

Relationship between serum glutathione peroxidase-1 activity with endothelial dysfunction level in patients with coronary artery diseases

Introduction

- Reactive oxygen species (ROS) ,such as superoxide and hydrogen peroxide, are generated in all cells by mitochondrial and enzymatic sources.
- These ROSs can cause oxidative damage to biomolecules such as .DNA , proteins and membrane lipids.

Introduction

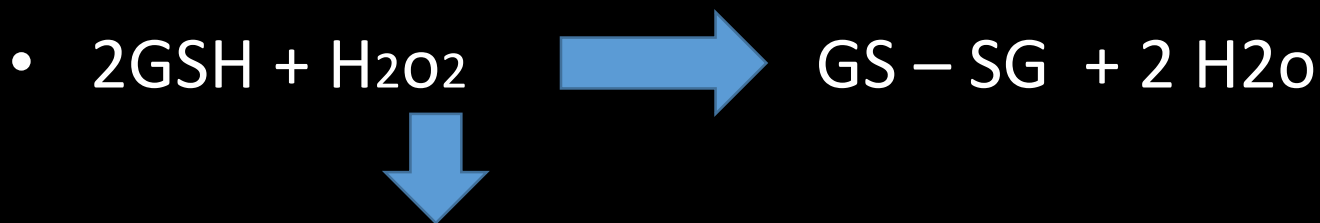
- Glutathione peroxidases (GPX s) are a large enzymatic family with peroxidase activity and several isoform in human body whose main biological role is to protect the organism from oxidative damage.
- Glutathione peroxidase isoenzymes are encoded by different genes, which vary in cellular location and substrate specificity.

Introduction

- Eight different isoforms of glutathione peroxidase (GPx 1 -8) have been identified in humans.
- Glutathione peroxidase -1 is the most abundant version, found in the cytoplasm of nearly all mammalian tissues, whose preferred substrate is hydrogen peroxide.

Introduction

- The main reaction that glutathione peroxidase catalyzes is:



Introduction

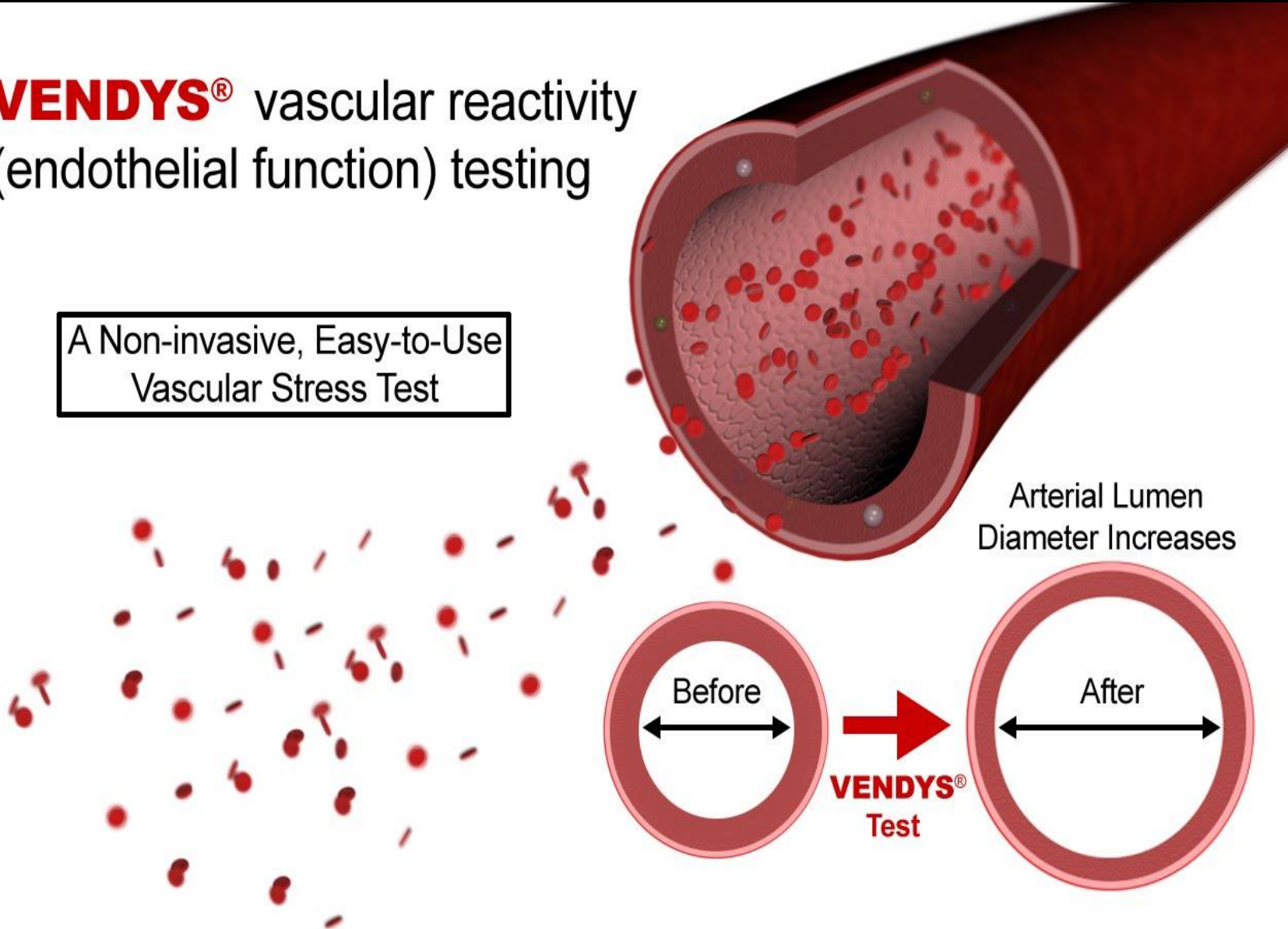
- It has been reported that peroxidase enzymes involved in pathogenesis of several diseases .
- According to peroxidase enzymes role, it is thought that peroxidase enzymes especially glutathione peroxidase-1 involved in atherosclerosis and cardiovascular diseases.

