INTRODUCTION

Can a volume challenge pinpoint the limiting factor in a Fontan circulation?

Wim DE MEY, MD; Bjorn COOLS, MD; Ruth HEYING, MD, PhD; Werner BUDTS, MD, PhD; Jacoba J. LOUW, MD; Derize E. BOSHOFF, MD, PhD; Stephen C. BROWN, MD; Marc GEWILLIG, MD, PhD

Dept. of Paediatric Cardiology, University Hospitals Leuven, Belgium; Dept. of Cardiology, University Hospitals Leuven, Belgium; Dept. of Paediatric Cardiology, University of the Free State, Bloemfontein, Zuid-Afrika.

Objective: It is difficult to determine whether the limitation in a failing Fontan circulation lies within the pulmonary vasculature or the heart. Such differentiation is crucial to direct adequate therapy. This study was set out to determine if a volume challenge could identify the limiting factor.

Methods and study population: Thirty-two catheterizations in 28 patients with a Fontan circulation were included. Pressures and oxygen saturations were measured before and after volume challenge (NaCl 0.9%; 15 cc/Kg). The changes in data were grouped based on the location of the major pressure increase. Ventricular function was measured in the resting state.

Results: The majority of the patients showed an increase in aortic oxygen saturation, mixed venous oxygen saturation, systolic, pulmonary and systemic venous pressures. The arterio-venous oxygen gradient decreased, suggesting an increase in cardiac output. Different patterns in pressure changes were observed. All patients showed similar increases in ventricular and pulmonary pressures and mean venous pressure (MVP). Some (n = 7) showed a lower increase in MVP, suggesting pulmonary reserve and recruitment; others (n = 8) showed a significant higher increase in MVP, suggesting increased pulmonary vascular resistance. Volume challenge was well tolerated.

Conclusion: Most patients were preload-responsive. The pressure changes following volume load showed patterns with a potential of differentiating between patients with a major pulmonary or cardiac limiting factor.

Keywords: Fontan – total cavopulmonary connection – circuit failure – volume challenge.
Patients

Patients presenting for a catheterization after Fontan operation between September 2005 and February 2011 were included. Patients who were not inclined to continue follow up after fully grown (especially in girls with pregnancy risk), with absence of fenestration or clinically indicated (paediatric, narco- sis-induced, protein losing enteropathy) or all Fontan patients had undergone extra cardiac total con- nector (TCPC) surgery to create an extracor- diac conduit. There were no right-to-left shunts at the time of volume challenge. The volume challenge during catheterization was performed after closure of the fenestration. Exclusion criteria were severe uncontrolled ophthalmalogy or missing data. The patients or their parents (if underage) (or other informed consent). Our institutional ethic-comitee on clinical investigation approved the procedure.

Procedures

Most catheterizations were done in general anaesthesia without oxygen supplements, one adult patient had a catheterization done under local anaesthesia. Normocapnia (pCO2 35-45 mmHg) and low positive pressures (maxi- mal PEEP: +5 cm H2O) were maintained during the procedure. This was done in order to reduce the influence on the haemodynamic measurements.2223 Gradually, catheterization was carried out. Volume challenge was done intravenously using a small catheter bolus of 15 cc/Kg (NaCl 0.9%). Full diagnostic catheterizations (with fluid-filled catheters) were performed both before and after the volume challenge. We measured mixed venous pressure (Pv), pulmonary wedge pressure (PcW), and ventricular end-diastolic pressure (VEDP) and ventricular end-systolic pressure (VESP) before and after fluid challenge. All measurements were performed during dimensional ventriculography and/or echocardiography. Data analysis

Data was inserted in an Excel© spreadsheet (Micro- soft Office 2013©). The following data was extracted from the patient’s file for each catheterization: age at completion of Fontan operation, gender, indication for catheterization, cardiac pathology, and intravenous med- ication and STEMI-identification. The total data were collected during catheterization before and after volume challenge. The difference in pressures and cardiac output before and after volume challenge was calculated.

Statistical analysis

All values were expressed as mean ± standard devia- tion. A P-value < 0.05 was considered to denote statisti- cal significance.

RESULTS

Age and gender

Thirty-one catheterizations with volume challenge were done in 35 patients. Most catheterizations were done under general anaesthesia (n = 38). Seven catheterizations were excluded due to missing data. Thirty-two catheterizations in 28 patients formed the basis of our analysis (17 males and 11 females). The mean age of the patients at the time of the catheterization was 10.5 ± 5.9 years (range: 3.1-26.0). The mean interval between completion of Fontan surgery and catheteriza- tion was 5.6 ± 4.8 years (range 0.2-18.3).

