Adiponectin and Vulnerable Coronary Plaques: a VH-IVUS study

LEE Chi-Hang, Ronald MD, FACC

Associate Professor
Yong Loo Lin School of Medicine
National University of Singapore

October 29, 2010 4:25-4:40 am

National University Heart Centre, Singapore

Intravascular Ultrasound Diagnostic Evaluation of Atherosclerosis in Singapore (IDEAS)

- To correlate anatomical and functional significance of intermediate lesions in small coronary artery (published)

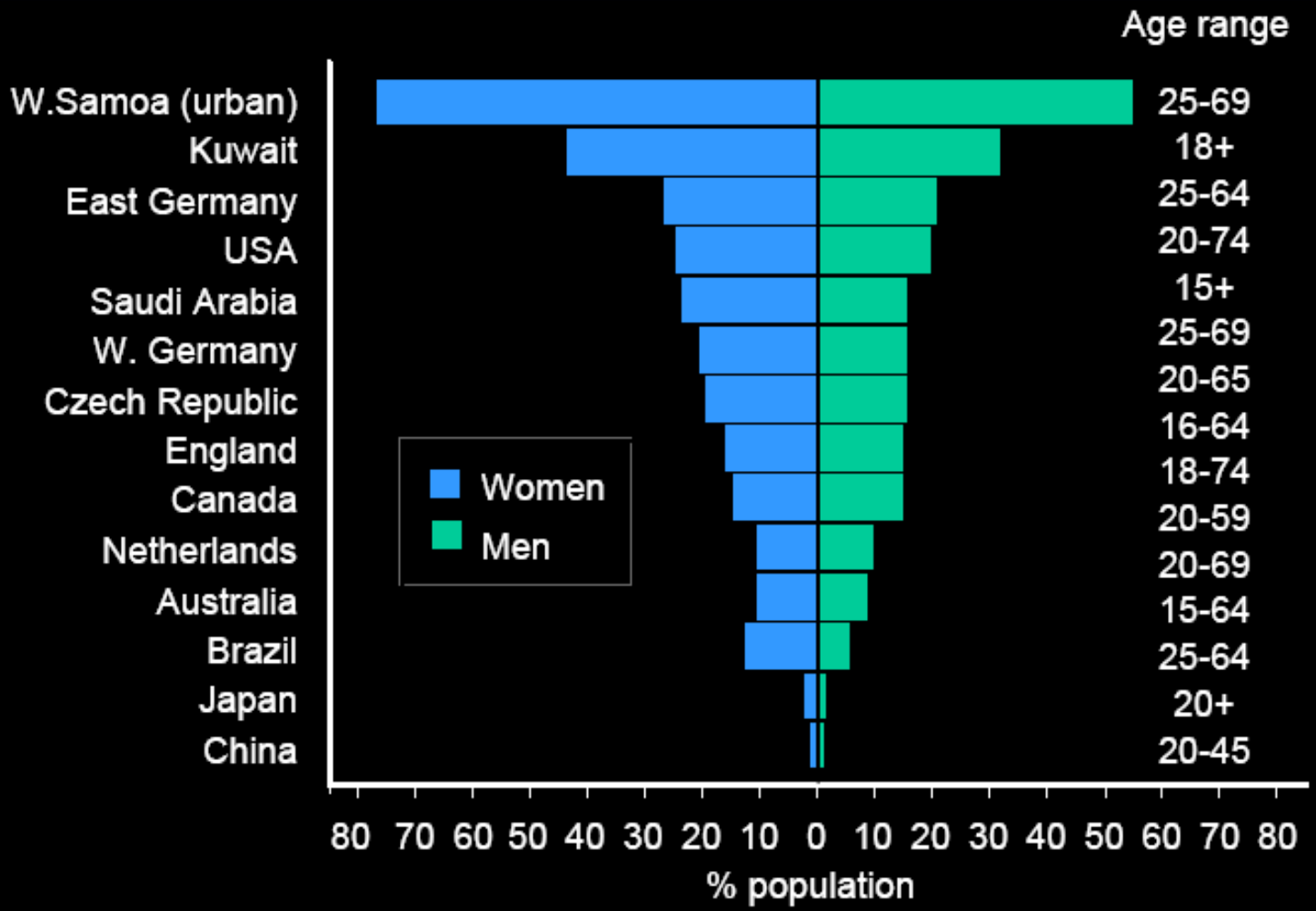
- Relationship between HDL and coronary artery modeling (submitted)

