Endothelial function in patients with cardiovascular risk factors evaluated with PET

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Ischemic cardiopathy: the importance of an early diagnosis

• 1st cause of death in Mexico
• 1 out of 3 Mexicans has at least one cardiovascular risk factor
• 30% mortality in the first 30 days after an AMI; half of these patients die within the first hour.
• 5% 1-year mortality after surviving an AMI

Salud México 2005. SSA. México
Cardiovascular Risk Factors

- Endothelial damage
- Atherosclerosis
- Atherotrombosis
- Myocardial damage
- Asymptomatic
- Chronic ischemia
- ACS
- C.H.F.
Endothelial Dysfunction

Oxidative Stress

- Loss of vasodilator predominance
- Prothrombotic and less thrombolytic
- Loss of anti-adherence
- Disturbance in vascular permeability
- Allows the proliferation of smooth muscle cells
Associated factors
Coronary endothelial Dysfunction

- Dyslipidemia
- Diabetes mellitus
- Smoking
- High Blood Pressure
- Metabolic Syndrome
- Rheumatologic diseases

Endothelial Function evaluated with PET

- Absolute quantification of the coronary blood flow in ml/g/min
- Dynamic quantification of the coronary blood flow with different physical or pharmacologic stimuli
- Evaluation of myocardial perfusion

Alexánder E. Arch Cardiol Mex 2006
Radiotracers

- Techniques
  - PET

Ammonia

Oxygen

Rubidium

Courtesy Turku PET Center, Finland
Coronary blood flow

$[^{13}\text{N}]-\text{ammonia PET}$

- Rest
  - EDVI
  - CFR
  - $\text{EDVI} \geq 1.5$
  - $\text{CFR} \geq 3.0$

- CPT

- Stress

Alexánderson E. Arch Cardiol Mex. 2005
Endothelial dysfunction

Stress CBF

Rest CBF

Stress CBF

Rest CBF
Associated factors
Coronary endothelial Dysfunction

- Dyslipidemia
  - Diabetes mellitus
  - Smoking
  - High Blood Pressure
  - Metabolic Syndrome
  - Rheumatologic diseases

Coronary Flow Reserve in Hypercholesterolemic Patients Without Overt Coronary Stenosis


Control Familial Hyperchol.
Secondary Hyperchol.
Familial Hyperchol.

CFR

p < 0.01
p < 0.5

Dyslipidemia: CFR and EDVI before treatment

n = 20

EDVI preTx, 1.28
CFR preTx, 2.79

Alexánderson E et al. Arch Cardiol Mex 2008
Dyslipidemia: CRF and EDVI after treatment with statins

n = 20

IVED preTx, 1.28
IVED posTx, 1.65
MFR preTx, 2.79
MFR posTx, 3.14

n = 20

Alexánderson E. Enviado a J Nucl Cardiol 2009
Effect of Cholesterol-Lowering Therapy in Patients with Early stages of Coronary Atherosclerosis

Baller et al. Circ 99:2871, 1999
Effect of Short-Term Cardiovascular Conditioning and Low-Fat Diet on CFR

Czernin et al. Circulation 92:197, 1995
Associated factors
Coronary endothelial Dysfunction

- Dyslipidemia
- Diabetes mellitus
- Smoking
- High Blood Pressure
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DM and endothelial dysfunction

- DM is the first cause of death in Mexico, mainly due to ischemic cardiopathy
- DM is an equivalent of coronary artery disease
- The reduction of serum glucose levels is associated with a decrease in the incidence of MACE.

ENSA 2005. SSA. México
DM and endothelial dysfunction

• The endothelial damage, product of the chronic Hyperglucemia and Hyperinsulinism favors the development of endothelial dysfunction and oxidative stress.

