TURIN, 20TH—21ST NOVEMBER 2008

GREAT INNOVATIONS IN CARDIOLOGY

4TH JOINT MEETING WITH MAYO CLINIC

4TH TURIN CARDIOVASCLAR NURSING CONVENTION

SESSION III: **HOT SESSION**
NEW THERAPIES AND NEW TREATMENTS

A. Lind (Essen—Germany)

Part II New Treatment Option for Endstage CAD Patients by Extracorporeal Shockwave Myocardial Revascularization Therapy (ESMR)

New Treatment Option for Endstage CAD Patients by Extracorporeal Shockwave Myocardial Revascularization Therapy (ESMR)

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Mechanism of the Cardiac Shock Wave Therapy

- **Vasodilation** - Shockwaves acutely reduces arterial perfusion pressure on artificially perfused rabbit kidneys with immediate increase in blood flow around the treated area
- **Shear stress** - Shockwave exert a "cavitation effect" (inside and outside of cells) inducing localized stress on cell membranes that resembles shear stress.
- **NO synthesis** - Shockwave cause nonenzymatic nitric oxide synthesis from L -arginine and hydrogen peroxide
- **VEGF and flt-1 upregulation** - SW upregulates VEGF and its receptor, Flt-1, in endothelial cells in vitro and VEGF in the ischemic myocardium in vivo.
- **Neovascularization** - SW therapy induces neovascularization at tendon via upregulation of endothelial nitric oxide synthesis, VEGF, and proliferating cell antigen.
- **Local perfusion** - Myocardial perfusion in the ischemic myocardium was improved only where the SW's were applied.

Preclinical Studies

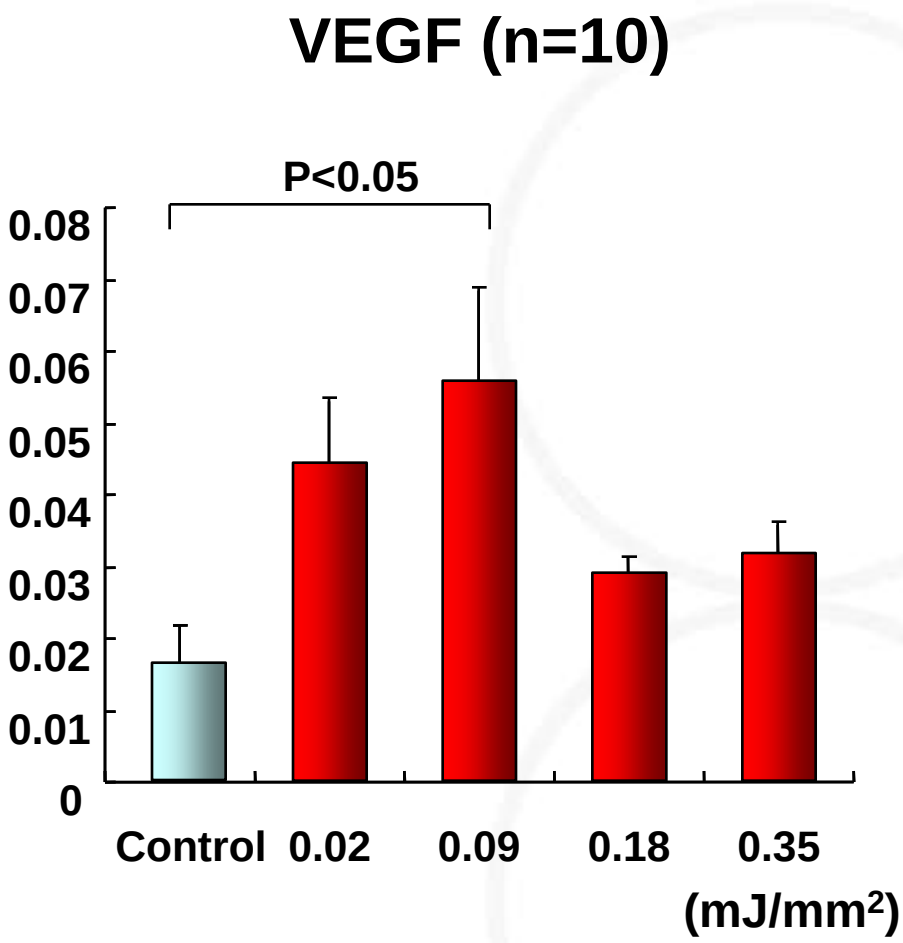
Extracorporeal Cardiac Shock Wave Therapy Markedly Ameliorates Ischemia–Induced Myocardial Dysfunction in Pigs in Vivo