- **Relationship between adiponectin and vulnerable coronary plaque**

National University Heart Centre, Singapore

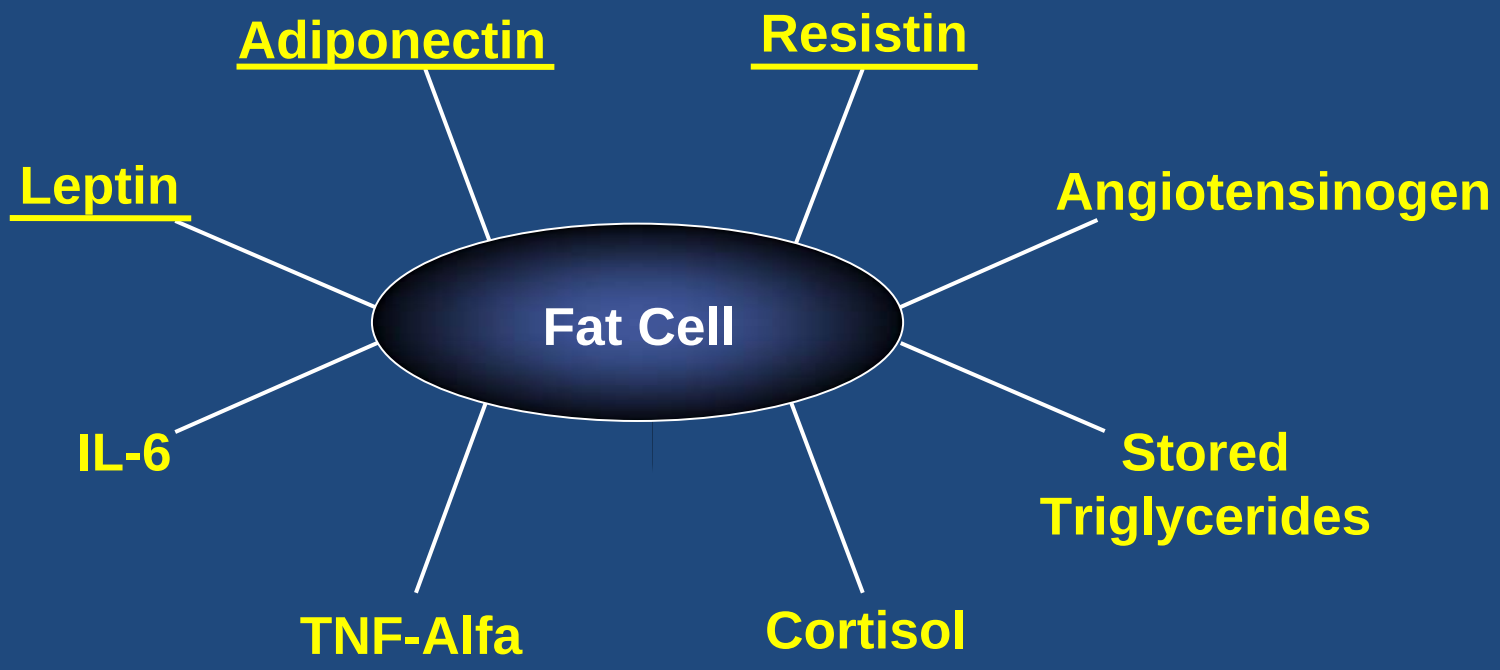
- Obesity, particularly intra-abdominal (visceral) obesity, is a leading cause of cardiovascular disease (CVD), insulin resistance, type 2 diabetes, dyslipidaemia, inflammation and thrombosis.

Global Prevalence of Obesity (BMI ≥30)



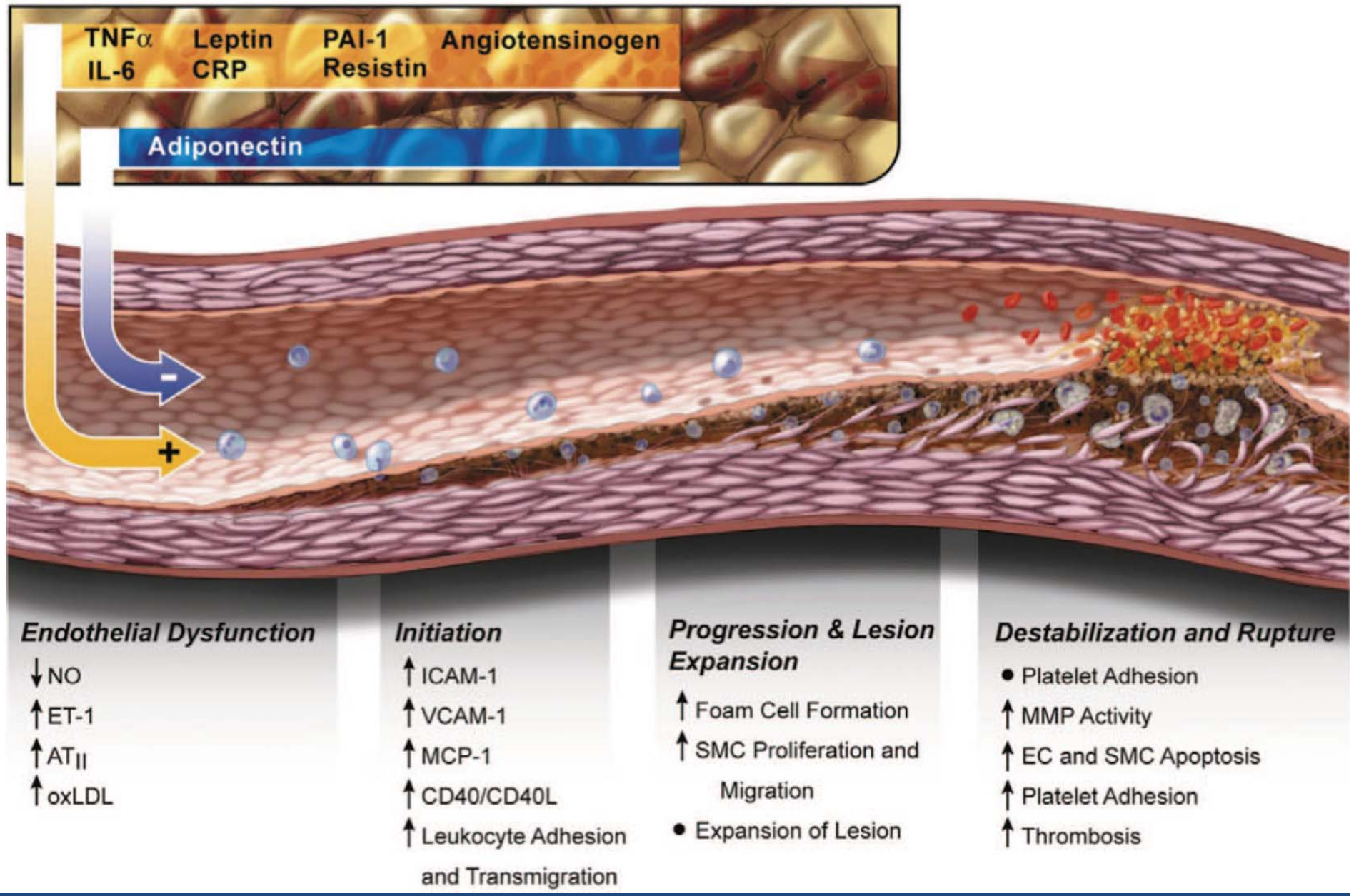
* Most recent available data. Surveys conducted between 1988 and 1994.

