Sedentary behavior and increased vascular disease risk

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Vascular Endothelial Dysfunction

Leisure time physical inactivity

Obesity prevalence

Type 2 diabetes prevalence
Endothelial Function: A “Barometer of Cardiovascular Risk”

Our Translational Vascular Biology Approach

Molecular phenotyping

Endothelial and smooth muscle cell culture studies

Functional studies in isolated arteries and 3D imaging

Vascular and metabolic studies in small and large pre-clinical animal models

Human vascular and metabolic basic science studies and interventional clinical trials
Sedentary behavior

↑ Vascular disease
Sedentary behavior

Loss of shear stress-induced protective effects on endothelial cells

↑ Vascular disease
Sedentary behavior
i.e. (excessive sitting)
↓ Shear stress
Endothelial dysfunction
↓
↑ Leg vascular disease

Restaino et al. 2015
Can a decrease in physical activity and increase in sitting time lead to a reduction in endothelial function in young healthy subjects?
Can a decrease in physical activity and increase in sitting time lead to a reduction in endothelial function in young healthy subjects?

11 healthy recreationally active young men

Boyle et al. J Appl Physiol 2013
Verification that activity was indeed reduced during sedentary lifestyle.
Popliteal artery FMD is impaired after 5 days of reduced physical activity

Boyle et al. J Appl Physiol 2013
PoPliteal artery FMD is impaired after 5 days of reduced physical activity

Brachial artery FMD appears to be preserved after 5 days of reduced physical activity

Boyle et al. J Appl Physiol 2013
Reduced physical activity and increased sitting time for 5 days impairs endothelial function in the lower extremities, likely as a result of a decrease in blood flow and shear stress stimulus.

Boyle et al. J Appl Physiol 2013
Is inactivity-induced leg endothelial dysfunction mediated by a reduction in shear stress?
Is inactivity-induced leg endothelial dysfunction mediated by a reduction in shear stress?

13 healthy recreationally active young men

- Reduced Daily Activity (<5,000 steps/day)
- Active (> 10,000 steps/day)

FMD Time Points

Teixeira et al. J Appl Physiol 2017
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Teixeira et al. J Appl Physiol 2017
Reduced leg blood flow-induced shear stress during physical inactivity may a key underlying mechanism mediating leg endothelial dysfunction. 

Teixeira et al. J Appl Physiol 2017
Does prolonged sitting impair endothelial function in the leg?
Does prolonged sitting impair endothelial function in the leg?

11 healthy recreationally active young men

Six hours of uninterrupted sitting
2 hrs prior to lab arrival

Ingestion of standardized meal

Assessment of popliteal artery blood flow and shear rate

Assessment of popliteal artery FMD
Pooploiteal artery blood flow is reduced during sitting

Blood Flow (mL/min)

During Sitting

Pre Sit  2hr  4hr  6hr  Post Sit

Restaino et al. Exp Physiol 2015
Uninterrupted sitting blunts endothelial function in the lower limbs

%FMD

* p<0.05 vs. Pre Sit; † p<0.05 vs. Post Walk

Restaino et al. Exp Physiol 2015
Is prolonged sitting-induced leg endothelial dysfunction mediated by a reduction in shear stress?
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11 healthy recreationally active young men

Heated Leg vs. Nonheated Leg

Assessment of popliteal artery blood flow and shear rate in both legs

Assessment of popliteal artery FMD in both legs
Time: p=0.449
Leg: p=0.011
Interaction: p<0.001

- Nonheated leg
- Heated leg

**Statistical Results**

**Legend**

† Significant difference between the nonheated and heated leg conditions

**Graph Description**

- The graph compares the mean shear rate (s⁻¹) between a nonheated leg and a heated leg at different sitting positions (Pre-Sit, 0hr, 1hr, 2hr, 3hr, Post-Sit).

**Significance Indicators**

- * Denotes a significant difference at each time point compared to the previous time point.

**Time Points**

- Pre-Sit
- 0hr
- 1hr
- 2hr
- 3hr
- Post-Sit

**Mean Shear Rate (s⁻¹)**

- The y-axis represents the mean shear rate in s⁻¹, ranging from 0 to 120.

**Legend**

- Black bars represent the nonheated leg.
- Grey bars represent the heated leg.
After 3 hrs of sitting
Prolonged sitting-induced leg endothelial dysfunction is mediated by a reduction in shear stress

Time: \( p=0.811 \)
Leg: \( p=0.023 \)
Interaction: \( p=0.008 \)
Can leg movement during sitting prevent sitting-induced leg endothelial dysfunction?
11 young healthy subjects

Assessment of popliteal artery blood flow and shear rate in both legs

Assessment of popliteal artery FMD in both legs
11 young healthy subjects

Assessment of popliteal artery blood flow and shear rate in both legs

Assessment of popliteal artery FMD in both legs

Fidgeting movement:

1 min on/4 min off
Average = ~250 taps/minute

Morishima et al. AJP-Heart 2016
Time: $P < 0.001$
Leg: $P < 0.001$
Interaction: $P < 0.001$
After 3 hrs of sitting

- Control leg
- Fidgeting leg

Time: $P < 0.001$
Leg: $P < 0.001$
Interaction: $P < 0.001$

Time: $P = 0.995$
Leg: $P = 0.015$
Interaction: $P < 0.001$
Prolonged sitting-induced leg endothelial dysfunction is prevented by fidgeting

Morishima et al. AJP-Heart 2016
Can prior exercise prevent sitting-induced leg endothelial dysfunction?

**Visit 1**
- Baseline
- 20 min
- 45 min
- 3 hours
- Post

**Visit 2**
- Exercise
- 0h
- 0.5h
- 1h
- 2h
- 3h

Assessment of popliteal artery blood flow and blood pressure
Assessment of popliteal artery FMD

**Figure A**

- **Graph Title:** Popliteal artery shear rate (sec^{-1})
- **X-axis:** Duration of sitting (Baseline, 0h, 0.5h, 1h, 2h, 3h, Post)
- **Y-axis:** Popliteal artery shear rate (sec^{-1})

- **Legend:**
  - Open Circle: Sitting without prior exercise
  - Filled Circle: Sitting with prior exercise

- **Key Points:**
  - Time: P < 0.001
  - Trial: P = 0.002
  - Interaction: P < 0.001

- **Significance Markers:**
  - *: P < 0.05
  - †: P < 0.01
Prior exercise prevents sitting-induced leg endothelial dysfunction

In the absence of exercise, standing represents an effective substitute to sitting for preserving leg endothelial function.
Popliteal artery shear rate (sec\(^{-1}\))

- Lying down with zero degree angles
- Lying down with hips and knees bent to 90 degrees

Leg bending with sitting largely contributes to the reduction in leg blood flow.
Does leg bending impair popliteal artery FMD?

**A**
- Both legs straightened
- 3 hours
- Both legs straightened

- Assessment of popliteal artery blood flow and shear rate in both legs
- Assessment of popliteal artery FMD in both legs

**B**
- Positioning of the transducer
  - During bending
  - During FMD

*Walsh et al. Physiol Reports 2017*
These findings support the hypothesis that the sitting vasculopathy may be attributable to limb bending.

People should limit extended periods of time with legs bent and immobile, regardless of whether this is in the setting of sitting or lying-down.
Sedentary behavior i.e. (excessive sitting)

↓Shear stress

Endothelial dysfunction

Padilla et al. AJP-Heart Circ 2017
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Endothelial dysfunction

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↑ Leg vascular disease

Type 2 diabetes
Smoking
Aging

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Padilla et al. AJP-Heart Circ 2017
Thank you for your attention!