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Exercise Capacity in Young Patients After Total Repair of Tetralogy of Fallot

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Abstract. Tetralogy of Fallot is the most common form of cyanotic congenital heart disease. Measurement of physical activity is usually performed as a routine part of the patient's cardiac evaluation. The aim of this study was to examine the exercise performance of young patients operated on for tetralogy of Fallot, assessing the possible influence of known negative prognostic factors related to the surgical repair. The study group comprised 41 consecutive patients (29 male and 12 female, ages 11.2 ± 3.9 years, range 6–16 years) operated on for tetralogy of Fallot. Patients in the study group were divided in subgroups in relation to the age of surgical intervention (before or after 2 years of life), the surgical approach (combined transatrial/transpulmonary approach or right ventriculotomy), and the presence of aortopulmonary shunts prior to performing total correction. Their data were compared with those of 33 aged-matched asymptomatic control subjects (19 male and 14 female, ages 11.9 ± 1.3 years, range 11–16 years). Blood pressure and heart rate measured at rest were similar between control and Fallot groups. A normal increase in systolic blood pressure was observed in response to exercise intensity for all subgroups. No significant difference between control and Fallot groups was found under conditions of mild or moderate exercise or for diastolic blood pressure at rest and in response to exercise. Lower maximal heart rate and systolic blood pressure values were recorded in all patients when compared with the control subjects. Significant differences in peak workload were detected between control and Fallot groups and between the control and each subgroup; however, no difference was found between subgroups. In conclusion, despite their very satisfactory clinical status, all patients showed a reduced peak workload, irrespective of the surgical approach, age at surgery, and aortopulmonary shunts prior to performing total correction.

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Tetralogy of Fallot is the most common form of cyanotic congenital heart disease. The current standard of its treatment is reparative operation in early infancy. Nevertheless, long-term success is hampered by the occurrence of arrhythmias and late sudden death [1, 9, 11].

Measurement of physical activity is usually performed as a routine part of the patient's cardiac evaluation because both physicians and parents are frequently involved in efforts to maximize the participation of such patients operated on for tetralogy of Fallot in recreational and noncompetitive sports. Exercise testing after intracardiac repair of tetralogy of Fallot indicates that maximal working capacity is generally reduced by 10% to 30% in these patients when compared with control subjects [12, 24] and may be associated with right ventricular exercise dysfunction [23, 25]. The aim of this study was to examine the exercise performance of young patients operated on for tetralogy of Fallot and assess the possible influence of known negative prognostic factors on the exercise capacity, such as late repair, aortopulmonary shunts prior to performing the total correction and transventricular surgical approach.

Patients and Methods

The study group comprised 41 consecutive patients (29 male and 12 female, age at follow-up 11.2 ± 3.9 years, range 6–16 years) operated on for tetralogy of Fallot between 1981 and 1991 (age at surgery 2.4 ± 1.2 years, duration of follow-up 8.2 ± 3.2 years) recruited from a cohort of children followed regularly in the outpatient cardiac clinic of Paediatric Cardiology Division — Monaldi Hospital of Naples. The exercise test was used as a routine part of the patient's cardiac evaluation. A detailed explanation of the exercise test was given to the subjects and/or parents, and informed consent was obtained.

Patient's data were evaluated and compared with those of 33 aged-matched asymptomatic control subjects (19 male and 14 female,

Table 1. Patients' characteristics

	Control group	Total Fallot group	Age at surgery (group A vs B)	Surgical approach (group C vs D)	Aortopulmonary shunts (group E vs F)
No. Patients	33	41	17 vs 24	26 vs 15	27 vs 14
Sex	19 M/14 F	29 M/12 F	13 M/4 F vs 16 M/8 F	14 M/12 F vs 15 M	20 M/7 F vs 9 M/5 F
Age at follow-up	11.9 ± 1.3	11.2 ± 3.9	11.5 ± 3.2 vs 11.1 ± 4.5	11 ± 2.9 vs 11.7 ± 5.4	11.2 ± 3 vs 11.4 ± 5.5
Height (cm)	159.8 ± 10.5	143.9 ± 24.1	146.1 ± 2.8 vs 142.5 ± 17.2	141 ± 26.6 vs 149.7 ± 17.6	144.4 ± 27.1 vs 142.9 ± 18.4
Weight (kg)	52.2 ± 11.6	45.7 ± 23.6	56.2 ± 32 vs 39.2 ± 13.5	46.4 ± 27.3 vs 44.5 ± 14.2	49.8 ± 26.5 vs 38.4 ± 15.4
Body surface (m^2)		1.3 ± 0.3	1.4 ± 0.3 vs 1.2 ± 0.3	1.3 ± 0.3 vs 1.4 ± 0.3	1.4 ± 0.3 vs 1.2 ± 0.3
Age at surgery		2.4 ± 1.2	1.4 ± 0.5 vs 3.2 ± 0.9	2.4 ± 1.3 vs 2.5 ± 0.8	2.1 ± 1.1 vs 3.1 ± 0.9
Follow-up (years)		8.2 ± 3.2	10.2 ± 3.1 vs 6.7 ± 2.3	8.8 ± 3.4 vs 7.1 ± 2.5	9.2 ± 3.2 vs 5.8 ± 1.6