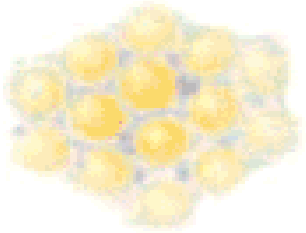
The Fat Cell Is a Veritable Endocrine Factory



Source: Underwood A, Adler J, Hand K, Ulick J. What You Don't Know About Fat. *Newsweek*. 2004;144:40-47.

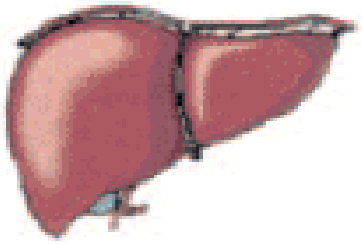
ADIPOKINES:


TNFα
IL-6
Leptin
CRP
PAI-1
Resistin
Angiotensinogen
Adiponectin
-
+
Endothelial Dysfunction
↓NO
↑ET-1
↑AT$_{II}$
↑oxLDL
Initiation
↑ICAM-1
↑VCAM-1
↑MCP-1
↑CD40/CD40L
↑Leukocyte Adhesion and Transmigration
Progression & Lesion Expansion
↑Foam Cell Formation
↑SMC Proliferation and Migration
• Expansion of Lesion
Destabilization and Rupture
• Platelet Adhesion
↑MMP Activity
↑EC and SMC Apoptosis
↑Platelet Adhesion
↑Thrombosis

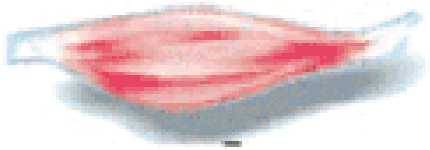


- A peptide hormone specifically produced by adipocytes
- Abundantly present in circulation
- Humans who are obese or who suffer from Type II diabetes show reduced levels of adiponectin

