Venous Properties in a Fontan Patient with Successful Remission of Protein-Losing Enteropathy
A Possible Marker for Venous Stagnation over Central Venous Pressure

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Summary
We present the case of a 1-year-old boy who developed protein-losing enteropathy (PLE) within 2 months of a fenestrated Fontan procedure. His fenestration rapidly closed despite bilateral pulmonary stenosis (BPS). Subsequent to PLE onset, both fenestration and the bilateral pulmonary artery were reconstructed, and the patient's PLE had been in remission, with additive use of medications, for more than 2 years. Notably, although fenestration closed again and central venous pressure (CVP) reduction was minimal, the surrogates of venous return resistance were markedly suppressed as shown by increased blood volume, reduced estimated mean circulatory filling pressure, and suppressed CVP augmentation against a contrast agent. Taken together, dynamic characteristics of venous stagnation, rather than the absolute value of CVP, were ameliorated by the pulmonary reconstruction and use of medications, suggesting a significant role of venous property in the physiology of PLE. In addition, simultaneous measures of CVP and ventricular end-diastolic pressure during the abdominal compression procedure suggested a limited therapeutic role of fenestration against PLE in this patient.

Key words: Fontan circulation, Venous characteristics, Hemodynamic, Fenestration

Protein-losing enteropathy (PLE) is a critical complication that can occur following the Fontan procedure, which is assumed to be the result of end-organ dysfunction induced by systemic congestion. Although this concept is supported by the fact that creation of fenestration may contribute to PLE remission, some of the patients who developed PLE had fenestration naturally closed despite optimal medications. We experienced a patient with hypoplastic left heart syndrome (HLHS) whose fenestration closed early after a Fontan procedure despite significant bilateral pulmonary stenosis (BPS), who developed PLE as early as 2 months after surgery. His PLE became remission after reconstruction of fenestration and release of PS. Intriguingly, venous characteristics had markedly changed while fenestration closed soon, and CVP was almost unchanged.

Case Report
A male infant diagnosed with HLHS had a fenestrated Fontan procedure at the age of 1 year. Cardiac catheterization prior to total cavopulmonary connection (TCPC) indicated a pulmonary arterial pressure (PAP) of 12 mmHg and a transpulmonary pressure gradient (TPG) of 3 mmHg, with an estimated pulmonary resistance of 0.92 Um². His pulmonary arterial index was 122 mm/m², and the ventricular ejection fraction was 56%, with mild tricuspid regurgitation.

Within a few days of surgery, the fenestration flow became undetectable despite heparinization. The arterial oxygen saturation (SaO₂) increased to 97% with the percentage of inspiratory oxygen (FiO₂) at 60%, which was 94% with FiO2 at 100% at the patient's intensive care unit (ICU) arrival after operation. Although ascites and pleural effusion kept the patient in the ICU, he became free of circulatory support using pulmonary vasodilators and diuretics and left ICU on postoperative day (POD) 10. As BPS was suspected by echocardiogram, cardiac catheterization was performed on POD 43. The hemodynamic study demonstrated CVP of 13 mmHg with a cardiac index (CI) of 2.7 L/minute/m². The pressure gradients between bilateral pulmonary arteries and TCPC conduit were 3 mmHg on average, suggesting significant BPS as Fontan circulation (Figure 1A). Percutaneous transluminal angioplasty for the bilateral pulmonary arteries and TCPC conduit was also performed with the aim of improving Fontan circulation.
The TPG was 3 mmHg, and the right ventricular end-diastolic pressure (RVEDP) was 8 mmHg, which was considered to be acceptable at this point, and we decided to follow him up as an outpatient. His medication included flosemide, tolvaptan, sildenafil, and ACE inhibitor.

Two months after the surgery, the patient was brought to the clinic with massive systemic edema. His body weight had increased by 2 kg (+25% of his body weight) as compared with his weight at his latest clinical visit, and serum levels of albumin and total protein were 2.4 and 4.6 g/dL, respectively. No proteinuria was detected, and the 99mTc-human serum albumin scans clearly indicated protein leakage to the digestive system; this convinced us the patient had developed PLE (Figure 1B). After continuous albumin infusion coupled with diuretics, systemic edema disappeared. Blood volume (BV) estimated using Indocyanine Green (ICG) was 64.4 mL/kg. Augmented IVC pressure elevation by the occlusion test, with suppressed BV, implied augmented mean circulatory filling pressure (mcfP). Mild abdominal compression implied reduced pressure gradient between ventricle and CVP, thus possibly compromised advantage of the fenestration (Figure 2A). Importantly, the increase in RVEDP was steeper than that of the increase in CVP, and the two pressure amounts became similar at 18-20 mmHg (Figure 2B). Accordingly, we suspected that fenestration closure might have resulted from the suppressed pressure gradient between the conduit and EDP, particularly when ventricular volume was loaded early after the operation.

