From ejection to filling and back again: is diastole independent from systole?

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Cardiac function and mechanics

Interactions between systole and diastole

- Afterload-dependence of systolic function
- Impact of systolic contraction on myocardial relaxation and early diastolic filling
- Preload dependence of systolic function – Frank Starling relationship
- Implications for diagnosis and monitoring
- Load-insensitive or load-independent indices of contractile function – isovolumic acceleration and force-frequency relationship
Development of tension in isolated papillary muscle
Increased by increased afterload

Konishi T et al, Int J Cardiol 1992; 35: 333-341
Influence of left ventricular systolic pressure profile on early diastolic relaxation

- **EARLY**
  - Delayed onset of fall in systolic pressure, without altering rate of fall

- **LATE**
  - Late increase in pressure induced earlier onset of fall in pressure but at a slower rate

7 open-chest dogs, intra-aortic balloon

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Influence of late-systolic increases in LV pressure on early diastolic relaxation

![Graph showing the relationship between peak LV pressure increase and Tau increase.]

Influence of timing of increases in LV systolic pressure on early diastolic relaxation

Impact of arterial load (AI) on LV function (n=303)

Fukuta H et al, Circ J 2010; 74: 1900-5
Correlation of *long-axis* systolic & diastolic function

Yip G et al, 
*Clin Science* 2002;102:515

Vinereanu D et al, 
*Eur J Heart Fail* 2005;7:820
Wave intensity in the ascending aorta
\[ \text{W/m}^2 \]

Velocity of shortening
\[ \text{m/s} \]

Left ventricular origin of waves in the ascending aorta

0. Aortic valve opening
1. Peak aortic flow
   Onset of reflections
   \( V_{\text{max}} \) of radial function
2. \( V_{\text{max}} \) long-axis function
3. Peak aortic pressure
4. Aortic valve closure

Diastolic suction precedes AV closure

Page C et al,
Int J Cardiol
2010;142:166-71
Suction generated by LV before aortic valve closure correlates with early diastolic relaxation and filling.

Expansion wave amplitude

\[ r = -0.77 \ (p < 0.001) \]

Ohite N et al, Heart Vessels 2003
Propagation velocity of mitral inflow during early diastole
Validation as a load-insensitive index of ventricular suction

\[ V_p \text{ (cm/sec)} \]

\[ \tau \text{ (msec)} \]

\[ R = -0.78 \]
\[ y = 592.21x^{-0.8838} \]
\[ p < 0.001 \]

Garcia M et al, J Am Coll Cardiol 2000; 35: 201-8
Increased mitral valve gradient during exercise results from a fall in minimum LVP without a change in LAP, i.e. increased suction

Effects of exercise on left ventricular torsion in healthy subjects

Apical rotation and untwist in HFNEF

LV torsion in early diastole produces ventricular recoil, annular motion, & suction

Y Tan and J Sanderson, JACC 2009; 54: 36-46
“Experiments carried out in this laboratory have shown that in an isolated heart [...] (within physiological limits) the larger the diastolic volume [...] the greater is the energy of its contraction.”

Length-dependence of tension (intact Frank Starling mechanism) facilitates synchrony of stress & strain
The Frank-Starling Mechanism
Preload dependence of LV systolic function

Otto Frank & Ernest Starling

Ventricular interaction & restrictive filling pattern
Monitoring of hypervolaemic haemodilution
Development of ventricular interaction

19 Jehovah’s witnesses, aged 22-70 years
1 litre of Dextran / Ringer’s lactate in 10 minutes, x 3

Thermodilution catheter

Transgastric short-axis TEE

van Daele M et al, Anesthesiology 1994; 81: 602-9
Preload dependence of myocardial velocities – 30 mmHg lower body negative pressure

Frigiola A et al, JACC 2001; 37: 409A
Effect of No or cGMP on myocardial relaxation

Differential effects of amlodipine vs atenolol (ASCOT)

Difference in magnitude but not timing of reflections

\[ \Delta \text{wave reflection index} = 3.5\% \]
Lowering central aortic pressure in hypertension improves diastolic function and longitudinal LV diastolic and systolic function (ASCOT Substudy)