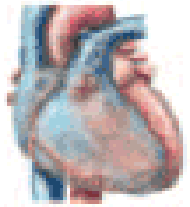
Adiponectin



↓ glucose output
↓ fat accumulation
↓ inflammation



↑ glucose uptake
↓ fat accumulation
↑ energy expenditure

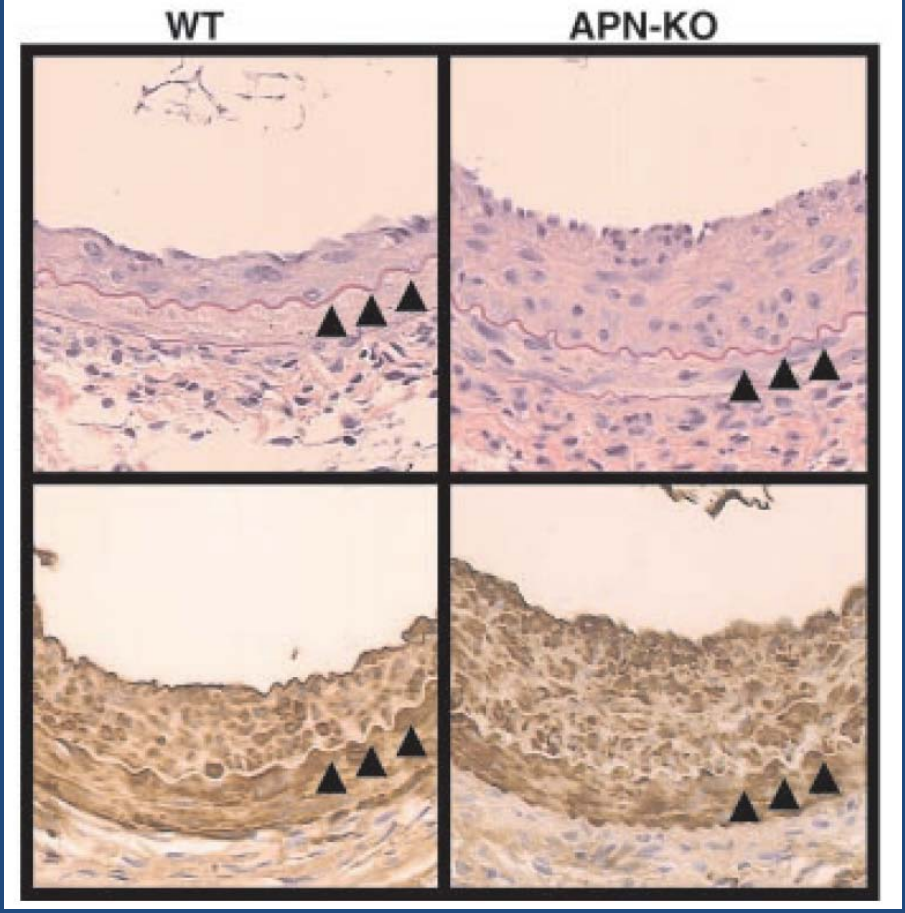


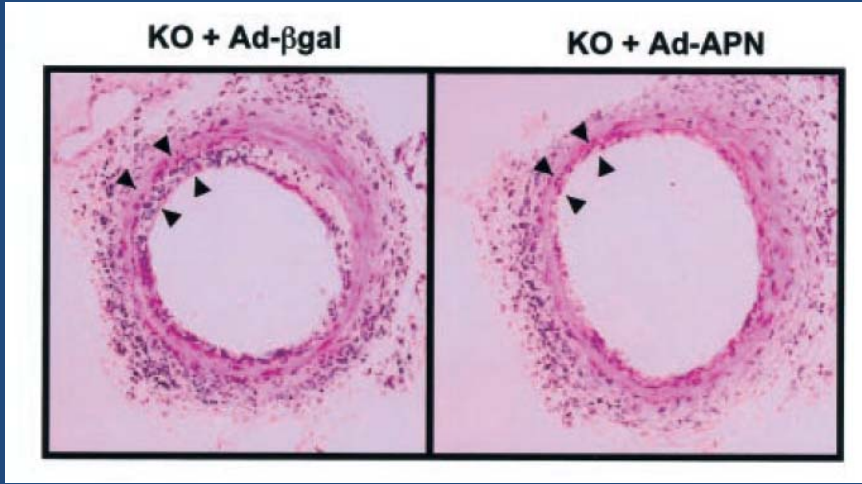
↓ inflammation
↓ endothelial adhesion
↓ foam cell formation

Protection from:

- Insulin-resistance
- Type 2 diabetes
- Coronary artery disease

Higher intimal thickening after injury in adiponectin knock-out mice

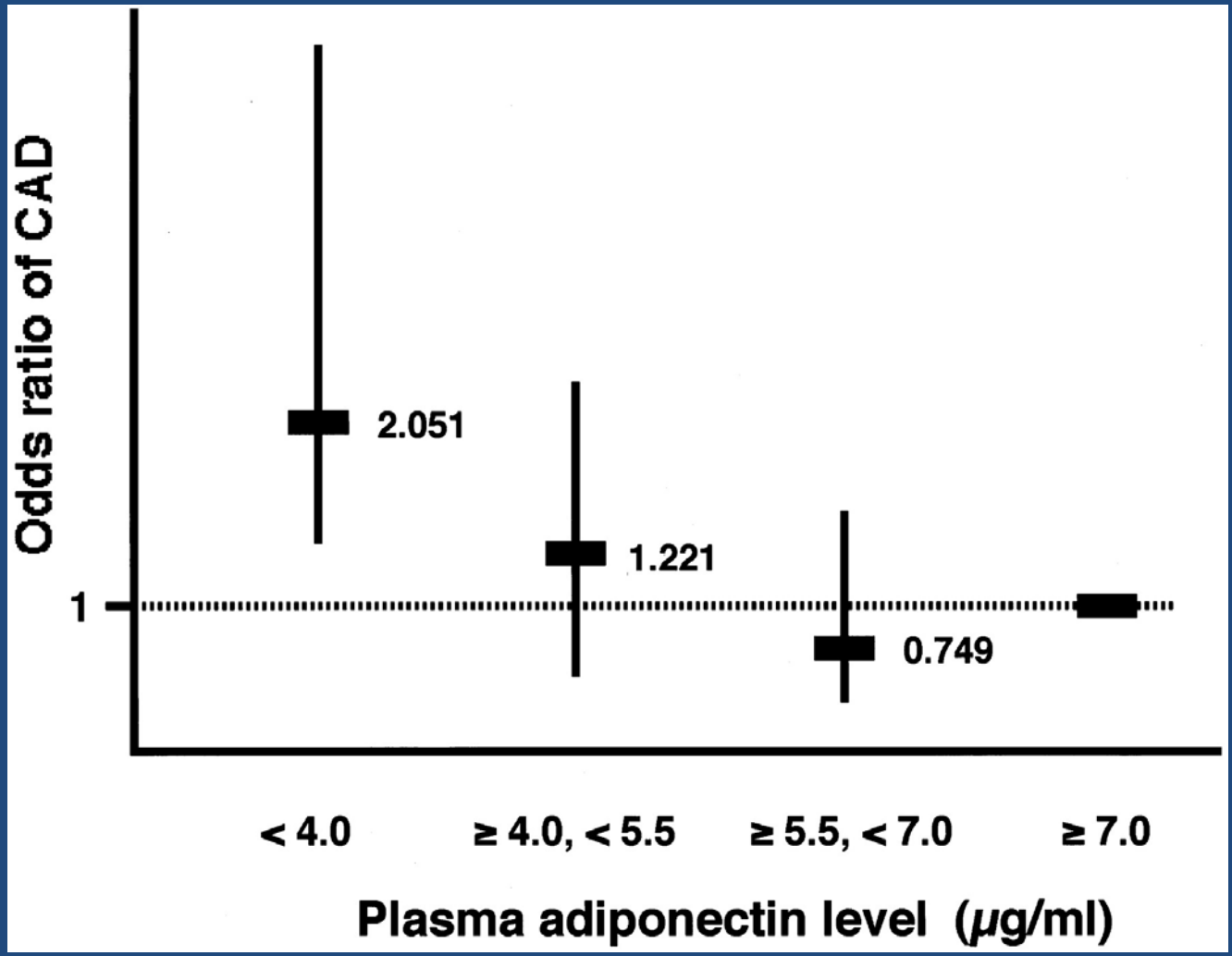




Effect of adenovirus-mediated supplement of adiponectin

National University Heart Centre, Singapore

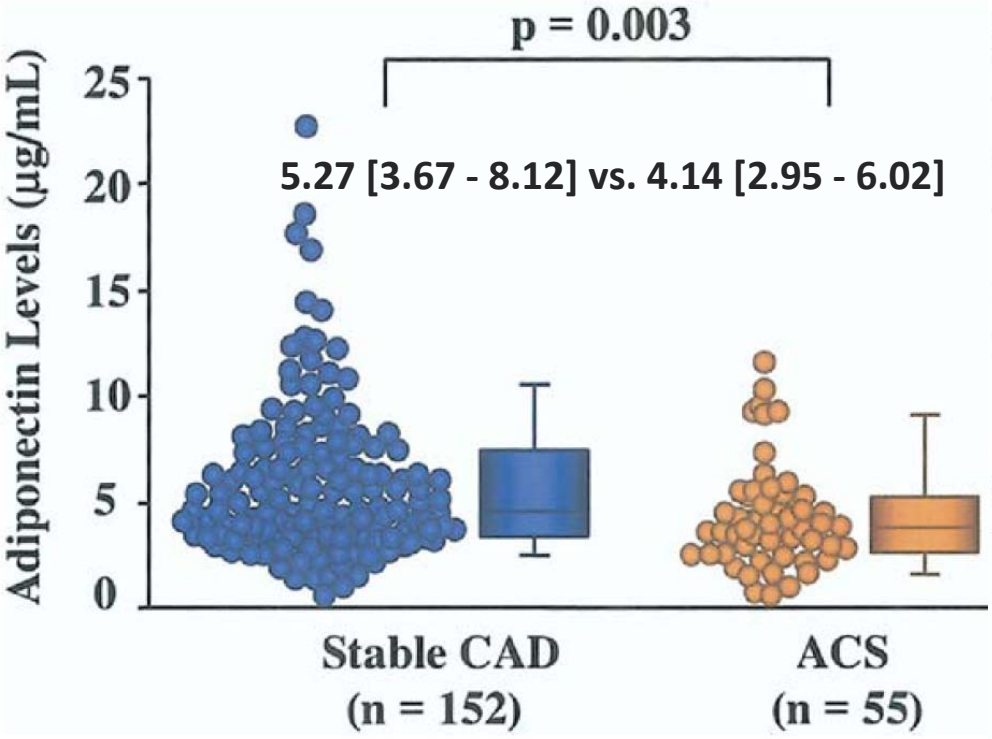
Association of Hypoadiponectinemia With Coronary Artery Disease in Men