Diagnosis, indication and current therapy

Anatomic diagnoses were: tricuspid atresia (n = 9), pulmonary atresia with intact ventricular septum (n = 6), single ventricle: dominant left (n = 10), single ventricle: dominant right (n = 2), functional single ventricle (n = 1). Indications for catheterization were: routine follow-up (n = 17), closure of fenestrations (n = 7) and clinical dete-rioration (n = 8). All patients received medication at the time of catheterization: acetylsalicylic acid (n = 23), clopidogrel (n = 10), vitamin K antagonist (n = 5), low-molecular-weight heparin (n = 2), diuretics (n = 6), beta blockers (n = 2), angiotensin-converting enzyme inhibitors (n = 8), and/or digoxin (n = 3). Only 1 patient received pulmonary vasodilators (bosentan).

Satisfaction

The acute saturation and mixed venous oxygen saturation before and after volume challenge was shown...
in table 1. The mean MVP sat increased from 65 ± 8.7% (range: 45–77.1%) after volume challenge to a mean pressure increase of 13.7 ± 6.3 mmHg (range: 3.0–29.0; P < 0.01) after volume load. The MVP sat increased from 10.0 ± 4.4 mmHg (range: 2.0–19.0) to 18.3 ± 3.3 mmHg (range: 10.5–21.0) after volume challenge.

Haemodynamics

Data of individual haemodynamic changes after vol-

ume load are summarized in table 1. All but two had a bigger increase in VEDP than in MVP. No patient (n = 8) had a bigger increase in MVP than VEDP. Others (n = 7) reacted to volume load with a bigger pressure increase in VEDP than in MVP. Three

patients (n = 3) had a bigger increase in MVP than in VEDP, but within the range of ± 2 mmHg. Some (n = 2) showed a similar pressure increase at the pre-cardiac and pre-pulmonary sites (increase

of MVP = VEDP, range: ± 2 mmHg). Most (n = 17) showed a different pattern of pressure changes. Pre- and post-volume load were compared with the haemodynamic situation after initiating treatment with bosentan. This patient showed a different response to volume load after almost 4 years of treatment. During the

two subsequent catheterizations showed no common

trend. These subsequent catheterizations were done in regular follow-up, and their second catheterization was indicated after developing clinical

suspicion (cyanosis). The difference in pressure change in these subsequent catheterizations showed no common

trend.

Table 1: Mean haemodynamics and oxygen saturations of total study population and subgroups

Subgroup with subsequent catheterizations

Four patients were included twice at different phases after the completion of the TCPC. In four of the four

patients the first catheterization with volume challenge was done in regular follow-up, and their second

catheterization was done after developing clinical

suspicion (cyanosis). The difference in pressure change in these subsequent catheterizations showed no common

trend.

The next patient catheterization was done to evaluate the remodelling changes after including treatment with bosentan. This patient showed a different response to volume load 4 years after treatment. During the

first volume challenge the mixed venous pressure rose with 1 mmHg. The patient showed a different response
to volume load after almost 4 years of treatment. During the

second volume challenge the mixed venous pressure was

Table 1: Mean haemodynamics and oxygen saturations of total study population and subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Pre Post Pre Post Pre Post Pre Post Pre Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population</td>
<td>18.0±48.5</td>
</tr>
<tr>
<td>Group 1</td>
<td>14.6±2.8</td>
</tr>
<tr>
<td>Group 2</td>
<td>14.6±2.8</td>
</tr>
<tr>
<td>Group 3</td>
<td>14.6±2.8</td>
</tr>
</tbody>
</table>

This table summarizes the mean haemodynamics and oxygen saturations of the total study population and subgroups. The mean values are given for each subgroup. The statistical significance of differences between the subgroups was assessed by analysis of variance (ANOVA) and post-hoc analysis with the Tukey Honestly Significant Difference (HSD) test. The significance level was set at P < 0.05.
DISCUSSION

Prevention and treatment of late circulatory failure in a Fontan circulation becomes important in the postoperative management. Therapeutic strategies will only be successful when aimed at the limiting factor.

The search for the limiting factor, causing late circulatory failure in a Fontan circulation, has led to a dichotomy in therapeutic strategies. Several studies attributed the failure of the circulation to a primary cardiac increase of MVP (2 mmHg) and a higher increase in VEDP (4 mmHg). The trans-pulmonary gradient and the PVR at rest was reduced from 5.5 mmHg and 0.16 Woods units to 3.0 mmHg and 0.08 Wood units, respectively, after treatment.

Complications

No complications occurred following fluid application or general anaesthesia.