• The endothelial dysfunction secondary to DM explains the progression of microvascular and macrovascular complications in this group of patients.
Coronary disfunction measured with PET

Abnormalities in Glucose metabolism

Endothelial dysfunction in DM

Treatment of Endothelial Dysfunción with Glimetal in Patients with DM2

- 16 patients recently diagnosed with DM2 were studied
- Two groups were randomly created, the first one recieved Glimepiride/Metformin (4mg/1000) and the second one recieved Metformin (1000 mg).
- A PET was performed before the treatment and a control PET was performed at the 10th week of treatment
Endothelial dependent
Vasodilation Index after 10 weeks of treatment with Glimetal

P < 0.001

Alexanderson et al. Arch Cardiol Mex. En Prensa
Changes in the Endothelial Dependent Vasodilation Index after 10 weeks with Metformin

PRE

POST

P = N.S.

Alexanderson et al. Arch Cardiol Mex. En Prensa
Comparison of the average EDVI before and after treatment in patients treated with Glimetal or Metformin

Glimetal P < 0.001
Metformina P= N.S.

Alexanderson et al. Arch Cardiol Mex. En Prensa
Prevalence of endothelial dysfunction before treatment in patients with DM2

- D.E.: 77%
- Sanos: 23%

Prevalence of endothelial Dysfunction after treatment with Glimet in patients with DM2

- 75%
- 25%
Associated factors

Coronary endothelial Dysfunction

- Dyslipidemia
- Diabetes mellitus
- **High Blood Pressure**
- Metabolic Syndrome
- Smoking
- Rheumatologic diseases

High Blood Pressure

• HBP is one of the biggest health issues in the world

• Approximately 1/3 of the Mexican population has High Blood Pressure
High Blood Pressure

• HBP causes a chronic increase of shear stress in the arterial wall

• This leads to an important decrease in NO release and a rise in the endothelial secretion of vasoconstrictor prostanoids and pro-inflammatory cytokines causing Endothelial dysfunction

• These factors accelerate the atheromatous plaque’s formation and growth

Shimokawa H; J Atheroscler Thromb; 1998; 4(3):118-127
Endothelial dysfunction in patients with systemic hypertension

Protocolo en estudio, Erick Alexánderson y cols.
Associated factors
Coronary endothelial Dysfunction

- Dyslipidemia
- Diabetes mellitus
- High Blood Pressure
- Smoking
- Metabolic Syndrome
- Rheumatologic diseases

Smoking

• Exposure to environmental tobacco smoke increases the risk of CAD and mortality in adults

• There is evidence that smoking increases platelet aggregation, acceleration of lipid peroxidation and inflammatory markers leading to Endothelial Dysfunction

• The ED is smoke-dose dependent

• Long term tobacco exposure causes ED in active and passive smokers even since childhood

Kallio K et al. Circulation; 2007; 115:3205-3212
Nagel G et al. Eur Heart J; 2009; 1885-1893
ED associated with Cotinine levels in 11 year-old passive smokers
Endothelial dysfunction associated with tobacco consumption

Czernin et al. Circulation 1995;91:2891
Associated factors

Coronary endothelial Dysfunction

- Dyslipidemia
- Diabetes mellitus
- High Blood Pressure
- Smoking
- Metabolic Syndrome
- Rheumatologic diseases

Metabolic Syndrome

- Overweight and obesity are associated with a progressively lower CFR

- BMI is associated with an impairment of total coronary vasodilatory reserve.

Motivala et al. JNC; 2008; 15(4):510-517
CFR and EDVI in patients with Metabolic Syndrome

N=6

Protocolo en estudio, Erick Alexánderson y cols
Associated factors
Coronary endothelial Dysfunction

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Rheumatologic Diseases

- Patients with rheumatologic diseases have accelerated atherosclerosis development due to a chronic inflammatory state

- SLE patients aged between 35 and 45 have a 50-fold increase in Myocardial infarction rate

- Subclinical atherosclerosis can be documented in up to 40% of SLE patients

- Endothelial function is impaired in rheumatologic diseases (SLE; APS)

Piper M et al; Lupus; 2007; 16:84-88
Fischer K; Pol Arch Med Wewn. 2009; 119 (11): 736-742
Anti-phospholipid syndrome

Figure 5. EDVI and MFR in PAPS patients and HVs. NS, Not significant.
Conclusions

• Endothelial dysfunction is an early marker of Coronary Artery disease

• Coronary risk factors predispose to Endothelial dysfunction even in asymptomatic patients

• PET is a good technique to diagnose and evaluate ED and its variations with treatment