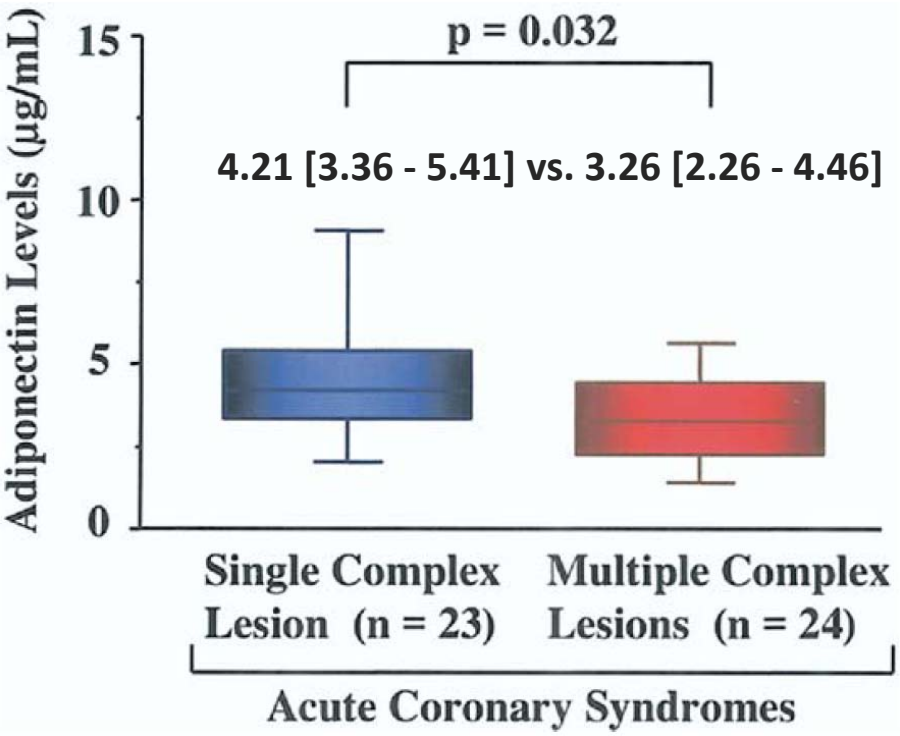


Kumada, M. et al. Arterioscler Thromb Vasc Biol 2003;23:85-89

National University Heart Centre, Singapore

Adiponectin, clinical presentation and lesion complexity in patients with coronary artery disease