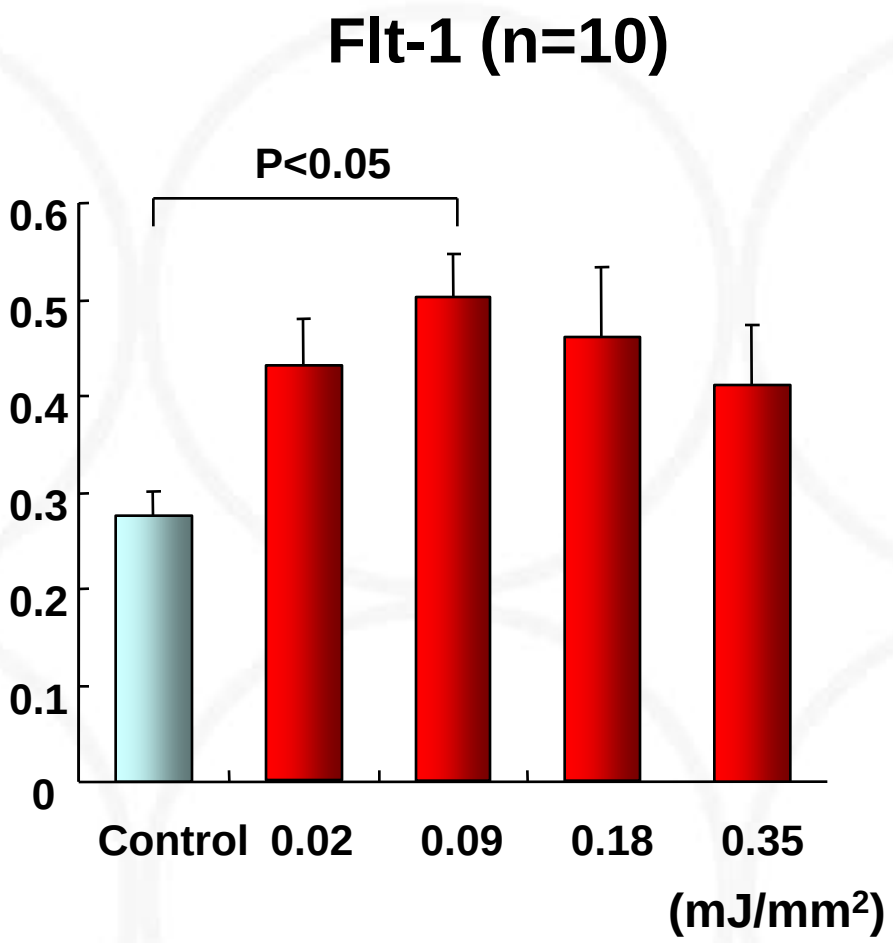
Nishida T, Shimokawa H et al.

Department of Cardiovascular Surgery, Cardiovascular Medicine, Kyushu University, Fukuoka, Japan

Circulation. 2004;110:3055-3061

SW Therapy Up-regulates mRNA Expression of VEGF and Flt-1 in HUVEC in Vitro (/GAPDH)