<table>
<thead>
<tr>
<th></th>
<th>Atenolol-Based Regimen (n = 411)</th>
<th>Amlodipine-Based Regimen (n = 413)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior wall thickness, systole, cm</td>
<td>1.58 ± 0.25</td>
<td>1.59 ± 0.23</td>
<td>0.510</td>
</tr>
<tr>
<td><strong>LV ejection fraction, %</strong></td>
<td><strong>69.48 ± 11.32</strong></td>
<td><strong>69.21 ± 12.19</strong></td>
<td>0.759</td>
</tr>
<tr>
<td>LVMI, g/m²</td>
<td>122.66 ± 30.92</td>
<td>118.80 ± 31.56</td>
<td>0.089</td>
</tr>
<tr>
<td>Relative wall thickness</td>
<td>0.51 ± 0.10</td>
<td>0.51 ± 0.10</td>
<td>0.412</td>
</tr>
<tr>
<td>Left atrial size, cm*</td>
<td>4.25 ± 0.59</td>
<td>4.14 ± 0.64</td>
<td>0.022</td>
</tr>
<tr>
<td>Transmural Doppler</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E wave, cm/s</td>
<td>60.08 ± 14.87</td>
<td>63.41 ± 15.01</td>
<td>0.001</td>
</tr>
<tr>
<td>A wave, cm/s</td>
<td>68.25 ± 14.63</td>
<td>75.08 ± 15.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>0.91 ± 0.29</td>
<td>0.86 ± 0.22</td>
<td>0.004</td>
</tr>
<tr>
<td>E-wave deceleration time, ms</td>
<td>0.20 ± 0.05</td>
<td>0.18 ± 0.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tissue Doppler</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic velocity (S’), cm/s</td>
<td><strong>8.2 ± 1.75</strong></td>
<td>9.5 ± 2.21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Early diastolic velocity (E’), cm/s</td>
<td><strong>7.91 ± 1.84</strong></td>
<td>8.76 ± 2.04</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Late diastolic velocity (A’), cm/s</td>
<td>10.76 ± 2.15</td>
<td>12.34 ± 2.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean E/E’ ratio</td>
<td>8.14 ± 2.38</td>
<td>7.76 ± 2.05</td>
<td>0.013</td>
</tr>
</tbody>
</table>

Tapp RJ et al, JACC 2010; 55: 1875-81
The VALIDD Study – Valsartan vs. placebo

384 patients with hypertension & diastolic dysfunction

Valsartan improved early diastolic function

Angiotensin receptor blockers ("sartans") have antifibrotic effects

( via $\sqrt{TGF \beta}$ )

*Solomon S et al, Lancet 2007; 369: 2079-87*
Effects of levosimendan on LV diastolic function
RCT in 23 patients after aortic valve replacement
Heart rate, mean arterial & central venous pressures constant

IVRT by transoesophageal echocardiography

Jörgensen K et al, Circulation 2008; 117: 1075-81
Isovolumic acceleration by tissue Doppler correlates with contractility (ees) & is load-insensitive.

Vogel M et al, Circulation 2003; 107: 1647
IVA in the RV is load-independent

Reduction of preload, by inflation of balloon in IVC

Increase of afterload, by inflation of balloon in main PA

Vogel M et al, Circulation 2002; 105: 1693-1699
Myocardial isovolumetric acceleration
Force-frequency relationship

\[ \text{dP/dt} \quad \text{mmHg/s} \quad \text{Aic [ IVA ] m/s}^2 \]

Vogel M et al, Circulation 2002; 105: 1693-1699
The force-frequency relationship

Wachter R et al, Eur Heart J 2009; 30: 3027-36
Inter-observer reproducibility of isovolumic acceleration 
Correlations and Bland-Altman analyses

Figure Bland Inter Andrei Dewi

R = 0.71, p < 0.0001
R = 0.90, p < 0.0001
R = 0.84, p < 0.0001

Normal
Type 2 DM
Heart Failure

Feasibility 97%
Coefficient of variation 20%

89%
16%
82%
25%

Margulescu A et al, JASE 2010; 23: 423-31
Cardiac function and mechanics

Interactions between systole and diastole

• Increased afterload especially in late systole delays myocardial relaxation

• Left ventricular filling volume and end-diastolic pressure influence LV systolic function

• Most echocardiographic indices of LV systolic and diastolic function are influenced by loading

• Assessment of intrinsic myocardial function can be made if loading is kept constant

• Isovolumic acceleration may be useful