Table 2

Table 2: Individual haemodynamics and oxygen saturations

<table>
<thead>
<tr>
<th>Cath. Age (years)</th>
<th>Fontan Age (years)</th>
<th>Diagnosis</th>
<th>NYHA FS rest (%)</th>
<th>MVP rest (mmHg)</th>
<th>VEDP rest (mmHg)</th>
<th>AVOG rest (%O2)</th>
<th>MVP VL (mmHg)</th>
<th>VEDP VL (mmHg)</th>
<th>AVOG VL (%O2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 13.8 26 Tri-A 1 10 2 – 11 5 –</td>
<td>2 2.9 5.4 DILV 3 35.00 11 6 35 21 7 –</td>
<td>3 2.9 9.1 DILV 2 37.50 13 11 37 15 15 22</td>
<td>4 3.25 4.2 DILV 2 37.78 12 4 14.5 4 –</td>
<td>5 3.25 6.1 DILV 1 30.00 14.5 12 24 19 7 –</td>
<td>6 3.3 5.8 DORV 1 30.61 13 6 37 15 7 35</td>
<td>7 3.3 7.1 DORV 1 33.33 11.5 2 48.5 15 3 –</td>
<td>8 3.7 14.7 Tri-A 1 30.77 15 14 26 21 17 44</td>
<td>9 3.7 15.3 Tri-A 3 30.00 16 10 23 9 –</td>
<td>10 5.6 9.9 Pu-A 1 30.00 16.5 2 34 21 7 24</td>
</tr>
</tbody>
</table>
inter-individual differences in mechanisms to cope with volume load. The capacity to recruit pulmonary vessels might be a major player in the volume load response of total cavopulmonary connections. Most patients showed a concordant increase in MVP and VEDP, suggestive of a Fontan circulation with reserve capacity. Fontan patients with a lower MVP increase (compared to VEDP increase) are assumed to have a pulmonary vasculature with reserve. This adaptive capacity of the lungs is probably due to recruitment. Patients showing a larger increase in MVP are assumed to have a pulmonary limiting factor: elevated PVR.

Catheterization performed to evaluate the hemodynamic situation after initiating treatment for pulmonary hypertension (bosentan; 4 years of treatment) showed a lower transpulmonary gradient and PVR after treatment. The pattern of pressure change (after volume challenge) evolved from a pattern with pronounced MVP increase to a pattern with equal increase in MVP and VEDP. These findings support our hypothesis and show that the pattern of pressure change after volume challenge can indicate patients who might benefit from a treatment with pulmonary vasodilators.

Volume challenge (a surrogate for physiological stress) acts as a stressor on the circulation. Healthy individuals will have enough reserve capacity to cope with the additional stress (increase in cardiac output and minor pressure increase). A patient whose circulation functions at its limits will respond to the volume challenge with pressure increase. Nowadays, the connections itself, such as the current ratio pulmonary connections, is no longer a limiting factor; elevated and stable flow distribution have become more common. This study had good ventricular functions, so the limiting factor will most likely be found within the pulmonary vasculature.

The pressures measured at rest in the Fontan circulation showed a pattern consistent to previous findings in Fontan patients (figure 1). As expected in a heterogeneous population of Fontan patients (clinically stable vs clinical deterioration) we observed a heterogeneous response to pressure changes after volume challenge. The heterogeneous pattern in pressure changes suggested unique individual differences in mechanisms to cope with volume load. The capacity to recruit pulmonary vessels might be a major player in the volume load response of total cavopulmonary connections.

Most patients showed a concordant increase in MVP and VEDP suggestive of a Fontan circulation with reserve capacity. Fontan patients with a lower MVP increase (compared to VEDP increase) are assumed to have a pulmonary vasculature with reserve. These findings support our hypothesis and show that the pattern of pressure change after volume challenge can indicate patients who might benefit from a treatment with pulmonary vasodilators.

Fig. 1. Schematic representation of the Fontan circulation and the pressure change. The Fontan circuit at rest (black line): the systemic veins are connected to the pulmonary artery, without a subpulmonary ventricle or systemic atrium. The pulmonary circulation (P) is connected in series with the systemic circulation (S). The systemic venous pressures are markedly elevated. The different patterns in pressure change following volume load are represented for each theoretical group: non-differentiating pattern (orange line: pressure increase MVP = VEDP), group with pulmonary limiting factor (red line: pressure increase MVP > VEDP) and the group with pulmonary recruitment (green line: pressure increase MVP < VEDP). Ao: aorta, LA: left atrium, MVP: mixed venous pressure, V: ventricle, VEDP: ventricular end-diastolic pressure, S: systemic circulation, P: pulmonary circulation.
The identification of different patterns following volume load adds a better understanding of the complex physiology of the Fontan circulation. But additional information is needed to determine the potential limiting factor in each Fontan patient. Furthermore, volume challenge could be an option to tailor treatment. However, the presence of different patterns in pressure change after volume load and not to identify any criteria to divide this population into clinical subgroups. Most patients underwent catheterization under general anesthesia which might introduce bias.

CONCLUSIONS

The mechanisms involved in controlling the cardiac output in a Fontan circulation are complex and currently understood. We analyzed the pressure changes after volume challenge in order to identify the lower limiting factor. A pattern with a larger increase in MVP is assumed to have a more important pulmonary limiting factor. Further investigation with evaluation of clinical and hemodynamic parameters and therapeutic response is necessary. Our findings open new perspectives to understand the complex physiology of the Fontan circulation and to tailor treatment.

CONFLICT OF INTEREST: None.

REFERENCES