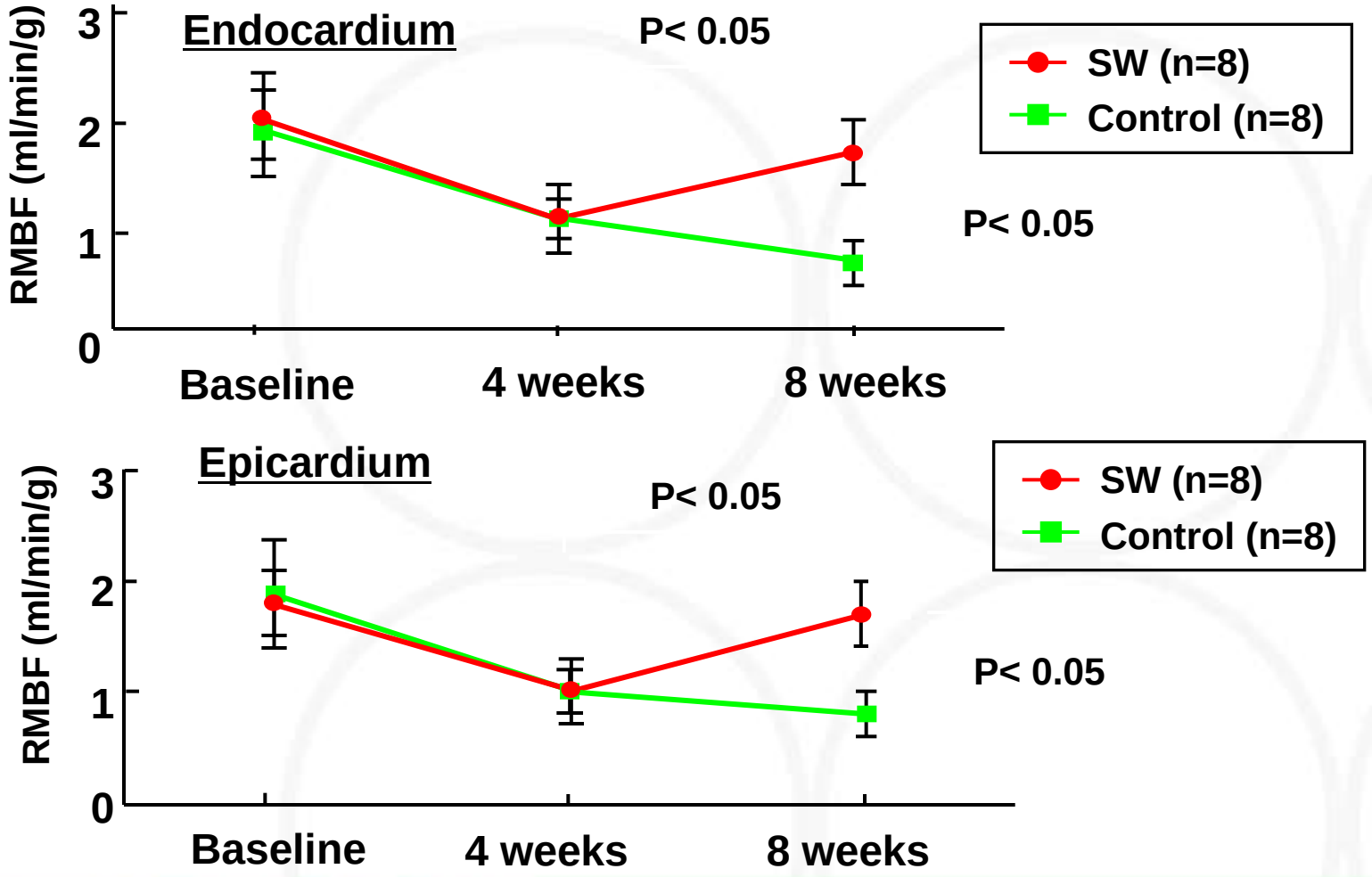
(Nishida, Shimokawa et al. Circulation. 2004.)

Study Design

- Animal:
  - Male pigs (n=16, 30-35 kg)
- Study Groups:
  - Group SW (n=8); SW treatment
  - Group Control (n=8); No treatment
- Chronic myocardial ischemia model:
  - Ameroid constrictor placed around the LCx

(Nishida, Shimokawa et al. Circulation. 2004.)

