Using a General Mathematical Model to Quantify the Fontan Paradox of Elevated Central Venous Pressure and Diminished Cardiac Output

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Introduction
Fontan procedure and its paradox
• Palliates patients with single ventricle (SV) physiology
  • Only one functioning ventricle for heart
• Connects the venous return and pulmonary circulation (Figure 1)
  • Low Cardiac output (CO) – Low tissue perfusion
  • High Central venous pressure (CVP) – High organ congestion
• However, common interventions either raise or lower CO and CVP simultaneously
  • This is called the “Fontan Paradox” 1
  • Clinical interventions not effective in preventing this paradox. 2

Limitations for current Fontan procedural models
• Computational models 3
  • Requires assumption of specified numerical values
  • Highly individualized; Cannot be applied to general population
• Animal models
  • Difficult to manipulate the mechanical properties affecting CVP and CO
• Human population is too fragile to experiment on

Benefits of Algebraic Formulas
• Numerical parameter values are not required
• Elegance to characterize different variations of Fontan physiology
• Ease of understanding

Purpose: to derive algebraic formulas for CVP and CO to enhance the understanding of Fontan Paradox

Characterizing the Cardiac Ventricle

Figure 2: Standard description of ventricular pressure-volume loop. End-systolic pressure-volume relationship (ESPVR) and end-diastolic pressure-volume relationship (EDPVR) are illustrated. Although ESPVR is understood to be non-linear, it is generally linearized to maintain simplicity (dashed line). Although loading the ventricle with different volumes alters pressure-volume loops, but ESPVR and EDPVR remain constant.

Standard Model Equations

Table 1: Model Equations

<table>
<thead>
<tr>
<th>Cardiac Ventricle</th>
<th>Cardiac Output</th>
<th>Volume</th>
<th>Ventricular end-systolic pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO</td>
<td>HR(Vsv − Voes)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psa</td>
<td>Psa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ppv</td>
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</tbody>
</table>

Table 2: Parameters

<table>
<thead>
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Methods

Minimal Closed-loop Heart Model

Figure 1: Minimal Closed-loop model of normal heart (top) and single ventricle heart after Fontan procedure (bottom). Arrows represent the blood flow. Systemic circulation is highlighted by the red rectangle, and the pulmonary circulation is highlighted by the blue rectangle. VR: venous return; other symbols are defined in Table 2.

Results & Discussion

Algebraic Formulas for CO and CVP

1. Theoretical stroke volume at zero ventricular pressure
2. Efficiency of heart-vascular interaction
3. Relate cardiac contractility
4. Theoretical CO at zero CVP
5. Relative pulmonary resistance

Solving the Paradox – pulmonary resistance

• Ideal interventions increases CO and decreases CVP
  • Negative correlation
• Altering some parameters eliminate the Paradox:
  • \( \Delta V \), \( E_{max} \),\( HR \), and \( R_s \)
  • Two most common parameters lead to the paradox:
    • \( R_s \) and \( P_{sa} \)

Circumventing the Paradox

• Most convenient clinical interventions:
  • altering blood volume (\( P_{sa} \)) or systemic resistance (\( R_s \))
  • Analyzed the sensitivity of CO and CVP from each parameter when \( R_s \) and \( P_{sa} \) are altered to elevate CO
    • Patients with stiff ventricle (high \( E_{max} \)) or high pulmonary resistance (high \( R_p \)) are less likely to suffer from the paradox
    • They have the most cardiac and pulmonary dysfunction

Conclusion

• Algebraic formulas explicitly relate parameters to CO and CVP to provide universal insight to Fontan physiology and Fontan paradox
  • Nonlinear pressure-volume relationships were assumed to be linear, but sufficient for our purposes.
  • Limited to see the trend and the relationship between parameters
  • Model suggests altering pulmonary resistance merits further study

References