Bidirectional Glenn Procedure Improves the Mechanical Efficiency of a Total Cavopulmonary Connection in High-Risk Fontan Candidates

Yoshihisa Tanoue, MD; Akira Sese, MD; Yasutaka Ueno, MD; Kunitaka Joh, MD; Takayuki Hijii, MD

Background—A total cavopulmonary connection (TCPC) is a widely performed surgical procedure for Fontan candidates. High-risk candidates who have undergone the bidirectional Glenn procedure (BDG) before TCPC have shown good results. The exact mechanism of this procedure, however, is still poorly understood. We hypothesized that a volume reduction with BDG improved ventricular contractility, thereby optimizing mechanical efficiency after TCPC.

Methods and Results—We measured percent normal systemic ventricular end-diastolic volume (%N-EDV), contractility (end-systolic elastance; E_{es}), afterload (effective arterial elastance; E_{a}), and mechanical efficiency (ventriculoarterial coupling; E_{a}/E_{es}) on the basis of the cardiac catheterization data before and after TCPC. Eighteen patients who underwent staged TCPC after BDG (staged group) were compared with 29 patients who underwent primary TCPC (primary group). E_{es} and E_{a} were approximated as follows: E_{es}=mean arterial pressure/minimal ventricular volume, and E_{a}=maximal ventricular pressure/(maximal ventricular volume−minimal ventricular volume), and E_{a}/E_{es} was then calculated. The ventricular volume was normalized with the body surface area. A canine experimental model with conductance catheter was used to validate the accuracy of this approximation of E_{es} and E_{a}. %N-EDV decreased after TCPC in both groups. In the staged group, a smaller ventricular volume resulted in better contractility (E_{es}). Although afterload (E_{a}) increased in both groups, the increment of E_{a} was smaller in the staged group. These changes resulted in an improvement of E_{a}/E_{es} in the staged group, whereas E_{a}/E_{es} increased in the primary group.

Conclusions—The volume reduction of BDG preceding TCPC allows for any afterload mismatch to be corrected, thereby improving ventricular energetics after TCPC. (Circulation. 2001;103:2176-2180.)

Key Words: Glenn ■ mechanics ■ cavopulmonary ■ Fontan

A total cavopulmonary connection (TCPC) is a widely performed surgical procedure for Fontan candidates. For high-risk Fontan candidates, the introduction of a bidirectional Glenn procedure (BDG) preceding TCPC may extend the indications for the Fontan procedure. High-risk candidates who have undergone BDG before TCPC have shown excellent results. The exact mechanism for the superiority of BDG, however, is still poorly understood.

We hypothesized that the volume reduction of BDG improved the ventricular contractility, thereby optimizing the mechanical efficiency after TCPC. To demonstrate this hypothesis, the approximation of the indices of both contractility (end-systolic elastance; E_{es}) and afterload (effective arterial elastance; E_{a}) was first introduced with a conductance catheter and a canine right-heart-bypass preparation. Second, we combined this approximation of the E_{es} and E_{a} with the cardiac catheterization data before and after TCPC and then compared the cardiac performance of the patients treated by staged TCPC after BDG with that of the patients treated by primary TCPC.

Validation of the Accuracy of the Approximation of E_{es} and E_{a}

Animal Preparations
A canine experimental model with conductance catheter was used to validate the accuracy of this approximation of E_{es} and E_{a}. Twenty-four adult mongrel dogs (16.8±2.7 kg, 14.0 to 24.0 kg) were used in the study. All animals were treated in compliance with the Guide for the Care and Use of Laboratory Animals published by the National Institutes of Health (NIH publication No. 85-23, revised 1985). This experiment was also reviewed by the Committee on the Ethics of Animal Experiments in the Faculty of Medicine, Kyushu University and carried out under the control of the Guidelines for Animal Experiments of the Faculty of Medicine, Kyushu University, and the Law (No. 105) and Notification (No. 6) of the government. All dogs were anesthetized intravenously with sodium thiamylal, intubated, and ventilated mechanically. A continuous infusion of fentanyl, midazolam, and pancuronium bromide was used to maintain anesthesia. ECG and systemic blood pressure were continuously monitored.

