Regulation of Coronary Blood Flow

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Dirk J. Duncker
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, ..., Duncker  *Compr Physiol* 2012
Canty & Duncker  *Braunwald’s Heart Disease* 2014
Cyclic Compression of the Coronary Microvasculature

![Diagram of heart with labeled vessels: RCA, LAD, LCx, Ao, RV, LV, PA.]

**GCV flow (ml/min)**

**RCA flow (ml/min)**

**LAD flow (ml/min)**

**Pressure (mmHg)**

- **Systole**
  - Ao
  - LV
  - RV

- **Diastole**

- **Systole**

**Time (s)**

0.0 0.4 0.8 1.2

Duncker & Merkus 2004

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Courtesy of Harold Laughlin
Unique aspects of the coronary circulation

- Cyclic compression of the vasculature
- High resting myocardial metabolic rate
  - Cardiac muscle: 1 ml/min/g flow
  - Skeletal muscle: 0.1 ml/min/g flow

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

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

**Coronary Flow**

- Myocardial O$_2$ consumption (ml/min/g)
- Hematocrit
- ArtSO$_2$
- CVSO$_2$

![Graphs showing coronary flow, hematocrit, ArtSO$_2$, and CVSO$_2$ against myocardial O$_2$ consumption.](image)

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Von Restorff et al. Pfluegers Arch 1977
Myocardial $O_2$ balance during exercise

- Myocardial $O_2$ balance
  - $O_2$ demand
    - Contraction
      - Heart Rate: 60%
    - Basal metabolism: ~0%
  - $O_2$ supply
    - Coronary flow: 80%
    - [O$_2$]$_{ART}$ - [O$_2$]$_{CV}$: 20%
Metabolic Vasodilation

Exercise

LVMBF = LV Myocardial Blood Flow
Laws of Hemodynamics

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

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

\( \Delta P \) = pressure difference
\( R \) = resistance
\( P_1 \), \( P_2 \) = pressures at points 1 and 2, respectively
\( L \) = length
\( r \) = radius
\( \eta \) = viscosity
\( R \) = resistance

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JR Levick  An Introduction to Cardiovascular Physiology 2010
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Distribution of Resistance in Coronary Microcirculation

![Diagram showing the distribution of resistance in the coronary microcirculation.](image)

The graph illustrates the microcirculatory pressure across different vessel diameters, comparing control and dipyridamole conditions. Arteries and veins are highlighted with distinct markers.

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**

- **CBF (ml/min)**
- **LV dP/dt (mmHg/s)**
- **MAP (mmHg)**
- **LVP (mmHg)**

<table>
<thead>
<tr>
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<th>Rest</th>
<th>Exercise at 5 km/h</th>
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<tr>
<td><strong>CBF (ml/min)</strong></td>
<td><img src="#" alt="Graphs" /></td>
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<td><strong>LV dP/dt (mmHg/s)</strong></td>
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Duncker & Merkus *J Physiol* 2007
Duncker & Bache *Physiol Rev* 2008
Laughlin, ..., Duncker *Compr Physiol* 2012
Control of Coronary Microvascular Tone

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Autoregulation

The ability of the heart to maintain flow constant in the face of a change in perfusion pressure without the intervention of any other external mechanism.
Coronary Autoregulation

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

Rubio and Berne, Prog CV Disease 1975

ETP April 24-26, 2014 (Courtesy of Bernard De Bruyne)
Autoregulatory Range

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

Rubio and Berne, Prog CV Disease 1975

ETP April 24-26, 2014 (Courtesy of Bernard De Bruyne)
METABOLIC VASODILATION

AUTOREGULATION

Davis et al. APS Handbook of Physiology 2008

Zhang, Rogers, Merkus, ... Chilian APS Handbook of Physiology 2008
Coronary Pressure-Flow Relation

\[ \Delta P = \text{Flow} \times R \]

\[ R_{\text{min}} = \frac{\Delta P}{\text{Flow}_{\text{max}}} \]

\[ C_{\text{max}} = \frac{1}{R_{\text{min}}} = \frac{\text{Flow}_{\text{max}}}{\Delta P} \]

P = pressure
R = resistance
C = conductance
Coronary Pressure-Flow Relation

**NORMAL**
- Maximum vasodilation
- Flow reserve normal
- Autoregulatory range
- Maximum vasoconstriction
- Flow reserve normal
- $P_{RA}$
- $P_{f=0}$

**STRESS**
- Increased resting flow
  - $\uparrow$ HR
  - $\uparrow$ SBP
  - $\uparrow$ Contractility
  - $\downarrow$ Hb
- Decreased maximum flow
- LV Hypertrophy
- Microvascular disease
- $\uparrow$ HR
- $\uparrow$ Preload
Coronary Pressure-Flow Relation

Subendocardial Vulnerability

Canty & Duncker  Braunwald’s Heart Disease 2014
Coronary Flow-Function Relation

Subendocardial vulnerability

A

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Coronary Pressure-Flow Relation

NORMAL

CORONARY FLOW (ml/min/gm)

Coronary Flow vs. Coronary Pressure Diagram
- Maximum vasodilation
- Flow reserve normal
- Maximum vasoconstriction
- Autoregulatory range
- $P_{RA}$
- $P_{f=0}$

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Canty & Duncker  Braunwald’s Heart Disease 2014
Stenosis

\[ \Delta P = f_1 \frac{Q}{A_s} + f_2 \left( \frac{1}{\sqrt{A_s}} - \frac{1}{\sqrt{A_n}} \right) \]

Flow separation

\[ f_1 = \frac{8 \pi \mu L}{A_s^2} \]

\[ f_2 = \frac{P}{2} \left( \frac{1}{\sqrt{A_s}} - \frac{1}{\sqrt{A_n}} \right) \]
Pressure Derived Fractional Flow Reserve, FFR

Aortic (Pao)
Coronary (Pd)

Coronary velocity
Adenosine

\[ FFR = \frac{P_d}{P_a} = \frac{105}{133} = 0.78 \]

CFR = 2.2
Assessment of Coronary Reserve

Flow velocity wire

PET/MRI/CT Perfusion

Pressure wire

Graph showing the relationship between distal coronary pressure and flow, with lines representing vasodilation, autoregulation, and fractional flow reserve.
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Coronary Pressure-Flow Relation

Influence of Coronary Microvascular Disease

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**Diagram Description:**

- **Normal Line:** This line represents normal coronary flow at various pressures.
- **CMVD Line:** This line indicates the flow reduction due to Coronary Microvascular Disease (CMVD) at different pressures.
- **70% Reduction Line:** This line shows a 70% reduction in flow compared to the normal line at the same pressure.
- **50% Reduction Line:** This line demonstrates a 50% reduction in flow compared to the normal line at the same pressure.

**Arterioles Diagram:**

- **Small Arterioles:** Represented as the most susceptible to CMVD with a pressure-sensitive response.
- **Intermediate Arterioles:** Less sensitive than small arterioles.
- **Large Arterioles:** Least sensitive, typically pressure sensitive.
- **Flow Sensitive:** Indicates the arterioles are sensitive to flow changes.

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**Axes:**

- **Coronary Flow (ml/min/gm):** Vertical axis ranging from 0 to 5 ml/min/gm.
- **Coronary Pressure (mm Hg):** Horizontal axis ranging from 0 to 100 mm Hg.

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**References:**

- Braunwald’s Heart Disease 2014
- Canty & Duncker

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**Event:**

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