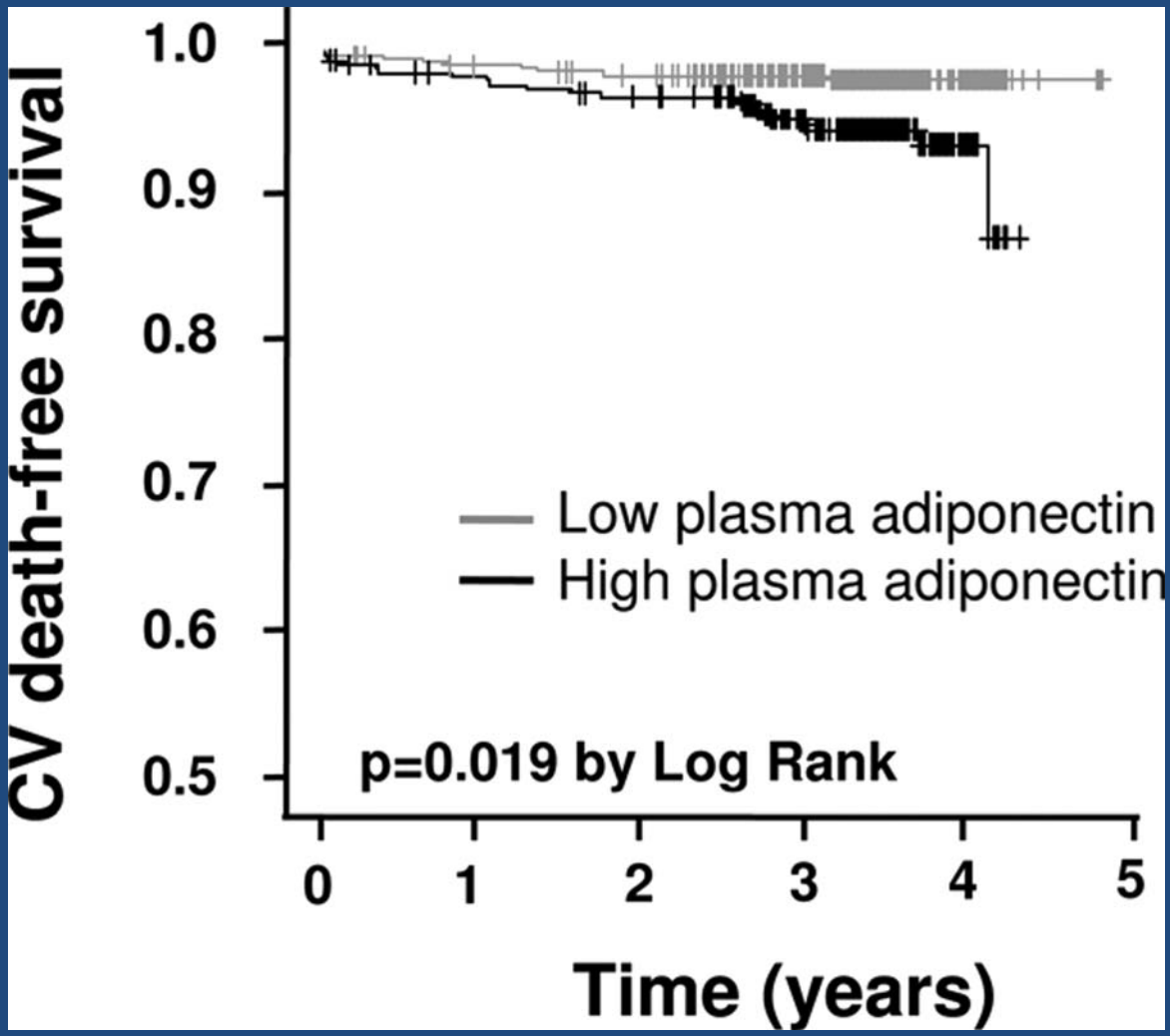




J Am Coll Cardiol 2006;48:1155– 62

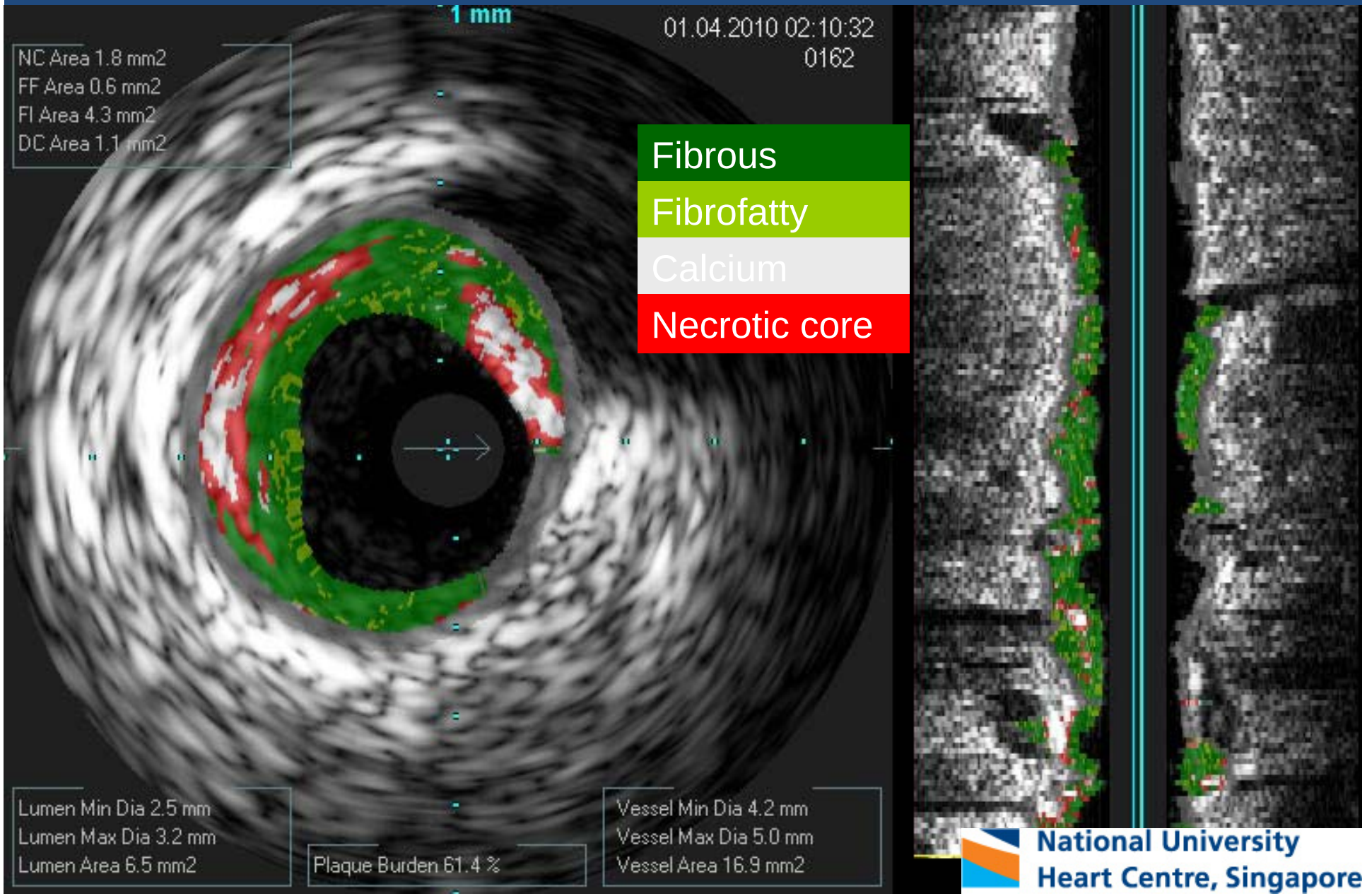
National University
Heart Centre, Singapore

Association of high-plasma adiponectin levels with CV death



Maiolino, G. et al. J Clin Endocrinol Metab 2008;93:3333-3340

Virtual Histology-Intravascular Ultrasound



National University Heart Centre, Singapore

Primary Objective

To compare the serum levels of adiponectin in patients with features of vulnerable coronary plaque

- Thin-capped fibroatheroma
- Positive remodeling
- Presented with acute coronary syndrome

National University Heart Centre, Singapore

Secondary Objectives

To study the relationships between serum levels of adiponectin and severity of coronary artery disease

- Number of vessel with >50% stenosis
- Percent atheroma volume

To study the relationships between serum levels of adiponectin and outcomes after PCI