Introduction

- Endothelial dysfunction is a systemic pathological state of endothelium which can be defined as an imbalance between vasodilating and vasoconstricting substances produced by (or acting on) the endothelium.
- Endothelial dysfunction can result from and/or contribute to several disease processes, as occurs in hypertension, hypercholesterolemia, diabetes and septic shock disease.

VENDYS[®] vascular reactivity (endothelial function) testing

A Non-invasive, Easy-to-Use
Vascular Stress Test

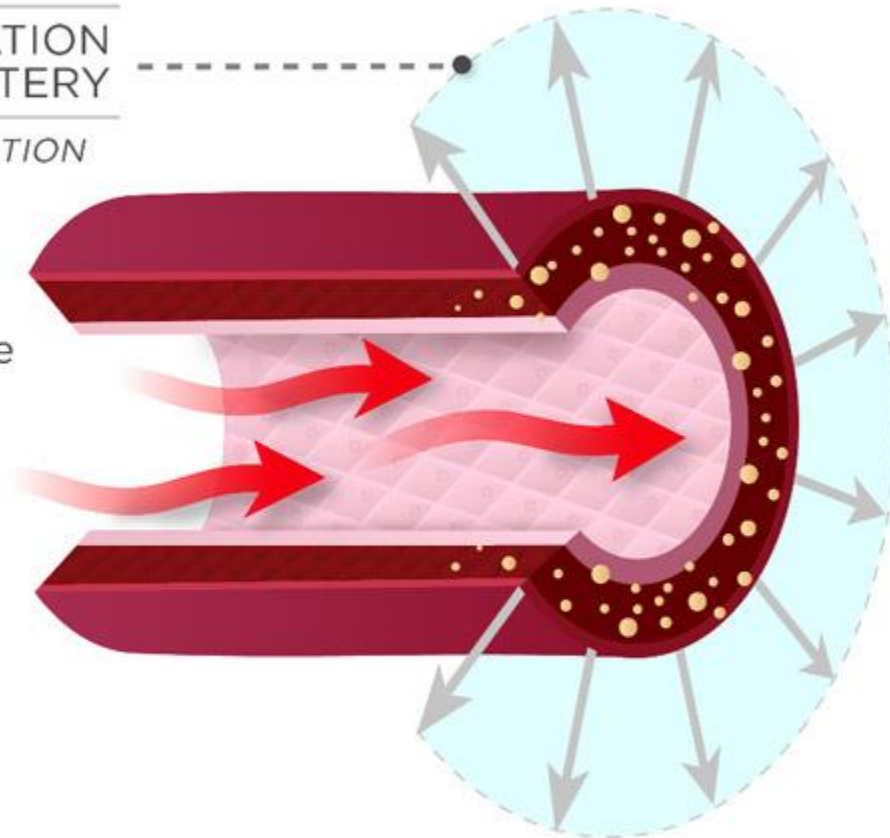


FLOW MEDIATED DILATION OF THE BRACHIAL ARTERY

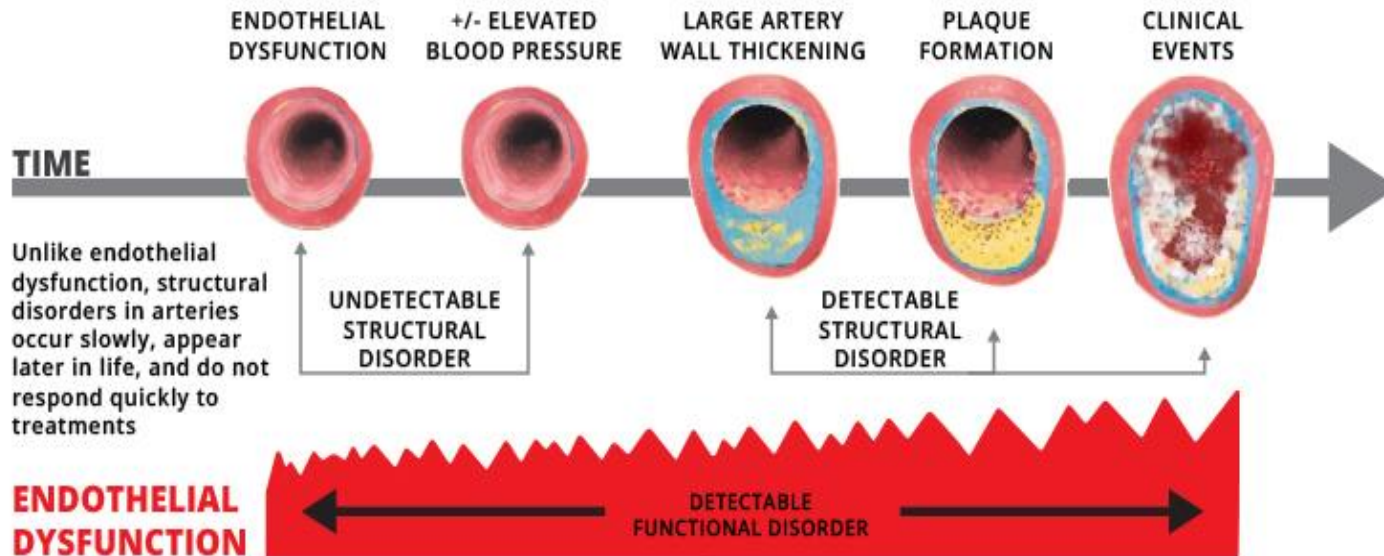
% FMD IS MEASURE OF DILATION

POST OCCLUSION...

- Increased blood flow rate
- Increased shear stress
- Endothelium releases **nitric oxide**
- Smooth muscle relaxes



NATURAL COURSE OF AETHEROSCLEROTIC CVD (HEART ATTACK, STROKE, PAD...)



Flow – mediated dilation (FMD)

- The gold standard for measuring endothelial function is angiography with acetylcholine injection.
- A noninvasive method to measure endothelial dysfunction is % Flow Mediated Dilation (FMD) as measured by Brachial Artery Ultrasound Imaging (BAUI).

