both ventricular physiology and adaptations to injury in various cardiovascular diseases, and those differences may be attributable to hormonal influences [18]. Interestingly, in our study the presence and the extent of RV-LGE and LV-LGE did not differ between the sexes.

In patients with early TOF repair, not only male sex but also the presence of RVOT aneurysm/akinesia was an independent predictor of biventricular dysfunction. Davlouros

Table 3. Logistic regression models predicting biventricular dysfunction (LVEF < 55% plus RVEF < 45%)

	All patients (n = 146)		Early correction (n = 54)		Late correction (n = 92)	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Predictors:						
Sex (for male sex)	8.6 (2.5–29.7)	0.0007	6.6 (1.2–36.3)	0.03	14.2 (1.8–113.1)	0.01
RVOT aneurysm/akinesia	–	–	5.7 (1.4–23.2)	0.015	–	–
Model performance: AUC (95% CI)	0.69 (0.61–0.77)		0.77 (0.63–0.87)		0.71 (0.61–0.80	

AUC — area under the curve; CI — confidence interval; LVEF — left ventricular ejection fraction; OR — odds ratio; RVEF — right ventricular ejection fraction; RVOT — right ventricular outflow tract

et al. [6] demonstrated a negative effect of RVOT aneurysm/akinesia on RVEF in a group of patients with repaired TOF with a median age at repair of 9.0 years. On the other hand, Wald et al. [19] proved that regional abnormalities in RVOT were negatively associated with global RVEF also in patients corrected earlier in life: median age at TOF repair was 1.2 years. The lack of association between RVOT aneurysm/akinesia and biventricular dysfunction in patients with late correction in our study may be attributable to the slightly lower, although insignificant, incidence of RVOT aneurysm/akinesia in this group compared to patients corrected earlier (37.0% vs. 45.2%, p = 0.55). This is probably the result of less aggressive surgical techniques in terms of relief of RVOT obstruction in patients with later surgical repair. Although the rates of RVOT patching in both subgroups were similar, the presence of RVOT akinetic and aneurysmatic region as demonstrated by Davlouros et al. [6] was not necessarily associated with the use of a patch during surgical repair, and there was a number of patients with RVOT aneurysm/akinesia in whom TOF repair had been performed without the use of a RVOT patch. We did not perform quantitative analysis of either RVOT dilatation or the extent of regional abnormalities in RVOT, thus we were not able to detect more nuanced differences between the subgroups [19, 20].

Previous studies have demonstrated that RVOT contractile dysfunction is associated with the presence of LGE [19, 20]. In our study, RV-LGE scores were higher in patients with RVOT aneurysm/akinesia and normal ventricular systolic functions; in patients with biventricular dysfunction the difference did not reach statistical significance, probably due to the small number of patients.

There were no differences in LVEF or RVEF between patients with early TOF repair vs. those corrected later in life, and the age at TOF repair did not prove to be an independent predictor of biventricular dysfunction. These results are in line with previous studies demonstrating that the age at TOF repair was not associated with ventricular systolic functions, and only patients corrected ≥ 18 years of age had a higher likelihood of LV dysfunction [5, 6]. Therefore, we excluded this group, leaving for analysis only patients with total repair performed < 18 years of age.

Neither the presence nor the extent of LGE (RV-LGE or total-LGE) was associated with impaired ventricular systolic functions. The small number of patients with LV-LGE outside the RV-LV hinge points (in the apex in four patients — probably associated with the use of a transapical LV vent during surgery [9]), consistent with previous studies [16, 19, 21], did not allow for any firm conclusions. Although previous studies in patients with repaired TOF have shown some association between LGE and impaired ventricular systolic function, the reported correlation coefficient between RV-LGE score and RVEF was not high, and some patients demonstrated LV-LGE typical of myocardial infarction [9, 19]. These results suggest that apart from ventricular fibrosis, other factors play a crucial role in the systolic function impairment.

Patients with biventricular dysfunction had higher RV and LV volumes than patients with normal biventricular systolic function. The fact that higher ventricular volumes are associated with lower ejection fractions is not surprising. Chronic volume overload ultimately causes failure of compensatory mechanisms, progressive ventricular dilatation, inadequate ventricular hypertrophy and consequently decreased global systolic function [1]. Moreover, it has been demonstrated that the indexed RV volumes are valid estimates of intrinsic RV contractility in patients with repaired TOF [22]. Thus, RV enlargement is directly linked to intrinsic RV dysfunction [22]. Although not directly demonstrated in our study, one can speculate that to preserve ventricular systolic function, all factors leading to ventricular dilatation should be targeted. Gatzoulis et al. [23] demonstrated that preserved ventricular systolic function heralds a positive outcome in patients with repaired TOF, and "aggressive intervention for right-sided haemodynamic abnormalities may have contributed to this outcome". During the follow-up, LV and RV systolic functions did not deteriorate, probably due to prompt surgical interventions treating PR and/or RV outflow obstruction [23]. By this aggressive approach, not only was ventricular systolic function preserved, but also cardiothoracic ratio remained stable, suggesting the preservation of ventricular volumes [23]. Whether biventricular dysfunction suggests or predicts irreversible injury is yet to be elucidated. This would require comparing the results of pulmonary valve replacement in

patients with biventricular dysfunction to those with normal ventricular systolic functions, a comparison beyond the scope of our study.