Since both BPS and fenestration closure were considered to have affected to the onset of PLE, surgical interventions to release the BPS and reconstruct the fenestration were implemented. Similarly to the original fenestration, a 4 mm punch-out in the conduit was made, and anti-platelet/coagulation was optimized. As acute increase of EDP could have resulted in another early closure of fenestration, we decided to keep the patient relatively dehydrated to avoid EDP augmentation, as implied by the abdominal compression procedure during previous cardiac catheterization. His SaO₂ was 95% with nasal oxygen supplementation of 3 L/minute. Despite efforts to keep the fenestration open, its signal faded on POD 28. At this point, SaO₂ increased to 97% with nasal oxygen supple-

Table 1. Hemodynamic Data

|                          | Post TCPC before PLE | Post TCPC after PLE | Post re-TCPC |
|--------------------------|----------------------|---------------------|-------------|
| SaO₂ (at cath lab entrance), % | 95                   | 95                  | 97          |
| CVP, mmHg                | 13                   | 14                  | 13          |
| RVEDP, mmHg              | 8                    | 8                   | 8           |
| CI, L/minute/m²           | 2.7                  | 3.4                 | 3.6         |
| Rp                       | 0.7                  | 1.2                 | 0.8         |
| Rs                       | 16.3                 | 10.4                | 13.2        |
| HR, bpm                  | 105                  | 111                 | 109         |
| PG pull-back             |                      |                     |             |
| LPA-conduit, mmHg        | 3                    | 3                   | 2           |
| RPA-conduit, mmHg        | 3                    | 4                   | 2           |

CI indicates cardiac index; CVP, central venous pressure; HR, heart rate; LPA, left pulmonary artery; RPA, right pulmonary artery; PG, pressure gradient; Rp, pulmonary arterial resistance; Rs, systemic arterial resistance; RVEDP, right ventricular end-diastolic pressure; and SaO₂, arterial oxygen saturation.
Figure 2. A: Abdominal compression acutely increased ventricular end-diastolic pressure to the level of CVP, which was likely to decrease the pressure gradient between CVP and ventricular diastolic pressure. B: The relationship between CVP and EDP during abdominal compression, as indicated by the arrow (A). CVP indicates central venous pressure, and EDP, end-diastolic pressure.
year\textsuperscript{11-13} and is considered to be multi-factorial. Surgical issues are one of the primary reasons; however, we employed the baffle punch-out method, which is reported to be robust for maintaining its patency.\textsuperscript{14} Traditionally, fenestration has been considered to close naturally when pulmonary circulation is so excellent that the circulation can be sustainable without it,\textsuperscript{15} although hemodynamic analyses in the Fontan patients have suggested that the early closure of fenestrations might be associated with a stiffened ventricular property.\textsuperscript{16} In the case presented here, abdominal compression during cardiac catheterization indicated a reduced pressure gradient between EDP and CVP at 18-20 mmHg or higher, which suggested that the patient’s ventricular end-diastolic pressure volume relationship at relevant preloading was too steep to further increase the preload by a small increment in diastolic pressure. This finding suggested that small increments of ventricular volume loading are likely to augment EDP, and the pressure gradient between CVP and EDP can thus easily decrease. We speculated that the unfavorable diastolic function coupled with postoperative myocardial edema caused suppression of the pressure gradient between the conduit and the EDP when small fluctuations in volume conditions were loaded, which then contributed to the early closure of the fenestration. The repeated natural closure of the fenestration in this patient despite anti-coagulation supports this concept.

Taken together, venous return characteristics, rather than the absolute value of CVP, might be useful dynamic markers of venous stagnation and thus end-organ dysfunction, including PLE. For patients who have a stiffened ventricular property, the exertion of fenestration is barely attained; thus, the release of venous stagnation by means of surgical or pharmacological interventions could be the only solution for PLE.
Venous Property Before and After Surgical Intervention

|                     | Post TCPC, after PLE | Post re-TCPC, after a year |
|---------------------|----------------------|---------------------------|
| IVC occlusion       | Mcfp, mmHg           | 45.1                      | 39.1                      |
|                     | ICG                  |                           |                           |
|                     | BV, mL/kg            | 64.4                      | 80                        |
| Contrast imaging    | Pre CVP, mmHg        | 12                        | 13                        |
|                     | Post CVP, mmHg       | 16                        | 15                        |

BV indicates blood volume; CVP, central venous pressure; ICG, indocyanine green; IVC, inferior vena cava; mcfp, mean circulatory filling pressure; PG, pressure gradient; PLE, protein-losing enteropathy; and TCPC, total cavo-pulmonary connection.

Conclusion

The absolute value of CVP alone may not properly indicate venous stagnation in the Fontan patients. Since the release of pulmonary stenosis or medications to reduce pulmonary resistance have provoked alteration in venous characteristics coincident with persistent PLE remission, dynamic venous properties, which are assessed by loading tests including volume loading or depletion, might be the promising guide for preventing Fontan-associated end-organ dysfunction. Although the pulmonary resistance may confound EDP augmentation, the abdominal compression procedure might be effective in detecting a non-responder of fenestration therapy against PLE.

Disclosure

Conflicts of interest: None.

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