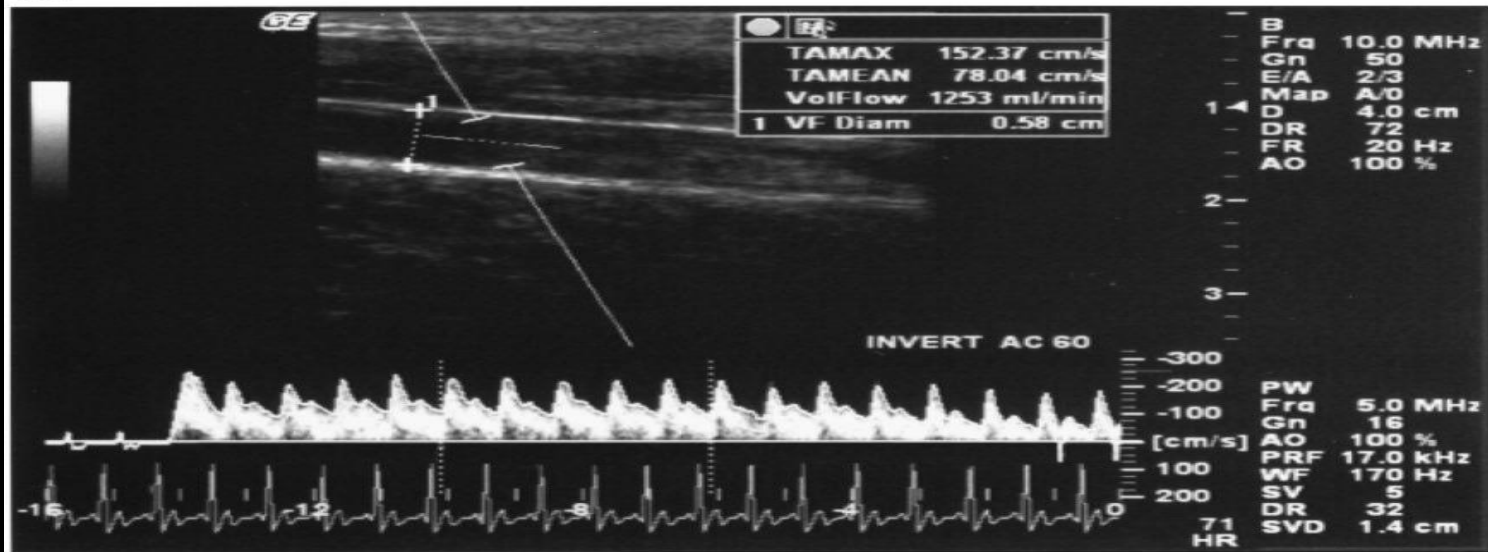
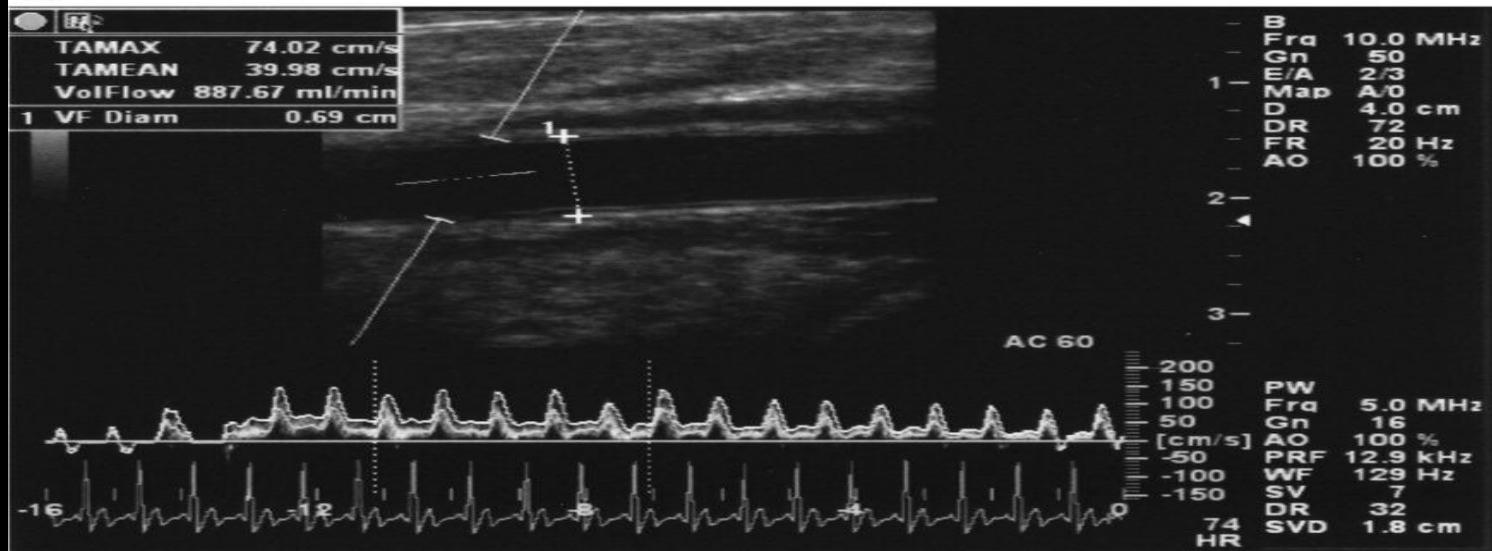
Measurement of Endothelial Dysfunction for Detection of Vulnerable Plaque and the Vulnerable Patient



Morteza Naghavi, MD

AHA – 2003

Orlando, FL

A**B**

Endothelial dysfunction

- Endothelial dysfunction can result from and/or contribute to several disease processes, as occurs in hypertension , hypercholesterolemia , diabetes and ,septic shock disease

Endothelial dysfunction

- IT can also result from environmental factors, such as from:
 - Smoking tobacco products
 - Exposure to air pollution
- E.D is more prevalent in shift workers