Finally, we have demonstrated that a substantial proportion of patients with repaired TOF, namely one fifth of the study population, had impaired both RV and LV systolic functions. Previous studies have proved that low RVEF and low LVEF are main predictors of a poor clinical outcome in this population [4]. Therefore, this significant population at risk for increased morbidity and mortality should be followed up closely. On the other hand, there was a large group of patients (about 45% of the study population) with both normal RVEF and normal LVEF. Either RVEF or LVEF, when normal, has been proved to be a reliable predictor for a favourable clinical outcome. Considering the continuously growing population of adolescents and adults with repaired congenital heart disease, and an increasing number of hospitalisations and outpatient visits due to congenital heart disease, the identification of patients at risk requiring close follow-up, and those with predicted good clinical outcome, may be of particular importance for healthcare systems and congenital heart disease centres. This approach could potentially reduce patient burden and costs. However, the assessment of outcomes in patients with normal and impaired ventricular systolic function was beyond the scope of this manuscript, and these speculations need to be confirmed in prospective studies.

Limitations of the study

Our study suffers from several limitations. It was a single centre cross-sectional study with all inherent limitations of this study design. A causal link between variables which demonstrated an association in the current study needs to be confirmed in prospective investigations.

We believe that ventricular dysfunction due to prolonged hypoxaemia, intraoperative myocardial ischaemia, or CAD was not a significant confounder of postrepair ventricular dysfunction. On the basis of medical history taking, which revealed typical/atypical angina, we excluded patients with CAD. There were only seven (4.8%) patients older than 45 years including four males. None of them gave symptoms suggesting the presence of obstructive CAD. None of the patients was older than 55 years. All patients were screened for the presence of risk factors for CAD, but the limited number of patients having any risk factor precluded statistical analysis. In one patient with typical angina, subsequent testing revealed the presence of obstructive CAD and the patient underwent percutaneous coronary intervention. This patient was excluded from the analysis. None of the patients had LGE of ischaemic pattern, which was consistent with no evidence of ischaemic injury. This is in agreement with the study by Muzarelli et al. [16] who demonstrated that ischaemic myocardial injury "is not likely to represent the most frequent cause of LV systolic dysfunction" in patients after TOF repair.

Patients with the lowest LVEF and RVEF were most probably not included in this study due to contraindications to CMR such as pacing systems and implantable cardioverter--defibrillators. Therefore, owing to this referral bias, the study population may not have been representative for all adults and adolescents with repaired TOF.

CONCLUSIONS

We demonstrated that impaired both RVEF and LVEF are common in patients with repaired TOF, with the vast majority being males. Additionally, RVOT aneurysm/akinesia was independently associated with biventricular dysfunction. On the other hand, neither the presence nor the extent of LGE was associated with impaired ventricular systolic functions. Considering the high risk for negative outcomes in these patients, as demonstrated in previous studies, a close follow-up of this population is warranted.

Conflict of interest: *Mateusz Śpiewak — speaker honoraria from Siemens.*

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Czynniki związane z obukomorową dysfunkcją skurczową u pacjentów po korekcji tetralogii Fallota

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Streszczenie

Wstęp: U pacjentów po korekcji tetralogii Fallota (TOF) często występuje dysfunkcja prawej komory (RV). Ponadto w tej populacji wykazano upośledzoną czynność lewej komory (LV). Nie są dostępne dane dotyczące pacjentów po korekcji TOF z obniżoną frakcją wyrzutową zarówno prawej (RVEF), jak i lewej komory (LVEF).

Cel: Hipotezą niniejszej pracy było, że znaczna część pacjentów po korekcji TOF charakteryzuje się upośledzeniem funkcji jednocześnie RV i LV. Celem pracy była charakterystyka pacjentów po korekcji TOF z obukomorową dysfunkcją skurczową.

Metody: Do badania włączono kolejnych pacjentów po korekcji TOF, u których wykonano rezonans magnetyczny serca. Badana grupa obejmowała 146 pacjentów (średni wiek: 26,4 ± 8,2 roku, zakres 13,6–51,3 roku), 60,3% stanowili mężczyźni. U 54 (37,0%) pacjentów korekcję całkowitą wady wykonano wcześnie (< 3 rż.), a u 92 (63,0%) w późniejszym okresie (≥ 3 rż.).

Wyniki: W badanej grupie było 31 pacjentów (21,2% całej badanej populacji; 90,3% mężczyzn) z obukomorową dysfunkcją skurczową. Prawidłowe wartości RVEF i LVEF stwierdzono u 65 (44,5%) osób. Ani obecność, ani stopień nasilenia późnego wzmocnienia pokontrastowego nie różniły się między pacjentami z prawidłową RVEF i prawidłową LVEF oraz pacjentami z obniżoną RVEF i obniżoną LVEF. Pomiędzy tymi grupami nie zaobserwowano różnic w wartości frakcji niedomykalności płucnej, maksymalnym gradiencie w drodze odpływu prawej komory (RVOT) ani w częstości występowania istotnej niedomykalności płucnej lub istotnego zwężenia RVOT (p = NS dla wszystkich porównań). W analizie regresji logistycznej wykazano, że płeć męska i obecność tętniaka/akinezy w RVOT wiązały się z występowaniem obukomorowej dysfunkcji skurczowej.

Wnioski: U pacjentów po korekcji TOF płeć męska i obecność tętniaka/akinezy w RVOT były w sposób niezależny związane z obukomorową dysfunkcją skurczową. Jednoczesne obniżenie RVEF i LVEF występuje często w tej populacji, ze znaczną przewagą wśród mężczyzn.

Słowa kluczowe: tetralogia Fallota, późne wzmocnienie pokontrastowe, niewydolność serca, rezonans magnetyczny

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