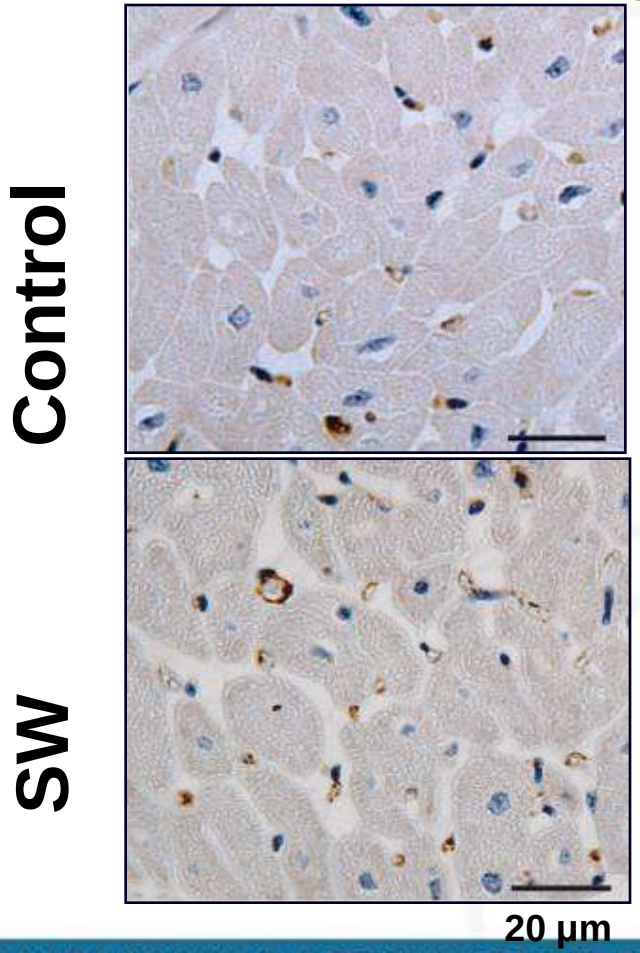
Improvement of Regional Myocardial Blood Flow (microspheres)



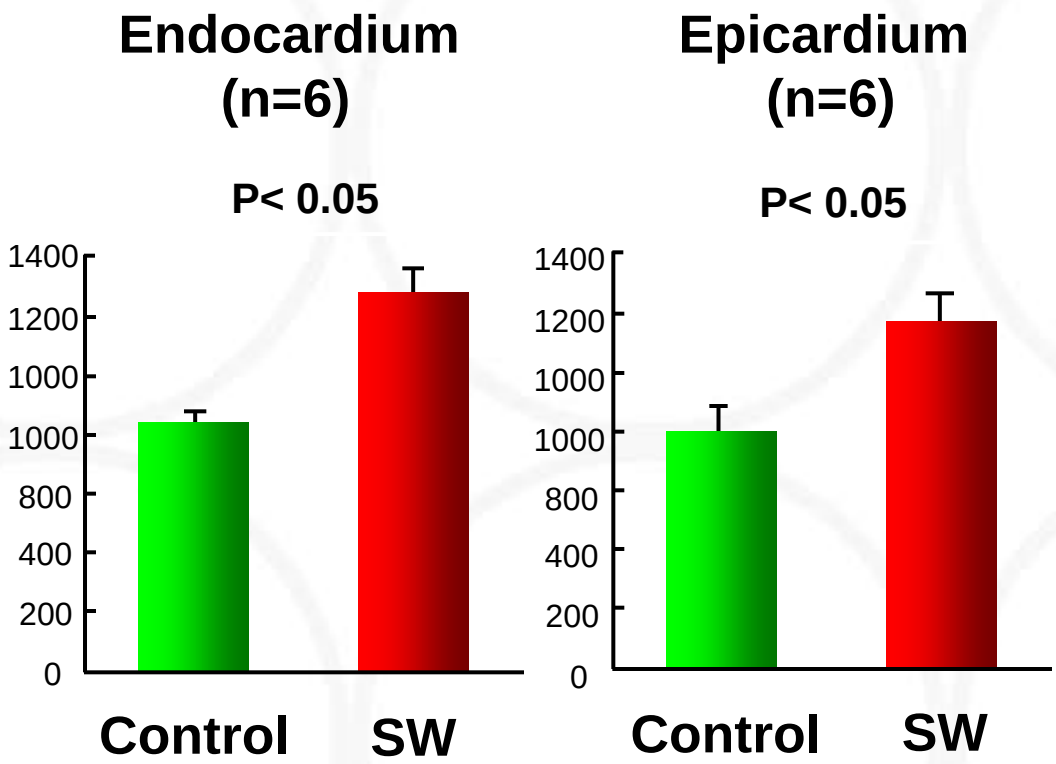
(Nishida, Shimokawa et al. Circulation. 2004.)

