Regulation of Coronary Blood Flow

23-04-2015

Dirk J. Duncker
Div Experimental Cardiology, Thoraxcenter
Erasmus MC, University Medical Center Rotterdam
The Netherlands
Regulation of Coronary Blood Flow

- Introduction
- Control of Coronary Resistance Vessels
- Autoregulation: Pressure Flow Relation
- Hemodynamic Effects of a Coronary Stenosis

Duncker & Bache  *Physiol Rev* 2008
Van de Hoeff et al  *J Mol Cell Cardiol* 2012
Laughlin et al  *Compr Physiol* 2012
Duncker et al  *Prog Cardiovasc Dis* 2015
Cyclic Compression of the Coronary Microvasculature

Pressure (mmHg)

LAD flow (ml/min)

RCA flow (ml/min)

GCV flow (ml/min)

Systole

Diastole

Systole

Time (s)

0.0 0.4 0.8 1.2

Ao LV RV

ETP April 23-25, 2015

Duncker & Merkus 2004

Courtesy of Harold Laughlin
Unique aspects of the coronary circulation

- Cyclic compression of the vasculature
- High ‘resting’ myocardial metabolic rate
  
  Cardiac muscle flow 1.0 ml/min/g
  Skeletal muscle flow 0.1 ml/min/g

- High myocardial capillary density
  
  Cardiac muscle 3000-4000/mm²
  Skeletal muscle 500-1000/mm²

- High myocardial oxygen extraction
  
  Cardiac muscle 60-80%
  Skeletal muscle 20-30%
Myocardial O$_2$ balance during exercise

Myocardial O$_2$ consumption (ml/min/g)

Coronary Flow

Hematocrit

ArtSO$_2$

CVSO$_2$

* * * *
Metabolic Vasodilation

Exercise

LVMBF = LV Myocardial Blood Flow

LVMBF = 0.012·HR-0.38
LVMBF = 0.016·HR-0.61
LVMBF = 0.021·HR-0.27
LVMBF = 0.019·HR-0.44

ETP April 23-25, 2015

Laughlin, Davis, ..., Bache, Merkus, Duncker Compr Physiol 2012
Laws of Hemodynamics

- Darcy’s law
  \[ \Delta P = \text{Flow} \times R \]
  \[ \text{Flow} = \frac{\Delta P}{R} \]

- Poiseuille’s law
  \[ R = \frac{8 \eta L}{\pi r^4} \]

Symbols:
- \( \Delta P \): pressure
- \( R \): resistance
- \( L \): length
- \( r \): radius
- \( \eta \): viscosity
Regulation of Coronary Blood Flow

• Introduction
• Control of Coronary Resistance Vessels
• Autoregulation: Pressure Flow Relation
• Hemodynamic Effects of a Coronary Stenosis

Duncker & Bache  *Physiol Rev* 2008
Van de Hoeff et al  *J Mol Cell Cardiol* 2012
Laughlin et al  *Compr Physiol* 2012
Duncker et al  *Prog Cardiovasc Dis* 2015

ETP April 23-25, 2015
Distribution of Resistance in Coronary Microcirculation

![Diagram of a heart with microcirculatory vessels and a graph showing the relationship between microcirculatory pressure and vessel diameter. The graph compares control and Dipyridamole conditions.](Chilian et al Am J Physiol 1989)
METABOLIC DEMAND OF THE MYOCARDIUM

Small arteries
Large arterioles

Flow sensitive

Intermediate arterioles
Pressure sensitive

Small arterioles
Metabolite sensitive

METABOLIC VASODILATION

CHANGE IN DIAMETER (%)

VEssel DIAMETER (μm)

Davis et al  APS Handbook of Physiology 2008
Zhang, ..., Chilian  APS Handbook of Physiology 2008
Control of tissue blood flow

“Blood goes where it is needed”

John Hunter 1794

“He must have wondered how blood “knows” where it is needed?”

LB Rowell JAP 2004
The ultimate cardiac challenge

Exercise

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Rest</th>
<th>Exercise at 5 km/h</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVP (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV dP/dt (mmHg/s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBF (ml/min)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Duncker & Merkus J Physiol 2007
Duncker et al JMCC 2012
Control of Coronary Microvascular Tone

Erythrocytes

Endothelium

ACE

ECE

bET-1

ET-1

TXA₂

5HT

Platelets

TXA₂

5HT

Platelets

TXA₂

5HT

Smooth Muscle

ET₂

ET₂

ET₂

ET₂

P₂Y

eNOS

COX-1

CYP450

O₂⁻⁻

shear stress

O₂

H₂O₂

K⁺

K⁺

K⁺

K⁺

K⁺

ACh

NE

α₁

α₂

H₁

H₂

P₂x

K⁺

K⁺

K⁺

K⁺

CO₂

adenosine

ATP

ADP

O₂

ATP

ADP

O₂

ECE eNOS COX-1 CYP450

Control of Coronary Microvascular Tone

ETP April 23-25, 2015

Laughlin et al Compr Physiol 2012
Regulation of Coronary Blood Flow

• Introduction
• Control of Coronary Resistance Vessels
• Autoregulation: Pressure Flow Relation
• Hemodynamic Effects of a Coronary Stenosis

Duncker & Bache  *Physiol Rev* 2008
Van de Hoeff et al  *J Mol Cell Cardiol* 2012
Laughlin et al  *Compr Physiol* 2012
Duncker et al  *Prog Cardiovasc Dis* 2015
Autoregulation

The ability of the heart to maintain flow constant in the face of a change in perfusion pressure...