- TIMI flow and corrected TIMI frame count
- PCI-related myocardial infarction
- One year clinical outcomes: Death, MI, TVR

National University Heart Centre, Singapore

Methods

- Patients who undergo coronary angiography and intervention for ischemic symptoms
  - Stable angina / silent ischemia
  - Unstable angina
  - NSTEMI
  - STEMI

- One identifiable culprit lesion

- VH-IVUS examination before balloon inflation (Thrombus aspiration is allowed)

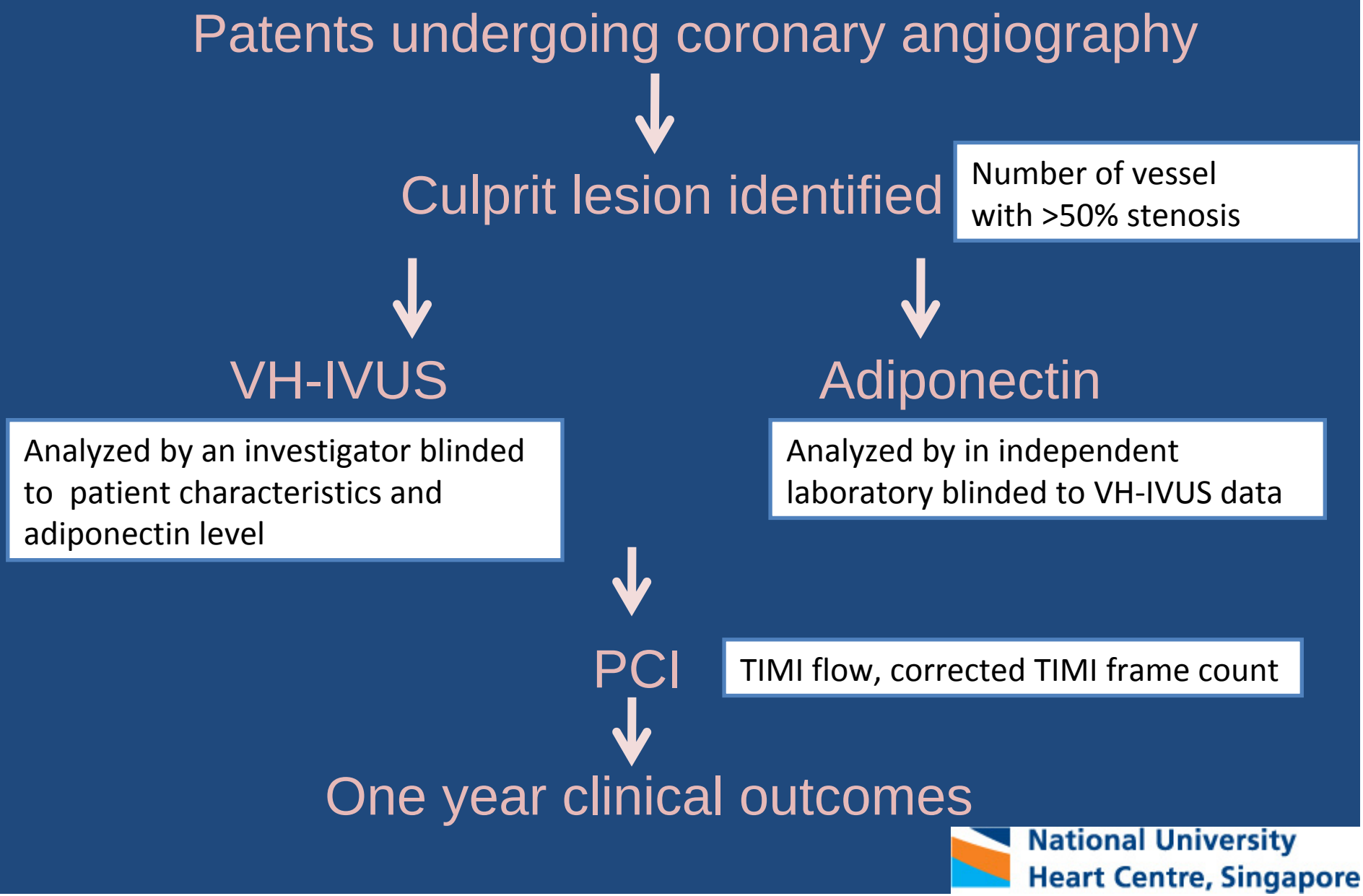
- Serum adiponectin measured by ELISA

National University Heart Centre, Singapore

Exclusion Criteria

- Thrombus-laden lesion after thrombus aspiration
- Instent restenosis
- Saphenous vein graft lesion
- Severe calcification
- Significant left main disease
- Renal failure on dialysis
- Severe angulation / tortuosity

Summary of study methodology



National University Heart Centre, Singapore

Study Status

- Total of 78 patients have been recruited
- Expected completion date: December 2010
- Number of patient/lesion analyzed: 68
- TCFA +ve: 27 (39.7%), TFCA –ve: 41 (60.3%)
- Adiponectin level: 7.4 vs. 4.3 μg/ml (TCFA +ve vs TCFA –ve, p=0.08)

National University Heart Centre, Singapore