Effect of Right Ventricular Anatomy on the Cardiopulmonary Response to Exercise
Implications for the Fontan Procedure

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Incorporation of the right ventricle (RV) into the pulmonary circulation of patients with tricuspid atresia undergoing a Fontan procedure has been advocated. The consequences of this approach on the exercise function of these patients was studied by examining the effects of progressive and steady-state bicycle exercise tests performed by 11 patients with right atrial (RA)–RV Fontan anastomoses, seven patients with RA–pulmonary artery (PA) Fontan anastomoses, 13 patients after repair of tetralogy of Fallot, and 34 normal control patients. All patients were in New York Heart Association class I. The exercise function of the patients undergoing RA-RV and RA-PA Fontan procedures were similar. They achieved peak work loads 60% and 67% of control and peak oxygen consumptions 60% and 64% of control, respectively. Both groups also displayed excessive ventilation, elevated dead space/tidal volume ratios, and depressed cardiac output during steady-state exercise. In contrast, tetralogy of Fallot patients achieved peak work loads and oxygen consumptions 83% of control and maintained normal cardiac outputs and dead space/tidal volume ratios during steady-state exercise. These results suggest that the presence of an RV within the pulmonary circulation of the Fontan patient does not result in improved exercise function. This may be due to the development of obstructive gradients across the RA-RV conduits during exercise or to the RV’s negative effect on left ventricular compliance. Moreover, in contrast with the postoperative tetralogy of Fallot patient, the hypoplastic RV of tricuspid atresia may not have sufficient myocardium to assume the active pumping function required by exercise. (Circulation 1990;81:1811–1817)

In the original Fontan operation for tricuspid atresia, the right ventricle (RV) was excluded from the pulmonary circulation.1 Since that time, various modifications of the Fontan procedure have been developed.2–8 Some centers have advocated incorporating the RV into the pulmonary circulation, whenever possible, by interposing a valved conduit between the right atrium (RA) and RV.5,7 Postoperative catheterization studies have demonstrated that these patients have a “ventricularized” pressure tracing within the RV. A prominent “v” wave also appears in the pulmonary artery (PA), reflecting the systolic contractile function of the RV.7–9 Doppler echocardiographic studies have demonstrated significant RV systolic contribution to PA blood flow in patients with RA-RV conduits.9,10 In contrast, individuals with direct RA-PA Fontan anastomoses do not have augmentation of PA pressure orflow during ventricular systole.8–10 Thus, Fontan patients with pulmonary ventricles appear to have hemodynamic characteristics that differ from those with direct RA-PA anastomoses. The functional and clinical implications of these hemodynamic alterations have not been thoroughly evaluated.

Tetralogy of Fallot is another congenital heart defect in which the RV is malformed. However, in contrast to the Fontan patient, the pulmonary ventricle of the repaired tetralogy of Fallot patient is neither absent, as in the Fontan patient with a direct RA-PA anastomosis, nor hypoplastic, as it is in the typical Fontan patient with an RA-RV anastomosis. The purpose of this study was to examine the exercise function of Fontan patients with and without pulmonary ventricles and to compare them to postoperative tetralogy of Fallot patients, as well as normal healthy control subjects, with the same protocols, equipment, and personnel. This format was chosen to

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study the role of the RV in the Fontan circulation and to explore other factors that might influence exercise performance after the Fontan operation.

Methods

Subjects

Eleven of 23 patients followed up at Babies Hospital after undergoing RA-RV valved conduit repair of tricuspid atresia participated in the study (RA-RV group) as did seven of 18 patients who had had direct RA-PA anastomoses for tricuspid atresia and other single ventricle equivalents (RA-PA group). Only patients who were in New York Heart Association class I, who were engaged in normal daily activities and required no cardiovascular medications, were included in the study. Hence, the performance of these subjects represents that of Fontan patients with the best clinical outcomes and excludes individuals in whom postoperative complications might have altered the patient’s status. A third group (tetralogy of Fallot group) comprised 13 patients who had undergone surgical repair of tetralogy of Fallot. They too were clinically well and were not receiving medications. A final group of 34 normal healthy control subjects was also studied. Three patients, all from the RA-RV group, had received previous Glenn shunts. Hence, for some analyses, the RA-RV group was subdivided into a group with and without previous Glenn shunts. Table 1 summarizes some of the characteristics of the subject groups. The groups were similar in most respects, except that the tetralogy of Fallot patients had open-heart surgery at a younger age than did the

<table>
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<tr>
<th>Table 1. Clinical Characteristics of the Subject Groups</th>
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<tr>
<td>Group</td>
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<tr>
<td>RA-RV</td>
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<td>RA-RV with Glenn shunt</td>
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<td>Control</td>
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BSA, body surface area; M:F ratio, male:female ratio; SaO₂, oxygen saturation; RA-RV, Fontan patients with right atrial–right ventricular valved conduits; RA-PA, Fontan patients with direct right atrial–pulmonary artery anastomoses; TOF, patients after repair of tetralogy of Fallot; NA, not applicable.