After a median sternotomy had been performed, the pericardium was incised and the heart suspended in a pericardial cradle. After
heparin had been administered intravenously, a right-heart-bypass preparation was established by an arterial cannula inserted into the main pulmonary artery and venous cannulas inserted into the superior and inferior venae cavae as previously described. The right heart bypass consisted of a centrifugal pump and a membrane oxygenator. An autonomic blockade was induced with hexamethonium bromide and atropine sulfate. The tapes around the superior and inferior venae cavae were snared to direct the systemic venous blood return into a reservoir. The blood was then pumped back to the main pulmonary artery. The venous cannula was placed in the right venous return through the right atrium to drain the entire coronary venous return, and the total coronary flow was measured by an in-line ultrasonic flow probe (Transonic Systems). The aortic flow was measured by an ultrasonic flow probe around the ascending aorta.

A 7F 12-electrode conductance catheter (Sentron) was inserted into the left ventricle through the apex. The catheter was attached to a signal generator/processor (Lecycom Sigma 5 DF, CardioDynamics). A catheter-tip micromanometer (MPC-500, Millar Instruments) was also inserted into the left ventricle, and then the left ventricular pressure-volume loop was measured. A right heart bypass was instituted to control the left ventricular venous return and to completely decompress the right ventricle, thereby eliminating any parallel conductance variation. The volume signal of the conductance catheter was calibrated by the aortic flow and the coronary flow, and the parallel conductance volume was calculated by the hypertonic saline technique.

Data Analysis
All signals were continuously monitored and online digitized at 200 Hz with an analog-to-digital converter (MacLab System, ADInstruments) and then were recorded on a digital computer (Macintosh PowerBook 540C). The digitized data were analyzed by computer algorithms using a C-language-type with an Intel Celeron-based personal computer (ThinkPad 240). The multiple left ventricular pressure-volume loops were obtained during transient preload reduction by reducing the right heart bypass flow.

The actual measurements of E_c and E_a were performed as follows. The end-systolic pressure-volume relation was fit by a linear regression analysis to obtain a slope (E_a). The concept of ventriculoarterial coupling between the left ventricle and the arterial system was also used. The left ventricular pressure was characterized by E_c and the arterial pressure was characterized by E_a. E_c was calculated as E_c = end-systolic ventricular pressure/end-diastolic ventricular volume – end-systolic ventricular volume. E_a was calculated as E_a = end-systolic arterial pressure/end-diastolic arterial volume.

The end-diastolic point was defined as the point of the upstroke of the first derivative of the LV pressure.

The approximations of E_c and E_a were performed as follows: E_c = mean arterial pressure/minimal ventricular volume; E_a = maximal ventricular pressure/(maximal ventricular volume – minimal ventricular volume).

E_c and E_a were approximated E_c and E_a, respectively. The correlations between E_c and E_a and between E_a and E_c were examined.

Statistical Analysis
The analysis of Pearson’s correlation coefficient was used to evaluate any correlations between E_c and E_a and E_c and E_a.

Analysis of Clinical Cases
Patient Information
Eighteen patients who underwent staged TCPC after BDG (staged group) were compared with 29 patients who underwent primary TCPC (primary group). These patients were consecutive, except for 2 children who died, and all underwent surgical intervention at Kyushu Kosei-Nenkin Hospital between July 1992 and September 1999. The operative strategy was selected by the chief pediatric cardiologist (K.J.). Informed consent for both the operation and cardiocatheterization was obtained from all parents of the children.

The median age of the patients was 3.9 years (1.8 to 14 years) in the staged group and 3.8 years (1.6 to 13 years) in the primary group. The mean weight was 18.0 ± 10.9 kg (10.4 to 49.5 kg) in the staged

<table>
<thead>
<tr>
<th>TABLE 1. Anatomic Diagnoses of Both Groups</th>
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<tbody>
<tr>
<td>Diagnosis</td>
</tr>
<tr>
<td>-------------------------------------</td>
</tr>
<tr>
<td>Tricuspid atresia</td>
</tr>
<tr>
<td>Pulmonary atresia with intact ventricular septum</td>
</tr>
<tr>
<td>Double-outlet right ventricle, hypoplastic left ventricle</td>
</tr>
<tr>
<td>Other complex functional right single ventricle</td>
</tr>
<tr>
<td>Other complex functional left single ventricle</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Operative Techniques
The operations were performed by 2 cardiac surgeons (A.S. and Y.U.). Anesthesia was done by the standard intravenous technique with fentanyl, midazolam, and pancuronium for muscle relaxation. Aortic and bicaval cannulations were performed thorough a standard median sternotomy, and cardiopulmonary bypass was instituted with a heart-lung machine consisting of a rotating pump and a membrane oxygenator. When heart arrest was necessary, myocardial preserva-