Age at surgery, age of surgical intervention [before (group A) or after (group B) 2 years of life]; surgical approach, combined transatrial/transpulmonary approach (group C) or right ventriculotomy (group D); aortopulmonary shunts prior to perform total correction, absence (group E) or presence (F).

age 11.9 ± 1.3 years, range 11–16 years). Patients in the study group were divided in subgroups in relation to the age at surgery [before (group A) or after (group B) 2 years of life], the surgical approach [combined transatrial/transpulmonary approach (group C) or right ventriculotomy (group D)], and the presence (group E) or the absence (group F) of aortopulmonary shunt (modified Blalock–Taussig shunt) prior to performing total correction. Specific inclusion criteria were as follows for all patients:

1. Ability to perform a symptom-limited bicycle ergometric stress test
2. The absence of any anamnestic, clinical, and instrumental evidence of heart failure and significant pulmonary regurgitation or right ventricular outflow tract obstruction
3. The absence of resting arrhythmias
4. The absence of abnormal lung function assessed by chest x-ray film, spirometry, and blood gas analysis
5. The absence of a previous history of symptomatic arrhythmia, syncope, pulmonary hypertension, or myocardial dysfunction
6. The absence of any significant arrhythmias on the electrocardiogram (ECG) Holter recordings (ventricular arrhythmias less than grade 1 according to the modification of Lown's criteria proposed by Deanfield et al. [5])
7. The absence of treatment with diuretics or cardioactive drugs (digitalis, beta-blockers, calcium channel blockers, and antiarrhythmics)
8. Age at the time of surgical repair less than 4 years

A maximal symptoms-limited exercise protocol was used with a bicycle ergometer with stepwise increments of 25 W every 3 min.

Twelve-lead ECGs and blood pressure measurements were recorded at rest before exercise, at the end of each workload, and at peak exercise. Blood pressure was measured by the same recorder from the right arm with a cuff of appropriate size. The test was terminated when one of the following endpoints was reached: target heart rate, severe fatigue, maximal systolic blood pressure during exercise, severe dyspnoea, or severe arrhythmias. All children were given considerable verbal encouragement to continue exercising as long as possible.

The following data were reported in the study: heart rate and blood pressure measured at rest, at the end of each step during exercise, and at peak exercise, peak workload expressed in watts, reasons for test termination, and diagnostic conclusions.

Statistics

Results are expressed as the mean value ± standard deviation. Differences in group means between the control group and Fallot group were analyzed with two-tailed unpaired *t*-test. One-way analysis of variance and Bonferroni's correction were used to evaluate any significant difference between control and study subgroups.

The chi-square test was used to test the significance of differences among the groups in terms of diagnostic conclusions of the ergometric stress test (maximal, submaximal, or not diagnostic). A p value of <0.05 was considered statistically significance.

Results

Patient characteristics are listed in Table 1. The resting ECGs of all the subjects revealed sinus rhythm. All the patients of the study group presented complete right bundle branch block, whereas no conductance disturbances were shown in the control group.

Ergometric stress test data of the control and study groups are summarized in Table 2. Blood pressure and heart rate measured at rest were similar for control and Fallot groups. A normal increase in systolic blood pressure was observed in response to exercise intensity for all subgroups. No significant difference between control and Fallot groups was found under conditions of mild or moderate exercise (75 W) as well as for diastolic blood pressure at rest and in response to exercise. Lower maximal heart rate and systolic blood pressure values were recorded in all patients when compared with those of the control subjects.