Increase in the Number of Capillaries

Factor VIII staining



Number of capillaries (/mm²)



(Nishida, Shimokawa et al. Circulation. 2004.)

ESMR Study

NI-CATh – Non-Invasive Cardiac Angiogenesis Therapy for myocardial ischemia in patients with refractory angina pectoris

CK Naber, A Lind, T Ebralidze, A Gutersohn, R Erbel

Essen University Hospital, Department of Cardiology

Inclusion Criteria

- Patient has documented myocardial segments with reversible ischemia or hybernation.
- Patient is classified as AP CCS of III or IV.
- Patients where angioplasty and bypass are not indicated because of anatomical or procedural reasons or frequent reocclusion / restenosis following traditional revascularization.
- Patient's condition should be stable and should have a life expectancy of >12 months.

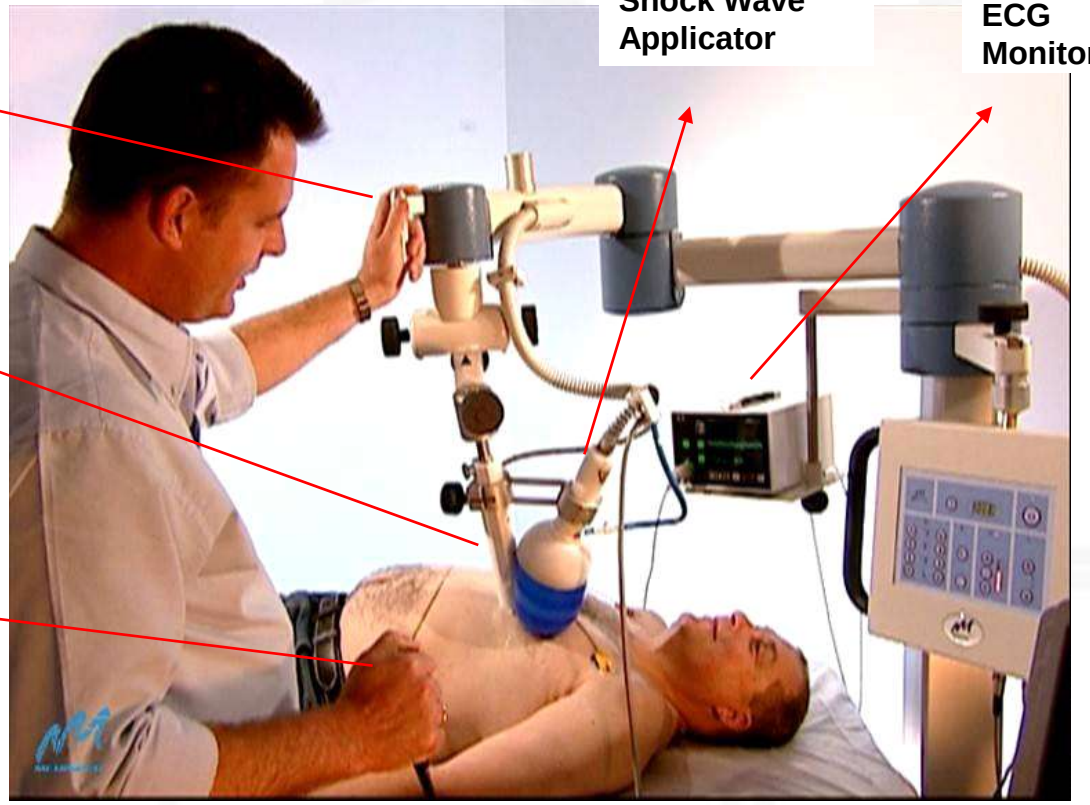
Exclusion Criteria

- Severe COPD
- MI less than 3 months prior to treatment
- Severe Valvular disease
- Intraventricular thrombus
- Pregnancy
- Patient with a malignancy