Statistical Analysis
The results are presented as mean ± SD. Student’s unpaired t test was used to compare the changes in the values before and after TCPC.
Validation of the Accuracy of the Approximation of \( E_{es} \) and \( E_a \)

The high correlations of \( E_{es} \) and \( E_{es}' \) and \( E_a \) and \( E_a' \) are shown in Figure 1. The correlation coefficient of \( E_{es} \) and \( E_{es}' \) was 0.966 \((P<0.001)\), and that of \( E_a \) and \( E_a' \) was 0.972 \((P<0.001)\).

**Analysis of Clinical Cases**

Preoperative and postoperative hemodynamic variables (mean pulmonary arterial pressure, the pulmonary arterial index of Nakata et. al.,\(^27\) systemic arterial oxygen saturation, and atrioventricular valve regurgitation) on cardiac catheterization are shown in Table 2.

The parameters of cardiac performance in both groups are shown in Figure 2. %N-EDV decreased after TCPC in both the staged and primary groups (from 131±38% to 111±35% and from 219±93% to 140±49%, respectively). Change before and after TCPC of %N-EDV between the staged and primary groups was significantly different (\(-20±26% \text{ and } -79±74\%\), \(P=0.002\), respectively). \( B, E_a \) increased in both the staged and primary groups (from 2.02±1.13 to 2.81±1.39 mm Hg · m\(^{-2}\) · mL\(^{-1}\), respectively). Difference in \( E_{es} \) between 2 groups was significant \((P=0.012)\). \( C, E_e \) increased in both the staged and primary groups (from 2.17±0.55 to 2.60±0.92 mm Hg · m\(^{-2}\) · mL\(^{-1}\) and from 1.58±0.67 to 2.46±0.78 mm Hg · m\(^{-2}\) · mL\(^{-1}\), respectively). Increment of \( E_a \) was smaller in the staged group. Difference in change before and after TCPC of \( E_a \) between the staged and primary groups was marginally significant \((0.43±0.81 \text{ and } 0.88±0.82 \text{ mm Hg} \cdot \text{m}^2 \cdot \text{mL}^{-1}, \text{respectively}, P=0.073)\). \( D, E/E_a \) decreased in the staged group (from 0.86±0.32 to 0.74±0.26, whereas it increased in primary group (from 0.88±0.34 to 1.08±0.63). Change before and after TCPC of \( E/E_a \) between the staged and primary groups was significantly different (\(-0.12±0.24 \text{ and } -0.20±0.53, \text{respectively}, P=0.019\)). Interaction of \( E/E_a \) between 2 groups was significant \((P=0.019)\). Values are expressed as mean±SD.

**TABLE 2. Preoperative and Postoperative Hemodynamic Variables in Cardiac Catheterization in Both Groups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Staged Group Before TCPC</th>
<th>After TCPC</th>
<th>Primary Group Before TCPC</th>
<th>After TCPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPAP, mm Hg</td>
<td>8.9±2.6</td>
<td>10.8±2.6</td>
<td>12.3±2.1</td>
<td>8.9±2.6</td>
</tr>
<tr>
<td>PAI, mm²/m²</td>
<td>254±75</td>
<td>221±99</td>
<td>421±130</td>
<td>272±82</td>
</tr>
<tr>
<td>SaO₂, %</td>
<td>82.1±3.8</td>
<td>89.8±7.4</td>
<td>81.0±5.0</td>
<td>90.5±5.3</td>
</tr>
<tr>
<td>AVVR, mild</td>
<td>2 (11.1%)</td>
<td>0</td>
<td>2 (6.9%)</td>
<td>0</td>
</tr>
</tbody>
</table>

mPAP indicates mean pulmonary arterial pressure; PAI, Nakata’s pulmonary arterial index; SaO₂, systemic arterial oxygen saturation; and AVVR, atrioventricular valve regurgitation. Data are mean±SD or the number and percentage of patients.