Methods

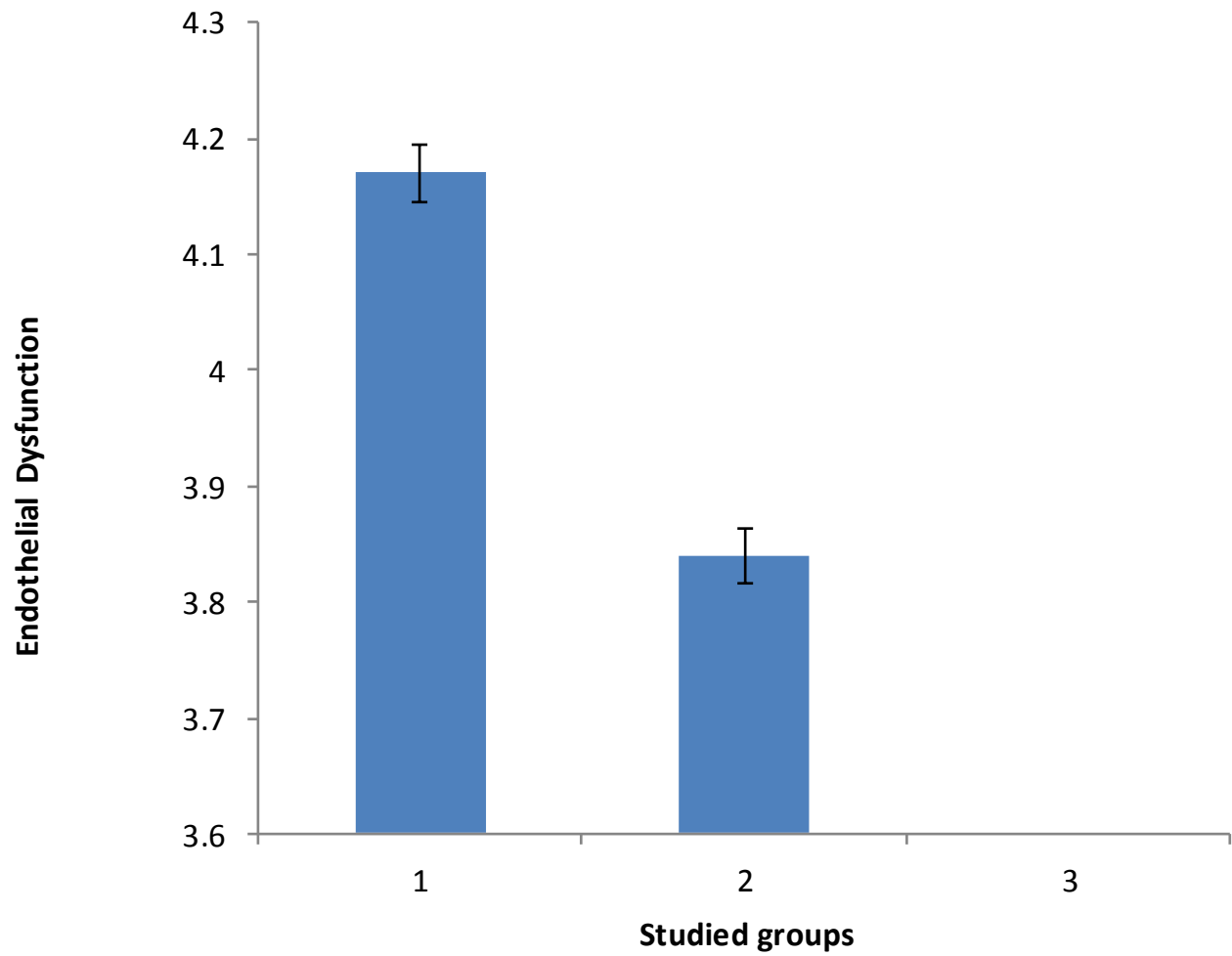
- By using Bio Vision 'Glutathione Peroxidase Assay Kit
- GPx reduce Cumene hydroperoxide, and oxidize GSH to GSSG.
- GSSG is reduced to GSH with consumption of NADPH.
- Decrease of NADPH is proportionally to GPx activity.
- The decrease of NADPH can be measured by absorbance at 340 nm.