Patients' Demographics

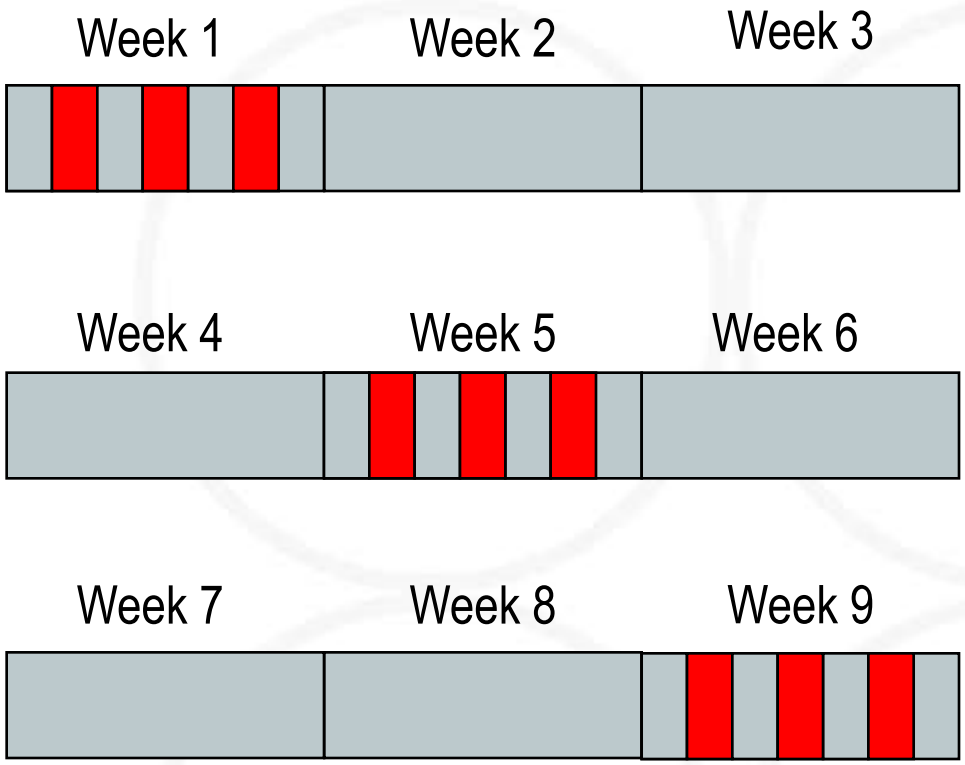
Male/Female	19/6	Beta Blocker	25 (100%)
Age	63.8±8	Statin	25 (100%)
BMI	29.9±4	ACE Inhibitor	19 (76%)
3 vessel disease	22 (88%)	Clopidorel	7 (28%)
CABG	19 (76%)	Aspirin	25 (100%)
Previous MI	5 (20%)	Nitrates	8 (32%)
Diabetes	6 (24%)		
Previous Smoking	8 (32%)		
Hyperlipoproteinemia	25 (100%)		
Hypertension	25 (100%)		