<table>
<thead>
<tr>
<th>Table 2. Clinical Characteristics of Individual Patients Undergoing Fontan Operation and Exercise Tests</th>
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<td>Patient</td>
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LVED pressure, preoperative left ventricular end-diastolic pressure; Shunt, history of aortopulmonary shunt; Glenn shunt, history of Glenn shunt; RV, incorporation of the right ventricle into the pulmonary circulation; Work load, percentage of control patients' predicted peak work load; Doppler, pulmonary artery Doppler blood flow pattern; V, ventricular augmentation; A, no ventricular augmentation; TA, tricuspid atresia; SV, single ventricle; TGA, transposition of the great arteries; VSD, ventricular septal defect; PS, pulmonary stenosis.
Table 3. Results of Progressive Exercise Tests

<table>
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<tr>
<th></th>
<th>Peak SaO₂ (%)</th>
<th>Peak work load (%)</th>
<th>Peak VO₂ (%)</th>
<th>Peak HR (%)</th>
<th>Peak VE (%)</th>
<th>Peak VE/VO₂ (%)</th>
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<tr>
<td>RA-RV</td>
<td>89.0±5.1†</td>
<td>59.6±10.0†</td>
<td>59.8±17.5†</td>
<td>97.7±5.7</td>
<td>81.5±30.7*</td>
<td>131.0±34.3*</td>
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<td>RA-RV with Glenn</td>
<td>83.7±2.1†</td>
<td>53.4±6.8†</td>
<td>48.6±12.4†</td>
<td>99.9±5.3</td>
<td>71.7±7.7†</td>
<td>145.9±47.2*</td>
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<tr>
<td>RA-RV without Glenn</td>
<td>91.4±4.4†</td>
<td>61.9±10.2†</td>
<td>64.9±16.4†</td>
<td>96.8±5.8</td>
<td>85.1±35.6</td>
<td>127.0±29.9*</td>
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<tr>
<td>RA-PA</td>
<td>92.1±4.0†</td>
<td>66.7±20.7†</td>
<td>63.7±18.9†</td>
<td>89.9±13.9</td>
<td>84.2±32.4</td>
<td>149.1±48.0†</td>
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<tr>
<td>TOF</td>
<td>95.8±2.6</td>
<td>82.6±18.3*</td>
<td>82.8±31.8*</td>
<td>96.8±8.5</td>
<td>84.8±20.1*</td>
<td>112.1±24.2*</td>
</tr>
<tr>
<td>Control</td>
<td>96.1±2.0</td>
<td>100.0±24.5</td>
<td>100.0±24.6</td>
<td>100.0±11.4</td>
<td>100.0±14.2</td>
<td>100.0±14.2</td>
</tr>
</tbody>
</table>

*p<0.05 vs. control; †p<0.05 vs. TOF.

Sao₂, oxygen saturation; VO₂, oxygen consumption; HR, heart rate; VE, minute ventilation; VE/VO₂, ventilatory equivalents for oxygen.

Fontan patients. Table 2 presents some of the clinical characteristics of the individual Fontan patients. Some of the data from the tricuspid atresia patients have been previously reported.11

Protocol

Details of the exercise protocol have been described.12 Briefly, each subject performed a progressive and steady-state exercise test. The protocol for the progressive exercise test required the subjects to pedal on an upright cycle ergometer at a rate of 60 rpm at an initial work load of 0 W. After a 4-minute washout period, the work load was increased at height-appropriate increments each minute until the 60-rpm rate could no longer be maintained. The subject then rested, at least 15 minutes, until the heart rate returned to baseline. Steady-state exercise testing was then performed. The subjects were required to pedal at 60 rpm at work loads of 0%, 25%, and 45% of their maximum work load. Steady state was defined as a constant mixed expired gas composition after 4 minutes of exercise at a given work load. All subjects completed at least two steady-state work loads.