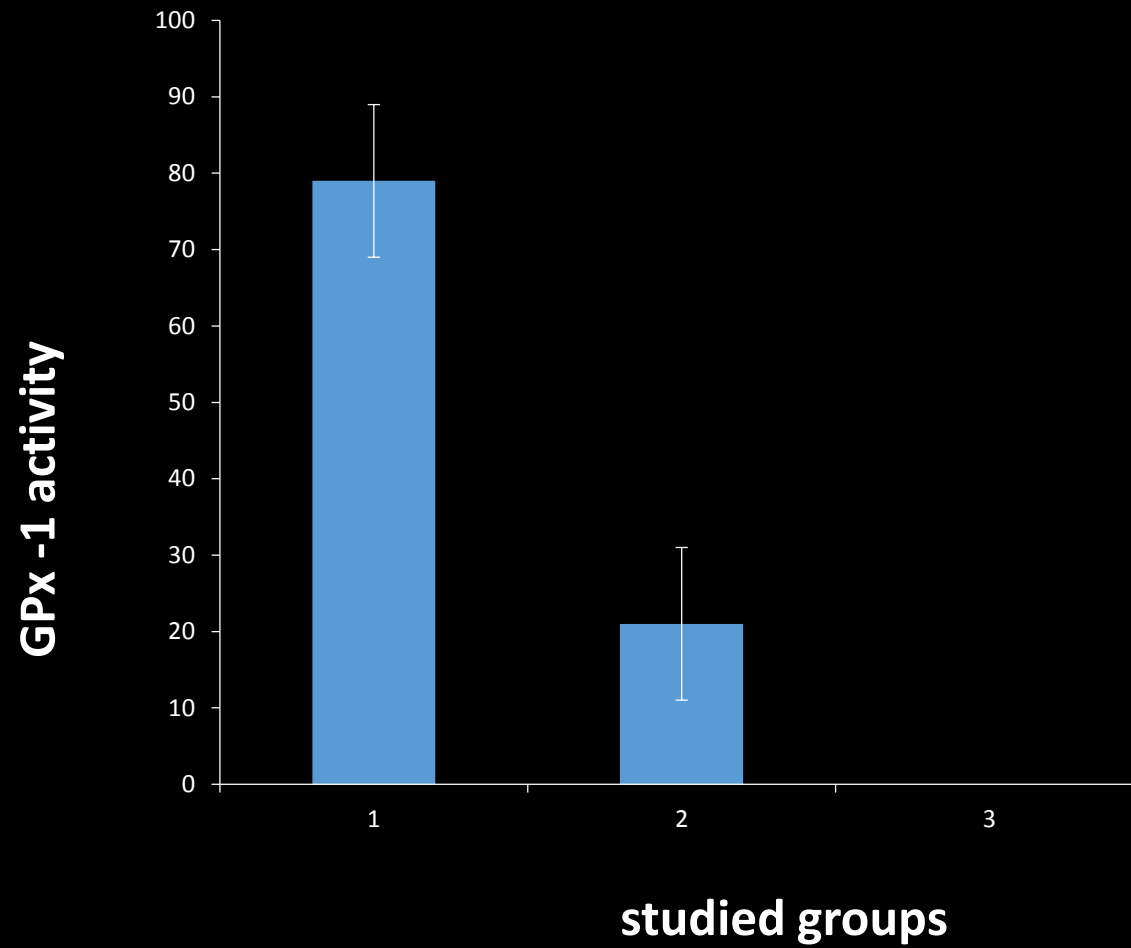


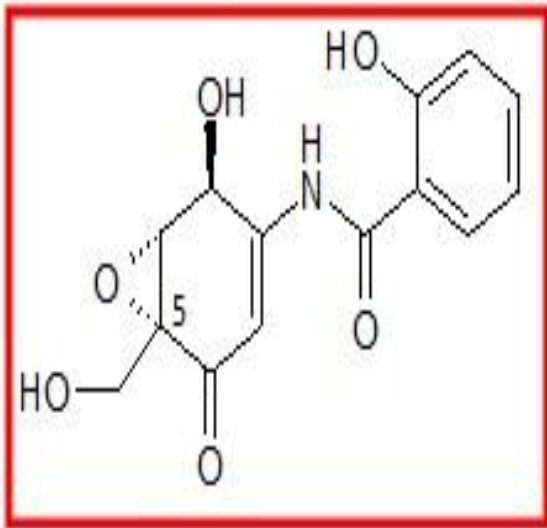
Blood collection

- Whole blood samples were collected in tubes from a peripheral vein using sterile soring and serum was isolated after proper time. Aliquots of serum were stored at -80°C for determination of GPx activity

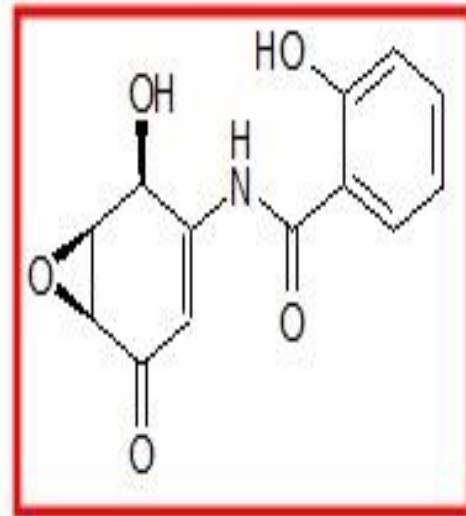
parameters	Group normal	Group coronary artery disease	p value
Age (years)	34.24±10.55	44.21±11.06	<0.001
SBP (mm Hg)	106.89±9.62	123.92±13.43	<0.001
DBP (mm Hg)	68.66±6.94	77.76±9.56	<0.001
Triglycerides, mmol/l	113.71±32.29	208.47±69.29	<0.001
Total cholesterol, mmol/l	176.03±40.32	208.58±41.47	<0.001
HDL-C, mmol/l	44.89±7.51	38.45±6.36	<0.001
LDL-C, mmol/l	89.24±23.92	97.82±22.51	<0.001
GPX, U/ml	79±38.6	21.7±13.5	0.001
ET-1(pg/ml)	71.44±132.82	145.73±223.03	0.008
FMD (%)	4.17±0.69	3.84±0.55	0.024