...while myocardial metabolism remains unchanged.
Coronary Autoregulation

Coronary Perfusion Pressure (mm Hg) vs. Coronary Blood Flow (mL/min)

ETP April 23-25, 2015 (Courtesy of Bernard De Bruyne)

Rubio and Berne, Prog CV Disease 1975
Autoregulatory Range

Coronary Perfusion Pressure (mm Hg)

Coronary Blood Flow (mL/min)

Rubio and Berne, Prog CV Disease 1975

ETP April 23-25, 2015 (Courtesy of Bernard De Bruyne)
Coronary Pressure-Flow Relation

Flow$_{\text{max}}$ / $\Delta P = \text{Conductance}_{\text{max}}$

**NORMAL**

- Maximum vasodilation
- Flow reserve normal
- Maximum vasoconstriction
- Autoregulatory range
- $P_{RA}$
- $P_{f=0}$
- 40 mm Hg

Coronary Flow (ml/min/gm)

Coronary Pressure

Duncker et al  Prog Cardiovasc Dis 2015

ETP April 23-25, 2015
Coronary Pressure-Flow Relation

NORMAL

- Maximum vasodilation
- Flow reserve normal

STRESS

- Maximum vasoconstriction

Increased resting flow:
- ↑ HR
- ↑ SBP
- ↑ Contractility
- ↓ Hb

ETP April 23-25, 2015
Duncker et al Prog Cardiovasc Dis 2015
Coronary Pressure-Flow Relation

**NORMAL**
- Flow reserve normal
- Maximum vasodilation
- Maximum vasoconstriction

**STRESS**
- Decreased maximum flow
- LV Hypertrophy
- Microvascular disease
- ↑ HR
- ↑ Preload

**Graphs**
- **Coronary Flow (ml/min/gm)** vs. **Coronary Pressure**
- **40 mm Hg**
- **Autoregulatory range**
- **P_{RA}**
- **P_{f=0}**

**ETP April 23-25, 2015**

Duncker et al. Prog Cardiovasc Dis 2015
Coronary Pressure-Flow Relation

**NORMAL**
- Maximum vasodilation
- Flow reserve normal
- Maximum vasoconstriction
- Autoregulatory range
- $P_{RA}$
- $P_{f=0}$
- $40 \text{ mm Hg}$

**STRESS**
- Decreased maximum flow
- LV Hypertrophy
- Microvascular disease
- $\uparrow$ HR
- $\uparrow$ Preload
- Flow reserve stress
- $60 \text{ mm Hg}$

Increased resting flow:
- $\uparrow$ HR
- $\uparrow$ SBP
- $\uparrow$ Contractility
- $\downarrow$ Hb

Duncker et al, Prog Cardiovasc Dis 2015
Regulation of Coronary Blood Flow

- Introduction
- Control of Coronary Resistance Vessels
- Autoregulation: Pressure Flow Relations
- *Hemodynamic Effects of a Coronary Stenosis*

Duncker & Bache *Physiol Rev* 2008
Van de Hoeff et al *J Mol Cell Cardiol* 2012
Laughlin et al *Compr Physiol* 2012
Duncker et al *Prog Cardiovasc Dis* 2015
Stenosis

\[ \Delta P = f_1 \frac{Q}{A_s} + f_2 (\frac{P}{2} \frac{1}{A_s^{1/3}}) \]

Flow separation

ETP April 23-25, 2015
Coronary velocity

Pressure Derived Fractional Flow Reserve, FFR

Aortic (Pao)
Coronary (Pd)

CFR = 2.2
FFR = Pd / Pao = 105 / 133 = 0.78
Assessment of Coronary Reserve

Graph showing the relationship between flow (ml/min/gm) and distal coronary pressure (mm Hg) with annotations for vasodilation, autoregulation, and 50%, 80%, and 90% pressure levels.
Assessment of Coronary Reserve

- Flow velocity wire
- PET/MRI/CT Perfusion

Graph showing the relationship between flow, distal coronary pressure, and stenosis percentage.
Assessment of Coronary Reserve

**Graphs:**
- **Left Graph:**
  - X-axis: Distal Coronary Pressure (mm Hg)
  - Y-axis: Flow (ml/min/gm)
  - Key points:
    - Vasodilation: 50%
    - Autoregulation: 80%
    - 90%
- **Right Graph:**
  - X-axis: Stenosis (%)
  - Y-axis: Relative Flow Reserve
  - Curve showing normal region and stenotic region.

**PET/MRI/CT Perfusion**

_Canty & Duncker  Braunwald’s Heart Disease 2014_
Assessment of Coronary Reserve

FLOW (ml/min/gm)

Vasodilation

50%

Autoregulation

80%

90%

DISTAL CORONARY PRESSURE (mm Hg)

FRACTIONAL FLOW RESERVE

\( \left( \frac{P_{\text{coronary}}}{P_{\text{aorta}}} \right) \)

Normal region

Pressure wire

Canty & Duncker  Braunwald’s Heart Disease 2014
Assessment of Coronary Reserve

Flow velocity wire

PET/MRI/CT Perfusion

Pressure wire

Canty & Duncker  Braunwald’s Heart Disease 2014
Regulation of Coronary Blood Flow

- Introduction
- Control of Coronary Resistance Vessels
- Autoregulation: Pressure Flow Relations
- Hemodynamic Effects of a Coronary Stenosis

Questions?

Duncker & Bache  *Physiol Rev* 2008
Van de Hoeff et al  *J Mol Cell Cardiol* 2012
Laughlin et al  *Compr Physiol* 2012
Duncker et al  *Prog Cardiovasc Dis* 2015