Peak work load, oxygen consumption (VO₂), minute ventilation (VE), and heart rate (HR) were determined from the progressive exercise test. CO₂ production, VO₂, VE, HR, end-tidal PCO₂, and mixed venous PCO₂ were measured during each steady-state work load. (Mixed venous PCO₂ was determined by the CO₂ rebreathe technique.)12,13 The dead space/tidal volume ratio (Vd/Vt) was calculated with the Bohr equation with arterial PCO₂ estimated from end-tidal CO₂.13,14 Cardiac output was calculated by the indirect Fick method for CO₂ with mixed venous and arterial CO₂ contents estimated from the mixed venous and end-tidal PCO₂ values, respectively.12,13

Predicted values from maximal VO₂, work load, and HR were obtained from standard equations.13 The data obtained from the normal control subjects’ steady-state exercise tests were used to construct regression lines for the graphs of cardiac output, VE, Vd/Vt, and HR versus VO₂. These regression lines were then used to obtain a “predicted” cardiac output, VE, Vd/Vt, and HR for each subject based on the VO₂ values achieved by the subject during the steady-state exercise tests. VO₂, cardiac output, and VE were normalized for body weight.

Doppler echocardiograms of resting pulmonary artery blood flow patterns of the Fontan patients were recorded with a GE PASS II (Melville, New York) or ATL Mark V (Northbrook, Illinois) echocardiography machine.

Statistical Analysis

The unpaired Student’s t test was used to compare the exercise measurements of the various groups. Multivariate analysis was used to further evaluate the consequences of including a ventricle within the Fontan patient’s pulmonary circulation. The following parameters were used as independent variables in the multivariate analysis: preoperative left ventricular end-diastolic pressure, history of systemic–pulmonary artery shunt procedures, history of a Glenn shunt, age at time of Fontan procedure, age at time of exercise, and whether the RV was included in the pulmonary circulation. Percent predicted for peak work load was used as the dependent variable. A p value less than 0.05 was considered significant.

Results

The control patients’ mean peak work load was 2.80±0.31 W/kg, peak VO₂ was 38.0±9.5 ml/kg, and peak HR was 174±17 beats/min. These values averaged 95±23%, 94±23%, and 88±10%, respectively, of predicted values. At peak exercise, the control subjects’ arterial oxygen saturation was 96.1±20%, VO₂ was 1.069±152 ml/kg, and VE/VO₂ was 28.2±4.0. The results of the progressive exercise tests for the patient groups are summarized in Table 3. The peak exercise function of the RA-RV and RA-PA groups was similar. Both groups had significantly diminished exercise capacity, performing approximately 60–65% of control for peak work load and peak VO₂. Both groups also manifested similar degrees of arterial desaturation at peak exercise. Although the Fontan patients’ VE at peak exercise was somewhat lower than control, their ventilation was excessive for their level of VO₂, as reflected by their elevated VE/VO₂ ratios. Multivariate analysis of the Fontan patients’ peak exercise function indicated that neither the presence of a pulmonary ventricle, nor any of the other clinical
variables studied, had a significant impact on peak work load.

The average exercise capacity of the postoperative tetralogy of Fallot patients fell in an intermediate range, between that of the Fontan and control subjects. The tetralogy of Fallot patients also maintained normal arterial oxygen saturations and did not ventilate as excessively as did the Fontan patients.

Results of the steady-state exercise tests are summarized in Table 4. A pattern similar to the progressive exercise test was once again seen: no significant difference existed between the RA-RV and RA-PA groups. The cardiac output at any given level of VO2 was decreased for both Fontan groups compared with control. In contrast, tetralogy of Fallot patients maintained normal cardiac outputs during submaximal exercise (see Figure 1). All three patient groups maintained HR appropriate for their levels of VO2. Hence, the Fontan patients' decreased cardiac output was due to their inability to maintain normal stroke volumes (i.e., cardiac output divided by HR) during submaximal exercise. On the other hand, the stroke volume of the tetralogy of Fallot patients was relatively well preserved. The Fontan patients also had elevated VE and Vd/Vt values during the steady-state exercise test. Tetralogy of Fallot patients once again functioned in an intermediate range, between the Fontan patients and control subjects (see Figures 2 and 3).