Methods: Shock Wave Application



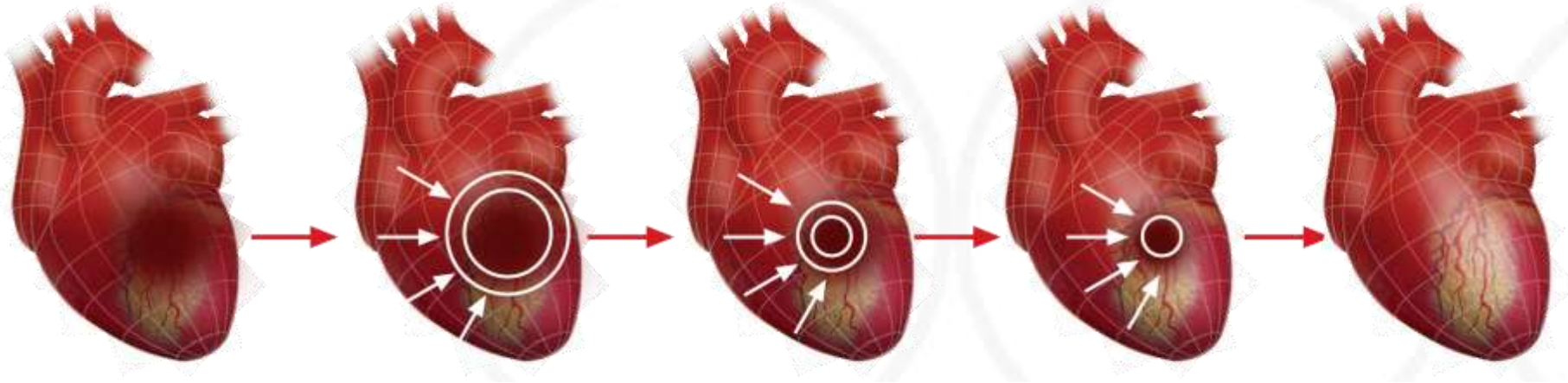
Energy Level: 0.09 mJ/mm^2; 500 shocks per treatment