Significant differences in peak workload were detected between control and Fallot groups as well as between the control and each of the subgroups. However, no difference was found between subgroups. Furthermore, no differences were found between the groups in terms of diagnostic conclusions of the ergometric stress test (maximal, submaximal, or not diagnostic).

Exercise-induced uniform ventricular premature complexes occurred in six patients in the study group. They were detected only during the immediate recovery period in three patients, during exercise only in one, and during both exercise and recovery in two.

Table 2. Ergometric stress test in the control and study groups

	Control group	Total Fallot group	Age at surgery (group A vs B)	Surgical approach (group C vs D)	Aortopulmonary shunts (group E vs F)
No. Patients	33	41	17 vs 24	26 vs 15	27 vs 14
Age	11.9 ± 1.3	11.2 ± 3.9	11.5 ± 3.2 vs 11.1 ± 4.5	11 ± 2.9 vs 11.7 ± 5.4	11.2 ± 3 vs 11.4 ± 5.5
Basal HR	91.7 ± 12.3	91.3 ± 12.5	94.9 ± 10.2 vs 88.6 ± 13.6	92.3 ± 12.5 vs 89.5 ± 12.8	92.9 ± 12.4 vs 88.2 ± 12.7
Basal SBP	107.9 ± 8	107.1 ± 11.9	111.4 ± 11.3 vs 103.9 ± 11.6	107.5 ± 10.6 vs 106.5 ± 14.2	108.9 ± 10.5 vs 103.6 ± 14.3
Basal DBP	64.5 ± 6.3	64.5 ± 8.9	67.1 ± 8.5 vs 62.6 ± 8.9	65 ± 9.6 vs 63.8 ± 7.9	66.4 ± 7.4 vs 60.9 ± 10.7
75 W HR	140.2 ± 24.8	149.7 ± 22	150 ± 15.2 vs 149.5 ± 27.2	152.9 ± 21.6 vs 144 ± 22.8	148.3 ± 20.4 vs 153.3 ± 26.9
75 W SBP	143.9 ± 10.6	149 ± 17.8	148.3 ± 11.1 vs 149.6 ± 22.4	146.9 ± 15.5 vs 152.5 ± 21.4	145.6 ± 14.7 vs 156.9 ± 22.4
75 W DBP	78 ± 4.3	76.2 ± 8.9	75.8 ± 6 vs 76.4 ± 11	75.6 ± 10.5 vs 77 ± 5.9	76.1 ± 8.7 vs 76.3 ± 9.9
Maximal HR	175.5 ± 17.5	167.5 ± 17.4	173.5 ± 17.4 vs 163.1 ± 16.4	168.4 ± 18.7 vs 166.1 ± 15.6	169.3 ± 18.4 vs 164.1 ± 15.4
Maximal SBP	166.8 ± 18.3	158.3 ± 25	159.2 ± 22.4 vs 157.6 ± 27.2	152.1 ± 25.3 vs 167.3 ± 22.4	153.5 ± 22.7 vs 166.3 ± 27.6
Maximal DBP	75.9 ± 5.5	78.8 ± 9.3	78.8 ± 6.8 vs 78.7 ± 10.9	77.9 ± 10.8 vs 80 ± 6.8	77.8 ± 9 vs 80.4 ± 10.1
Peak workload	136.4 ± 39.1*	92.9 ± 32.4	98.3 ± 37.2 vs 88.8 ± 28.6	87.5 ± 32.5 vs 101.9 ± 31.4	95.7 ± 33.4 vs 87.5 ± 31.1
Maximal EST	12	4	4 vs 0 pts	4 vs 0 pts	4 vs 0 pts
Submaximal EST	11	15	4 vs 11 pts	5 vs 10 pts	8 vs 7 pts
Not diagnostic EST	10	22	9 vs 13 pts	17 vs 5 pts	15 vs 7 pts

Age at surgery, age of surgical intervention [before (group A) or after (group B) 2 years of life]; surgical approach, combined transatrial/transpulmonary approach (group C) or right ventriculotomy (group D); aortopulmonary shunts prior to perform total correction, absence (group E) or presence (F); HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; 75 W HR, heart rate at moderate exercise (75 W); 75 W SBP, systolic blood pressure at moderate exercise (75 W); 75 W DBP, diastolic blood pressure at moderate exercise (75 W); maximal EST, number of subjects with maximal negative ergometric stress test; submaximal EST, number of subjects with submaximal negative ergometric stress test; not diagnostic EST; number of subjects with a not diagnostic ergometric stress test; pts = patients.
* $p < 0.0001$; Differences are calculated as total Fallot group vs control group.