Results

Validation of the Accuracy of the Approximation of \( E_{es} \) and \( E_a \)

Approximation of \( E_{es} \) and \( E_a \) was performed as follows:

\[
E_{es} = \frac{\text{mean arterial pressure}}{\text{minimal ventricular volume}}; \quad E_{es}' = \frac{\text{maximal ventricular pressure}}{\text{maximal ventricular volume}} - \frac{\text{minimal ventricular volume}}{\text{minimal ventricular volume}}.
\]

Curves indicate 95% confidence limits of regression.

between the 2 groups. A 2-factor ANOVA with repeated measures on 1 factor was used to clarify whether the interaction between the 2 groups was significant and whether the difference between the 2 groups was significant.

**Figure 1.** Validation of accuracy of approximation of \( E_{es} \) and \( E_a \). \( E_{es}' \) and \( E_a' \) indicate approximated \( E_{es} \) and \( E_a \), respectively. Approximation of \( E_{es} \) and \( E_a \) was performed as follows:

\[
E_{es} = \frac{\text{mean arterial pressure}}{\text{minimal ventricular volume}}; \quad E_{es}' = \frac{\text{maximal ventricular pressure}}{\text{maximal ventricular volume}} - \frac{\text{minimal ventricular volume}}{\text{minimal ventricular volume}}.
\]

Curves indicate 95% confidence limits of regression.

**Figure 2.** Parameters of cardiac performance in staged group (○) and primary group (●). A, %N-EDV decreased after TCPC in both staged and primary groups (from 131±38% to 111±35% and from 219±93% to 140±49%, respectively). Change before and after TCPC of %N-EDV between staged and primary groups was significantly different (\(-20±26% \text{ and } -79±74\%\), \(P=0.002\), respectively). B, \( E_a \) increased in both staged and primary groups (from 2.89±1.41 to 3.79±1.32 mm Hg · m\(^{-2}\) · mL\(^{-1}\) and from 2.02±1.13 to 2.81±1.39 mm Hg · m\(^{-2}\) · mL\(^{-1}\), respectively). Difference in \( E_{es} \) between 2 groups was significant \((P=0.012)\). C, \( E_e \) increased in both staged and primary groups (from 2.17±0.55 to 2.60±0.92 mm Hg · m\(^{-2}\) · mL\(^{-1}\) and from 1.58±0.67 to 2.46±0.78 mm Hg · m\(^{-2}\) · mL\(^{-1}\), respectively). Increment of \( E_a \) was smaller in staged group. Difference in change before and after TCPC of \( E_a \) between the staged and primary groups was marginally significant \((0.43±0.81 \text{ and } 0.88±0.82 \text{ mm Hg} \cdot \text{m}^2 \cdot \text{mL}^{-1}, \text{respectively}, P=0.073)\). D, \( E/E_a \) decreased in the staged group (from 0.86±0.32 to 0.74±0.26, whereas it increased in primary group (from 0.88±0.34 to 1.08±0.63). Change before and after TCPC of \( E/E_a \) between the staged and primary groups was significantly different (\(-0.12±0.24 \text{ and } -0.20±0.53, \text{respectively}, P=0.019\)). Interaction of \( E/E_a \) between 2 groups was significant \((P=0.019)\). Values are expressed as mean±SD.
The interaction of $E_a/E_{es}$ between the 2 groups was marginally significant ($P=0.012$). The interaction of $E_a$ between the 2 groups was not significant. Although the afterload ($E_a$) increased in both the staged and primary groups (from $2.17\pm0.55$ to $2.60\pm0.92$ mm Hg · m$^{-2}$ · mL$^{-1}$ and from $1.58\pm0.67$ to $2.46\pm0.78$ mm Hg · m$^{-2}$ · mL$^{-1}$, respectively), the increment of $E_a$ was smaller in the staged group. The difference in the change before and after TCPC of $E_a$ between the staged and primary groups was marginally significant ($0.43\pm0.81$ and $0.88\pm0.82$ mm Hg · m$^{-2}$ · mL$^{-1}$, respectively, $P=0.073$). The interaction of $E_a$ between the 2 groups was not significant. The difference in $E_a$ between the 2 groups was marginally significant ($P=0.056$). These changes resulted in an improvement of $E_a$ between the staged group (from $0.86\pm0.32$ to $0.74\pm0.26$, whereas $E_a/E_{es}$ increased in the primary group (from $0.88\pm0.34$ to $1.08\pm0.63$). The change before and after TCPC of $E_a$ between the staged and primary groups was significantly different ($-0.12\pm0.24$ and $+0.20\pm0.53$, respectively, $P=0.019$). The difference in $E_a/E_{es}$ between the 2 groups was not significant. The interaction of $E_a/E_{es}$ between the 2 groups was significant ($P=0.019$).