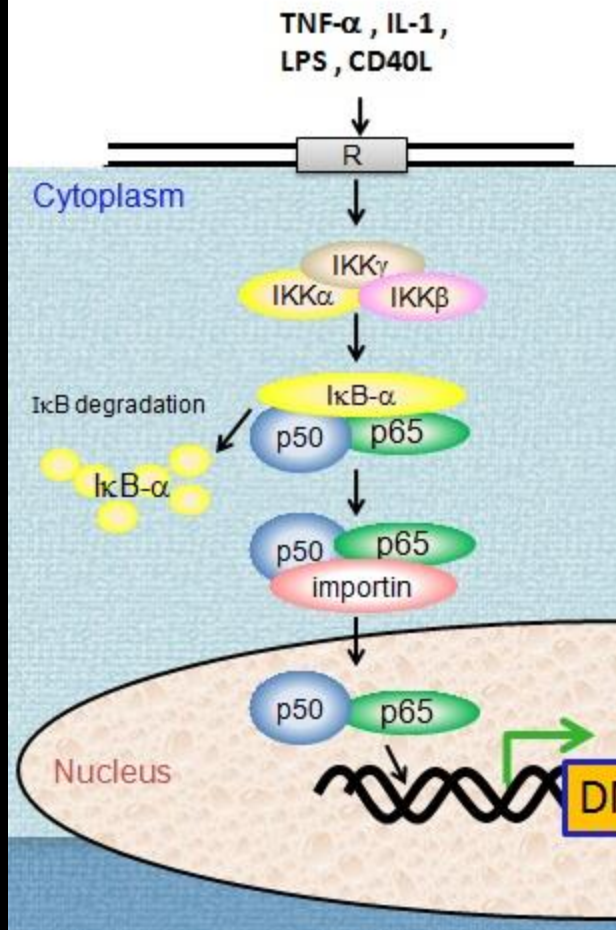


epoxyquinomicin C

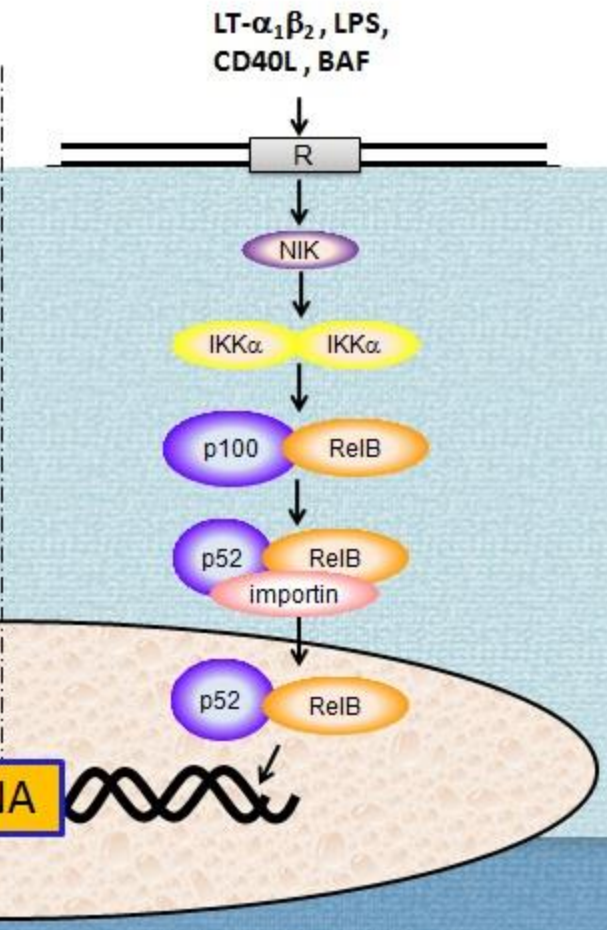


(-)-DHMEQ

canonical pathway



noncanonical pathway



Discussion

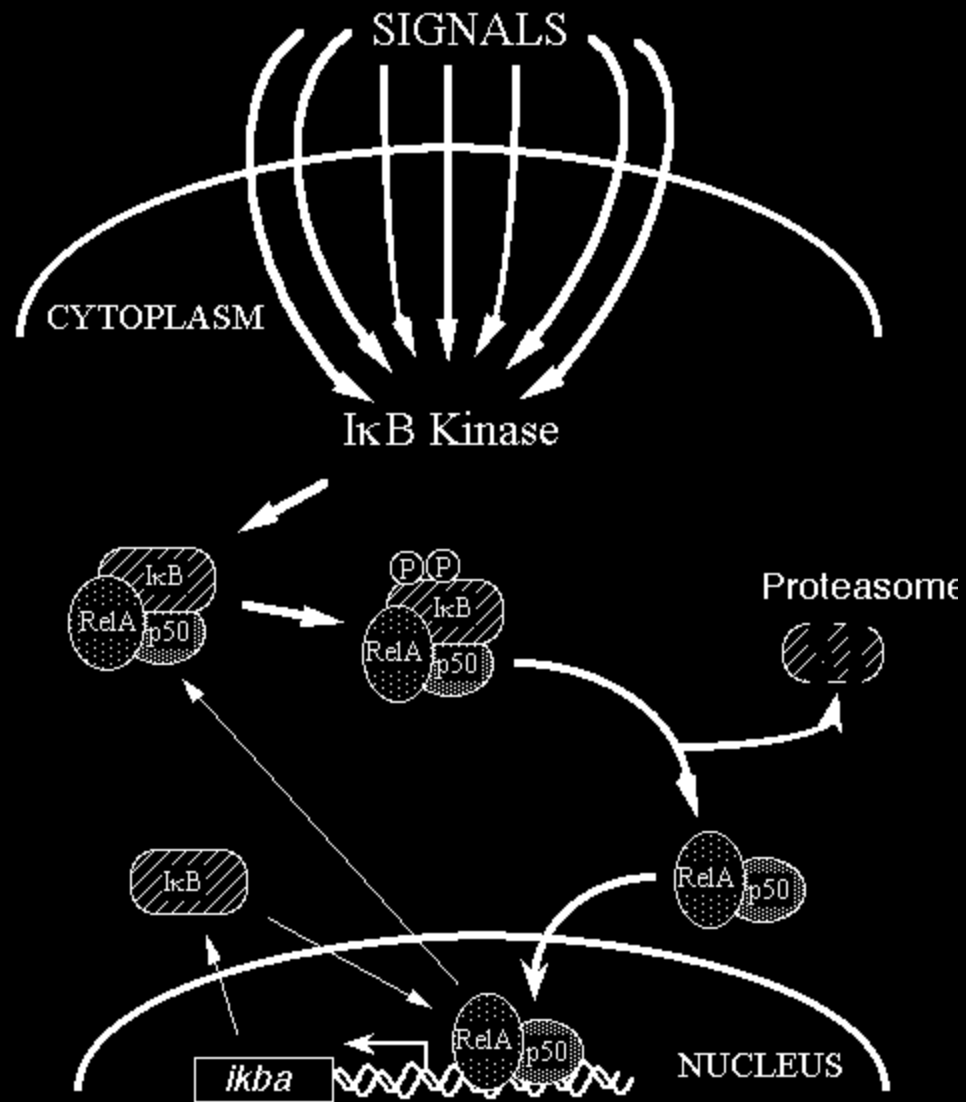
- 1- In coronary artery diseases, NO production decreased. (NO produces vasodilation).
- 2 - Shear stress is increased (if the shear stress is chronically induced)
- 3 - It leads to the upregulation of and release of inflammatory cytokines.
- 4 - LDL oxidation is increased.
- 5 - Smooth muscle cell proliferation

Continue

- 6 - Leukocyte adhesion and infiltration into the vessel.
- 7 Development atherosclerosis.

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Discussion

- To the best of our knowledge ,this is the first study in examine the relationship between serum GPx -1 activity levels and the endothelial dysfunction in patients with coronary artery diseases.

Discussion

Data presented in this study showed that serum GPx-1 activity in patients with CAD was significantly lower than healthy subjects.

Also

Endothelial dysfunction levels in patients with CAD was significantly lower than healthy subjects.

These observations are consistent with the results reported by Blankenberg et al. and others.

Conclusion

- Our data analysis showed a direct relationship between E.D and serum GPx-1 in patients with CAD.
- If we can find a relationship between E.D levels and levels of occultation in coronary artery can help me to diagnosis patients with CAD by an invasive technique including FMD technique.





