Serial follow-up of biventricular function, contractile reserve, exercise capacity, and NT-proBNP measurements in repaired tetralogy of Fallot

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Purpose

To study the course of biventricular size, function, and contractile reserve in patients with repaired tetralogy of Fallot, in relation to exercise capacity and NT-proBNP levels, with prospective serial follow-up, and to establish guidelines for CMR imaging intervals.

Methods

Patients: Serial follow-up was performed in 36 patients (25 male) with a 5 year interval.
CMR imaging: At rest and during dobutamine stress (7.5 µg/kg/min.), end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), ejection fraction (EF), and mass were calculated using a short axis set. Pulmonary regurgitation (PR) was calculated using flow measurements of the pulmonary valve. RV effective SV (RVeff.SV) (SV corrected for PR volume) was calculated additionally.
Results of stress testing are presented as absolute values or as change compared to the values at rest.
Two subgroups were created, based on RVEDV at follow-up, using a cut-off value of RVEDV 150 ml/m²; 9 patients had undergone a pulmonary valve replacement (PVR) during follow-up (1.9 ± 1.1 yrs after the baseline study) and were evaluated as third subgroup.
Exercise test: Patients performed a maximal bicycle exercise test (respiratory quotient at peak exercise ≥ 1.05). Results are presented as percentages of predicted values if appropriate.
NT-proBNP: Results of NT-proBNP measurements were compared with results in a group of healthy controls, matched for gender and age at study.

Results

Table 1: Baseline characteristics and results of exercise testing and NT-proBNP measurements

	Subgroup I (N = 15) RVEDV < 150ml/m²		Subgroup II (N = 12) RVEDV ≥ 150ml/m²		PVR subgroup (N = 9)	
Age at surgery (yrs)	0.9 ± 0.5		0.6 ± 0.3		1.0 ± 0.6	
Transannular patch	9 (60%)‡$		12 (100%)		9 (100%)	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Age at study (yrs)	14.1 ± 4.0	19.4 ± 4.1*	14.1 ± 5.1	19.4 ± 4.8*	18.0 ± 5.3	23.4 ± 5.4*
NYHA class	I: 13 (87%) II: 2 (13%)	I: 13 (87%) II: 2 (13%)	I: 11 (92%) II: 1 (8%)	I: 8 (67%) II: 4 (33%)	I: 7 (78%) II: 2 (22%)	I: 9 (100%) II: 0 (0%)
Peak workload (%)	92 ± 15	94 ± 14	89 ± 11	86 ± 11	88 ± 9	86 ± 8
VO_2 max. (%)	94 ± 21	90 ± 13	96 ± 18	84 ± 16	92 ± 9	88 ± 11
VE/VCO_2 slope	30 ± 5	30 ± 5	32 ± 3	32 ± 4	32 ± 5	29 ± 7
NT-proBNP (pmol/l)	11 ± 10	11 ± 9	18 ± 11	15 ± 10	13 ± 8	14 ± 11

Results are given as mean ± standard deviation or as counts (percentages).
* Significant difference between baseline and follow-up.
‡ Significant difference with subgroup II; $ Significant difference with PVR subgroup.

Exercise test: In subgroup II, VO_2 max. tended to decrease, but this was not statistically significant (table 1) (VO_2 max. 96 ± 18% vs. 84 ± 16%, p = 0.054). There were no significant changes from baseline to follow-up within the subgroups, nor were there significant differences between the subgroups at baseline or follow-up.
NT-proBNP: NT-proBNP levels were significantly higher in patients than in healthy controls (13 ± 10 pmol/l vs. 4 ± 3 pmol/l, p < 0.001). NT-proBNP levels did not change from baseline to follow-up within any of the subgroups, nor were there significant differences between the subgroups at baseline or follow-up.

Results, continued

CMR imaging: Biventricular contractile reserve was preserved in all patients (figure 1 / table 2). PR and RV volumes (EDV, ESV, SV) increased significantly at follow-up, but only within subgroup II. Biventricular EF, LV parameters, and biventricular contractile reserve remained stable in subgroups I and II and were not different at follow-up between all 3 subgroups.
PR and RV volumes decreased after PVR; RVEF at rest, RVeff.SV at stress and LV contractile reserve increased significantly after PVR.

Figure 1: Serial follow-up results of RVEDV, RVEF and LVEF at rest and at dobutamine stress