**Discussion**

In the present study, we showed the improvement in the ventricular energetics after staged TCPC compared with that after primary TCPC. To the best of our knowledge, this is the first report to focus its attention on the ventricular energetics after TCPC in clinical patients. The objective of this study is to elucidate the mechanism behind the excellent clinical results of BDG preceding TCPC for high-risk Fontan candidates.

Information on cardiovascular performance is provided if it is possible to measure the multiple pressure-volume relations of children. The measurement of ventricular volume is essential to both understand and assess the physical state of the cardiovascular system. It is difficult, however, to measure the ventricular volume in clinical situations, and it is actually impossible for unstable children before and after cardiac operation. Cardiac catheterization was performed on all children before and after BDG and TCPC to determine the optimal treatment strategy at our hospital. The present approximation of $E_a$ and $E_a$ enables us to evaluate ventricular contractility, afterload, and ventriculoarterial coupling from the cardiac catheterization data before and after a cardiac operation. This promising approximation of $E_a$ and $E_a$ can also be applied to other clinical cases.

The introduction of BDG preceding TCPC extends the indications for the Fontan procedure to high-risk candidates. Various studies have reported the clinical results of staged TCPC to be excellent. Various speculations and explanations have been made regarding its mechanism, including the preservation of ventricular function by relieving the volume load on the single ventricle, improvement in oxygenation, and improvements in pulmonary vascular function. The occurrence of a decreased volume load on the ventricle, however, conflicts with the concept of introducing BDG before TCPC. The reducing effect of the volume load on the ventricle after primary TCPC is more effective than that after BDG. In addition to this, the improvement in oxygenation after TCPC is also greater than that after BDG. The exact mechanism for the superiority of BDG, however, remains unclear. In the present study, we showed that BDG preceding TCPC improved ventricular contractility, thereby optimizing the mechanical efficiency after TCPC. Although many questions remain unanswered regarding the exact mechanism for the superiority of BDG, the improvement in the mechanical efficiency is considered to be one of the most important factors for the excellent results obtained for staged TCPC after BDG. Two early-period patients died after primary TCPC in our hospital before the introduction of BDG. These patients might have survived the operation if they had undergone BDG before TCPC.

Akagi and colleagues reported the systemic vascular resistance to increase after the Fontan operation, and this study demonstrated the afterload to increase after both staged TCPC and primary TCPC. Not only the short-term usage but also the long-term appropriate usage of vasodilatory agents thus play an important role in the therapeutic strategy for children after TCPC. In our hospital, amrinone infusion is performed in children who undergo TCPC while being weaned from cardiopulmonary bypass and in the early postoperative period, and enalapril is administered long-term after oral intake is established. These therapies are all considered to improve the ventricular energetics and hemodynamic characteristics, thus improving long-term outcome.

The approximation of $E_a$ and $E_a$ described in this study has thus far been validated only in an animal model. The validation of this approximation should therefore be performed not only on normal hearts but also on diseased hearts in human studies. Inherently, the staged group is a high-risk group, whereas the primary group is a low-risk group. It is therefore necessary to divide the groups more specifically, such as whether the morphological characteristics show the dominant ventricle to be the right or the left ventricle; whether the previous procedure was either a systemic-pulmonary shunt, pulmonary arterial banding, or not performed; and in the staged group, whether or not another source of the pulmonary blood flow remains. In particular, the role of the accessory pulmonary blood flow after BDG remains unclear. These specifications could not be performed, however, because of the small number of patients. Further studies comparing patients with or without a systemic-to-pulmonary shunt and with or without a forward flow from the ventricle are thus called for.

In conclusion, the volume reduction of BDG preceding TCPC allowed for any afterload mismatch to be corrected, thereby improving the ventricular energetics after TCPC. This improvement in the mechanical efficiency after staged TCPC is one of the mechanisms behind the excellent clinical results of BDG preceding TCPC in high-risk Fontan candidates. The long-term evaluations of $E_a$, $E_a$, and $E_a/E_{es}$ still need to be determined in future follow-up studies, however, before any definitive conclusions can be drawn.

**References**


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