RA-RV patients with previous Glenn shunts performed less well than the other Fontan patients with regard to VE and oxygen saturation at peak exercise; they did not differ with regard to the other parameters studied. When the patients with previous Glenn shunts were excluded from the analyses, the exercise function of the remaining RA-RV patients (i.e., those without previous Glenn shunts) remained similar to that of the RA-PA patients.

Doppler echocardiography was used to identify those Fontan patients with augmentation of pulmonary artery blood flow during ventricular systole. (Nine of the 11 patients in the RA-RV group manifested this echocardiographic feature; none of the RA-PA patients possessed it; see Table 2). The presence of this feature had no impact on exercise function. The patients' exact intracardiac anatomy (i.e., tricuspid atresia with normally related great vessels vs. other single ventricle equivalents) was also unrelated to exercise function (see Table 2).

**Discussion**

Previous studies have found Fontan patients to have impaired exercise function. Driscoll et al. found peak VO2 and exercise tolerance to average approximately 50–60% of predicted values. The mean peak VO2 and work load for the Fontan patients in the present study averaged approximately 60–65% of control work load. Driscoll et al and other investigators also described abnormalities in ventilation arterial saturation, cardiac output, and stroke volume similar to those documented in this study.

![Figure 1. Regression plot of cardiac output vs. oxygen consumption during submaximal steady-state exercise. RA-RV, Fontan patients with right atrial–right ventricular valved conduits; RA-PA, Fontan patients with direct right atrial–pulmonary artery anastomoses; TOF, patients after repair of tetralogy of Fallot. Solid lines represent regression line for the control patients ±2 SD. Tetralogy of Fallot patients maintained normal cardiac outputs, whereas the cardiac outputs of both Fontan groups were significantly depressed compared with control.](https://example.com/figure1.png)
Previous investigators have described abnormal exercise function among tetralogy of Fallot patients, characterized by reduced peak VO₂ values, exercise duration, and ventilatory thresholds, ranging from 70–90% of predicted values.\textsuperscript{19–21} VE during exercise and cardiac output at submaximal exercise levels has been shown to be relatively normal.\textsuperscript{19} The tetralogy of Fallot patients in this study achieved peak VO₂ and work load values 83% of control while maintaining near normal VE, Vd/VT ratios, and cardiac outputs during submaximal exercise.

This paper presents a unique comparison of tetralogy of Fallot and Fontan patients in the same laboratory. As a consequence of this approach, the comparison is more quantitative and reliable than that made between studies performed at different institutions, with different protocols, and carried out on one or the other of these patient populations. One of the principal findings of this study is the superior exercise function of the tetralogy of Fallot patient. Although neither group did as well as the normal control subjects, the tetralogy of Fallot patients out performed the Fontan patients in every parameter studied. This appears to underscore the importance of RV function in the cardiopulmonary response to exercise. However, among the Fontan patients, the principal finding from the comparison of subjects with and without pulmonary arteries is that incorporation of the RV into the pulmonary circulation of the Fontan patient appears to confer no significant benefit in terms of exercise function, despite its effect on the pulmonary artery blood flow pattern detected by Doppler echocardiography. For each parameter of exercise function studied, the small differences between patients with and without pulmonary ventricles did not achieve statistical or clinical significance. Furthermore, on multivariate analysis, no significant correlation emerged between peak work load and the presence of a pulmonary ventricle.

Another finding with possible clinical relevance was the absence of a significant relation between peak work load and the other clinical and hemodynamic parameters studied with multivariate analysis. This implies that, with proper patient selection and successful surgery, the exercise function of Fontan patients will not be affected by the presence of an RA-PA anastomosis, previous aortopulmonary shunt, previous Glenn shunt, older age, or moderately elevated left ventricular end-diastolic pressure.

Previous studies comparing the exercise function of Fontan patients with RA-RV and RA-PA anastomoses (i.e., with and without pulmonary ventricles) have been inconclusive. Driscoll et al\textsuperscript{15} found superior exercise function in patients with RA-PA anastomoses. However, they believed this difference was related to other factors (i.e., age at time of exercise) rather than the type of operation. These investigators also included patients with valved and nonvalved anastomoses within each study group. In contrast,
Fontan et al. found the exercise capacity of two patients with RA-RV valved conduits to be equivalent to that of 10 patients with RA-PA valved conduits and superior to that of 18 patients with nonvalved RA-RV anastomoses. He also found that the Fontan patient's exercise performance was adversely affected by the presence of a previous Glenn shunt.