Discussion

Impaired exercise capacity and ventricular arrhythmia have been proposed as risk factors for sudden death after repair of tetralogy of Fallot [8, 22]. However, the predisposing factors remain controversial [4], even though residual hemodynamic abnormalities after surgery [18, 19], age at surgery [5, 9, 19], and duration of follow-up [4, 28] are considered crucial.

The aim of the study was to evaluate the exercise performance of young patients operated on for tetralogy of Fallot and assess the potential influence of several known negative factors relative to the total surgical correction. Our data on general reduced maximal exercise tolerance agree with those of previous reports [6, 12, 20, 23–25, 27], even though the possible pathophysiological mechanisms that could explain our's and previous observations are only conjectural since limited information is available concerning the hemodynamic responses of these patients to exercise. However, recent studies suggest that, in the absence of significant lung function abnormalities and significant hemodynamic embalancement, the impaired exercise performance could be related to an abnormality of both left and right ventricular compliance [21].

Right and left ventricular myocardial fibrosis [13, 15] in addition to myocardial hypertrophy or increased ventricular volume, alone or in combination with the superimposition of the effects of cardiopulmonary bypass, ventriculotomy, inadequate myocardial protection, and the placement of nonfunctional patches, could cause abnormalities in ventricular compliance [3, 10, 21]. Severe abnormalities of diastolic function, could cause the right ventricle to become unfillable during atrial systole and act as a passive conduit, with an antegrade diastolic pulmonary blood flow coincident with atrial systole.

The reduced inotropic reserve or compliance of right ventricle and the increase in right ventricular end diastolic and pulmonary wedge pressures [7] could be responsible for the decrease in the stroke index [21] that, alone or in combination with the inability of heart rate to increase in proportions similar to those observed in control subjects, could result in a significant decrease in cardiac output and exercise capacity. However, the exercise capacity of these patients can be expected to be partly related to daily exercise habits. Although the attitudes of the majority of pediatricians and cardiologists are liberal concerning physical activity for children operated on for tetralogy of Fallot with a good hemodynamic repair, many patients are usually advised by their parents against exercise activities. The factor limiting exercise may not be the heart but rather skeletal muscle function [31]. In this setting, mild cardiac impairment in the presence of average physical training may not cause any obvious reduction in exercise performance even with maximal ergometric stress test [31].

One of the most important findings of this study was that, despite their very satisfactory clinical status, all pa-

tients showed a reduced peak workload, irrespective of the surgical approach used. Currently, the effects in young patients operated on for tetralogy of Fallot of the previously mentioned negative prognostic factors in terms of exercise performance and right or left ventricular function are not clear and quite controversial. Although the correlation between ventricular tachycardia or impaired exercise tolerance and older age at first repair was described in previous reports [14, 16, 17, 20], it is not universally supported [2, 28]. Nevertheless, it has been shown [26] that prior aortopulmonary shunt procedures were not more frequent among patients with ventricular arrhythmias and reduced exercise performance, as noted previously [17, 28], despite reports of such association [30].

In this study it could be supposed that the lack of differences in terms of exercise performance between the subgroups could be related to the fact that all the previously mentioned factors, such as the abnormality of both left and right ventricular compliance and of right ventricular diastolic function, the reduced cardiac output, and the reduced physical activity, may all contribute to an abnormal exercise response despite the presence or absence of the known negative prognostic factors. Furthermore, although our data are not in agreement with data from previous reports that indicated that better exercise performance is associated with earlier primary repair and a lesser degree of residual impairment [14, 20], the strict patient selection criteria used in this study must be taken into account.

All the patients enrolled were operated on in early infancy, which has been associated with a lesser degree of ventricular dysfunction; all had a good hemodynamic repair (no intracardiac shunts or pulmonary incompetence and a right ventricular systolic pressure at rest of <60 mmHg); and none had a previous history of symptomatic arrhythmia, syncope, pulmonary hypertension, or heart failure.

Furthermore, the effect of the shorter follow-up and the young age of the patients at follow-up must also be considered. Although it has been shown that in patients operated on for tetralogy of Fallot the exercise tolerance did not change significantly over time [29], it is possible that exercise performance might decrease with longer follow-up in a different way in the selected groups. Further studies are warranted to explore this possibility.

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From PediHeart

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