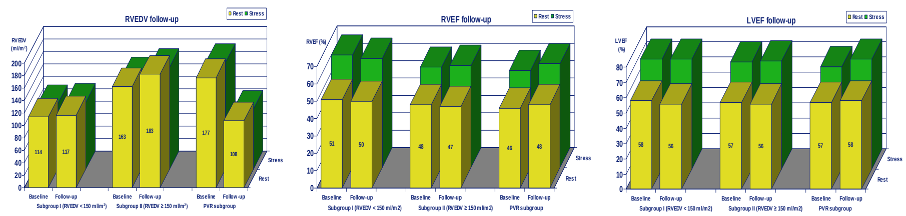


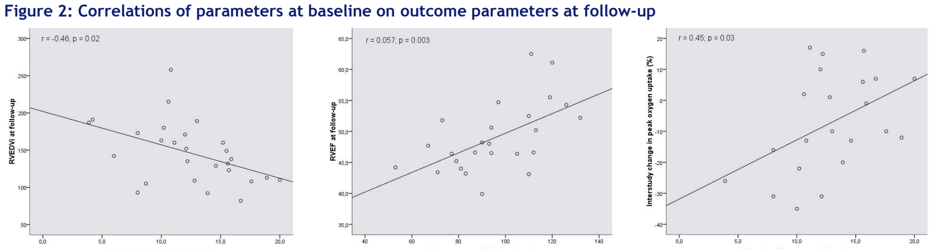
Table 2: CMR imaging results at rest and at dobutamine stress at baseline and at follow-up

	BASELINE						FOLLOW-UP					
	Subgroup I (N = 15) RVEDV < 150 ml/m²		Subgroup II (N = 12) RVEDV ≥ 150 ml/m²		PVR group (N = 9) Before PVR		Subgroup I (N = 15) RVEDV < 150 ml/m²		Subgroup II (N = 12) RVEDV ≥ 150 ml/m²		PVR group (N = 9) AfterPVR	
	Rest	Change	Rest	Change	Rest	Change	Rest	Change	Rest	Change	Rest	Change
PR (%)	19 ± 12‡$	0 ± 4	43 ± 9	-1 ± 7	40 ± 6	4 ± 6#	20 ± 13‡$	-4 ± 3#	48 ± 7*$	-4 ± 4#	6 ± 8*	-1 ± 1*#
RVEDV (ml/m²)	114 ± 24‡$	-8 ± 9#	163 ± 25	-13 ± 11#	177 ± 42	-5 ± 9	117 ± 20‡	-9 ± 8#‡	183 ± 29*$	-19 ± 12*#	108 ± 14*	-11 ± 7#
RVESV (ml/m²)	56 ± 17‡$	-19 ± 7#	85 ± 16	-22 ± 7#	96 ± 30	-19 ± 11#	59 ± 15‡	-19 ± 6#‡	98 ± 21*$	-29 ± 12*#$	56 ± 11*	-17 ± 8#
RVeff.SV (ml/m²)	47 ± 8	7 ± 5#	45 ± 6	5 ± 10	49 ± 9	2 ± 4	46 ± 6	10 ± 7#	44 ± 6	9 ± 6#	49 ± 6	7 ± 4*#
RVEF (%)	51 ± 6	14 ± 4#‡$	48 ± 4	10 ± 3#	46 ± 5	10 ± 4#	50 ± 6	13 ± 4#	47 ± 4	12 ± 5*#	48 ± 4*	12 ± 4#
LVEDV (ml/m²)	82 ± 11	-2 ± 6	81 ± 8	-5 ± 5#$	87 ± 12	1 ± 5	86 ± 11	-5 ± 6#	83 ± 10	-4 ± 6#	84 ± 7	-7 ± 6*#
LVESV (ml/m²)	35 ± 6	-12 ± 4#	35 ± 5	-12 ± 3#	37 ± 7	-9 ± 5 #	36 ± 8	-14 ± 7#	37 ± 5	-13 ± 5#	35 ± 3	-14 ± 3*#
LVEF (%)	58 ± 4	14 ± 4#	57 ± 4	13 ± 4#	57 ± 3	10 ± 4#	56 ± 5	16 ± 4#	56 ± 3	15 ± 5*#	58 ± 4	14 ± 3*#

Results are given as mean ± standard deviation.
Significant difference between rest and dobutamine stress; * Significant difference between baseline and follow-up.
‡ Significant difference with subgroup II (ANOVA, Bonferroni); $ Significant difference with PVR group (ANOVA, Bonferroni).

Correlations: Correlations were assessed in non-PVR patients; the most remarkable correlations are displayed in figure 2 and in this subsection): A lower RVEF at baseline correlated with a larger RVEDV at follow-up (RVEF: r = -0.42, p = 0.03). The increase in biventricular SV at stress, the increase in RVeff.SV at stress, and biventricular contractile reserve at baseline correlated positively with the interstudy change in VO_2 max. (LV contractile reserve: r = 0.61, p = 0.003).

Figure 2: Correlations of parameters at baseline on outcome parameters at follow-up



Conclusions

- PR and RV volumes increased in 5 years time, but only in patients with an RVEDV ≥ 150 ml/m² at baseline. VO_2 max. tended to decrease in these patients, but biventricular function, contractile reserve, and NT-proBNP levels remained stable and were not different between all 3 subgroups at follow-up. After PVR, RVEF and LV contractile reserve increased.

- We believe a conservative approach towards CMR imaging intervals and PVR is justified in patients with an RVEDV < 150 ml/m². A 2-3 year interval between CMR imaging studies seems justified in patients with an RVEDV ≥ 150 ml/m², in the absence of clinical deterioration.

- CMR stress imaging might be of additional value in the follow-up of patients after TOF repair.