Thus, factors that could explain the RV's inability to enhance the exercise performance of the Fontan patient, despite the apparent contribution to resting pulmonary artery blood flow, include 1) the previous Glenn shunts, 2) use of valved conduits to construct the RA-RV anastomoses, and 3) hemodynamic and anatomic features unique to the Fontan patient with a pulmonary ventricle.

**Presence of Patients With Glenn Shunts**

Patients with Glenn shunts are known to develop pulmonary arteriovenous fistulas, which may adversely affect exercise function. In addition, bicycle exercise increases blood flow primarily to the lower extremities. In a Fontan patient without a Glenn shunt, this increased venous return would be distributed to both lungs. In the Fontan patient with Glenn shunt, the increased venous return from the lower extremities can flow only to the left lung. This maldistribution of pulmonary blood flow may also impair exercise tolerance. Despite these considerations, the average exercise performance of the three patients with previous Glenn shunts was only slightly worse than that of the other Fontan patients. It is possible that more significant differences would have emerged if a larger group had been studied. However, when the three patients with Glenn shunts were excluded from the analyses of this study, the average performance of the remaining Fontan patients with RA-RV anastomoses remained practically indistinguishable from that of patients with RA-PA anastomoses. Hence, the presence of subjects with Glenn shunts did not account for the lack of difference in the exercise performance of patients with and without pulmonary ventricles.

**Use of Valved Conduits**

Ben Shachar et al. found that Fontan patients may develop gradients across their conduits during exercise, even if little or no gradient is present at rest. This factor may have impaired the exercise function of the RA-RV patients, all of whom had valved conduits, but it would have had less relevance for the patients without pulmonary ventricles, all of whom had direct RA-PA nonvalved anastomoses.

**Hemodynamic and Anatomic Features Unique to the Fontan Patient**

In patients with RA-RV anastomoses, the left ventricle typically shares a common septum with a small, ventriculotomy scarred chamber that invariably has elevated diastolic pressures. Subsequent right-to-left diastolic bowing of the interventricular septum may cause decreased left ventricular diastolic compliance and increased left ventricular filling pressures. These sequelae would tend to impede pulmonary blood flow, particularly in a Fontan patient. Furthermore, this effect would be magnified during exercise, because the Fontan patient's right-sided pressures are known to rise markedly with exercise. Hence, the beneficial hemodynamic effects of RV systolic function may be counterbalanced by the RV's deleterious impact on left ventricular compliance.

Postoperative catheterization studies have also emphasized the limited functional capacity of the RV of the Fontan patient. Bull et al. found that the RV did not perform any positive work when included in the pulmonary circulation of Fontan patients. Although Coles et al. found that the RV of patients with RA-RV valved conduit connections did perform some mechanical work at rest, the absolute magnitude of the work was small, resulting in a mean PA pressure that exceeded mean RA pressure by only 3.6 mm Hg, a pressure step-up far below the amount achieved by the normal resting RV. These findings suggest that the intrinsically hypoplastic RV of tricuspid atresia, though able to perfuse the pulmonary circulation at rest, simply does not have sufficient myocardium to assume the active vigorous pumping function required of the normal RV during exercise. This appears to explain the differences between Fontan patients with pulmonary ventricles and postoperative tetralogy of Fallot patients. The RV of tetralogy of Fallot patients, though abnormal, is not intrinsically hypoplastic. Unlike the RA or the hypoplastic RV of the tricuspid atresia patient, it can actively assist in the hemodynamic adjustments required by the demands of exercise. Hence, the exercise function of the postoperative tetralogy of Fallot patient is superior to that of the Fontan patient, whether or not a "ventricle" was included in the pulmonary circulation.

In conclusion, the exercise function of the Fontan patient is inferior to that of the tetralogy of Fallot patient and does not appear to be improved by the inclusion of the RV in the pulmonary circulation. The theoretical benefits expected to result from the presence of an active right-sided pumping chamber in the Fontan circulation may be negated by other hemodynamic and anatomic factors that arise as a consequence of this approach. This study indicates that the use of an RA-RV valved conduit, with the likely need for replacement, may not be warranted for most tricuspid atresia patients, although it may be appropriate for a patient with an unusually well-developed RV. The role of a nonvalved atroventricular anastomosis in the management of tricuspid atresia remains to be addressed.

**References**


Key Words • tricuspid atresia • single ventricle • tetralogy of Fallot
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