Methods: Treatment Protocol



3 treatments / week at 5 zones, 100 shocks / zone

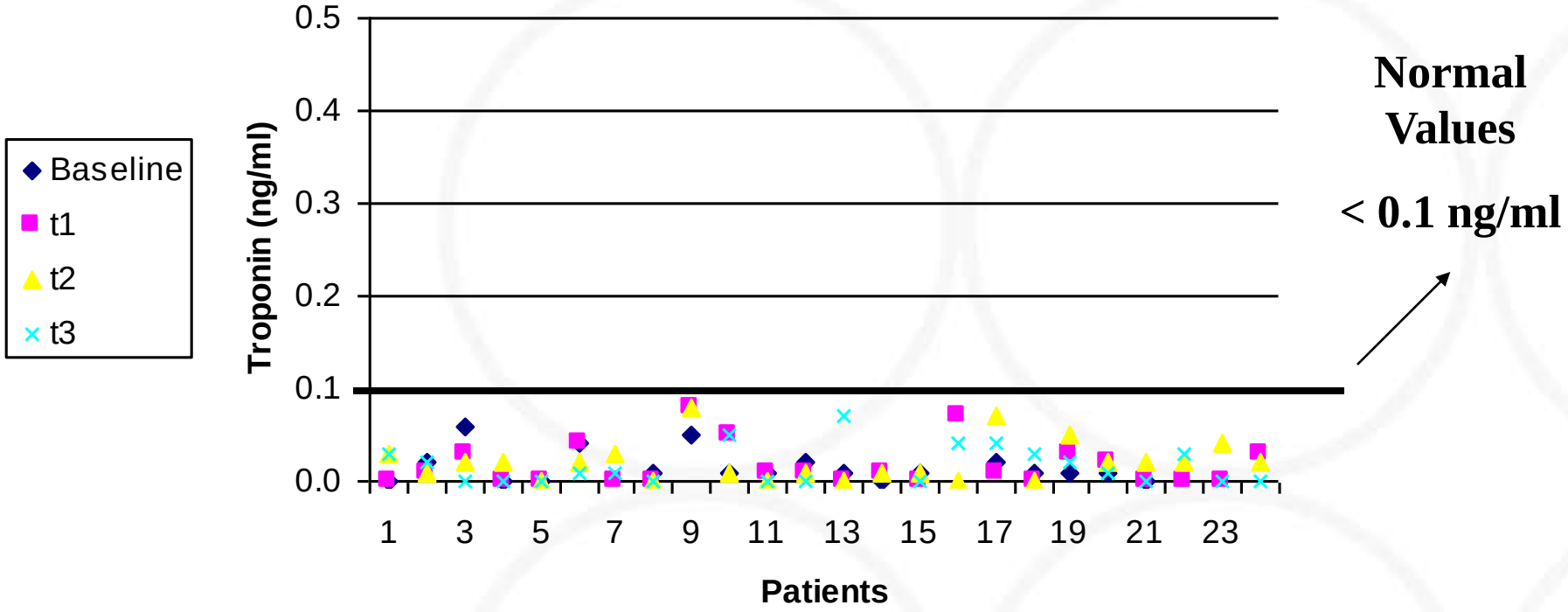
Methods: Treatment Strategy



3 treatments / week at 5 ischemic zones, 100 shocks / zone

Energy Level: 0.09 mJ/mm^2; 500 shocks per treatment

Safety – Troponin I levels

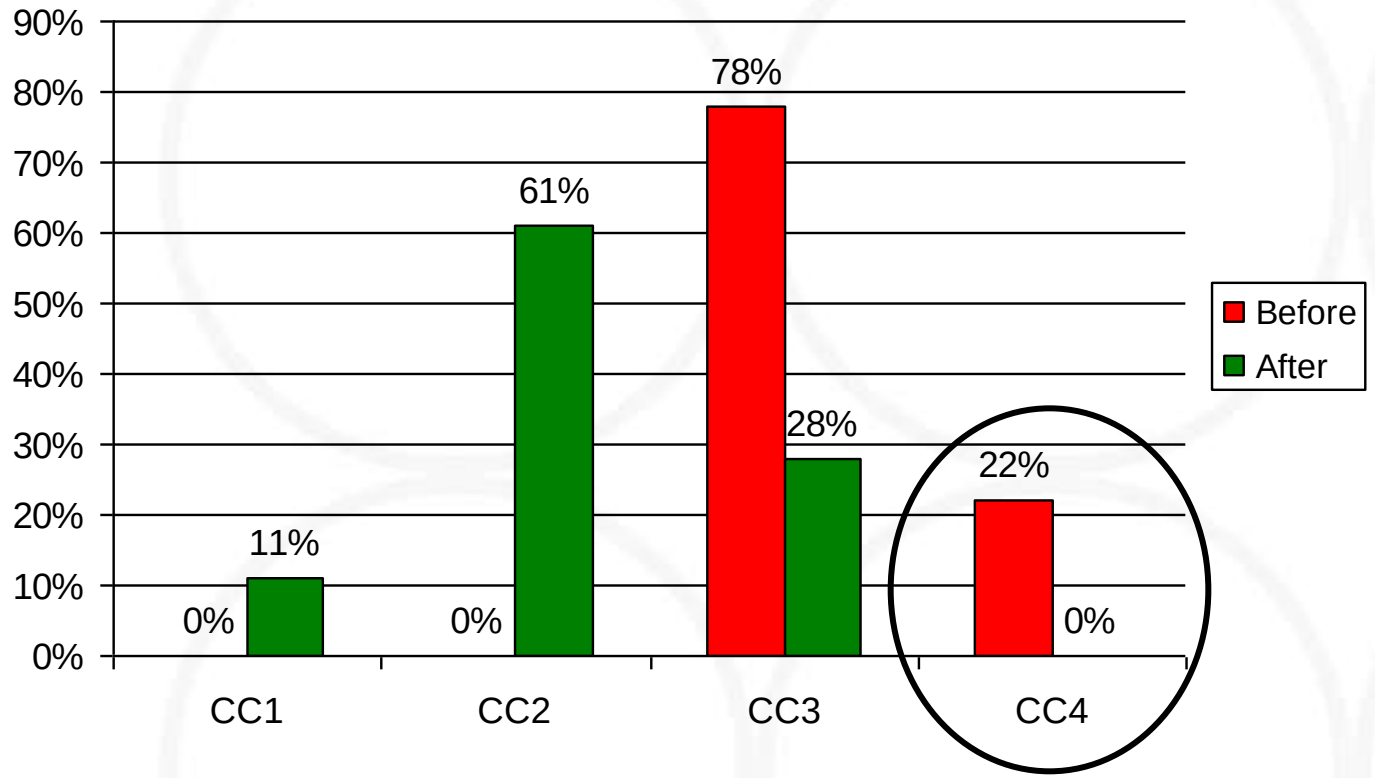


	Baseline	t1	t2	t3
Troponin I	0.015	0.017	0.020	0.016
SD	0.017	0.023	0.021	0.020

N = 25

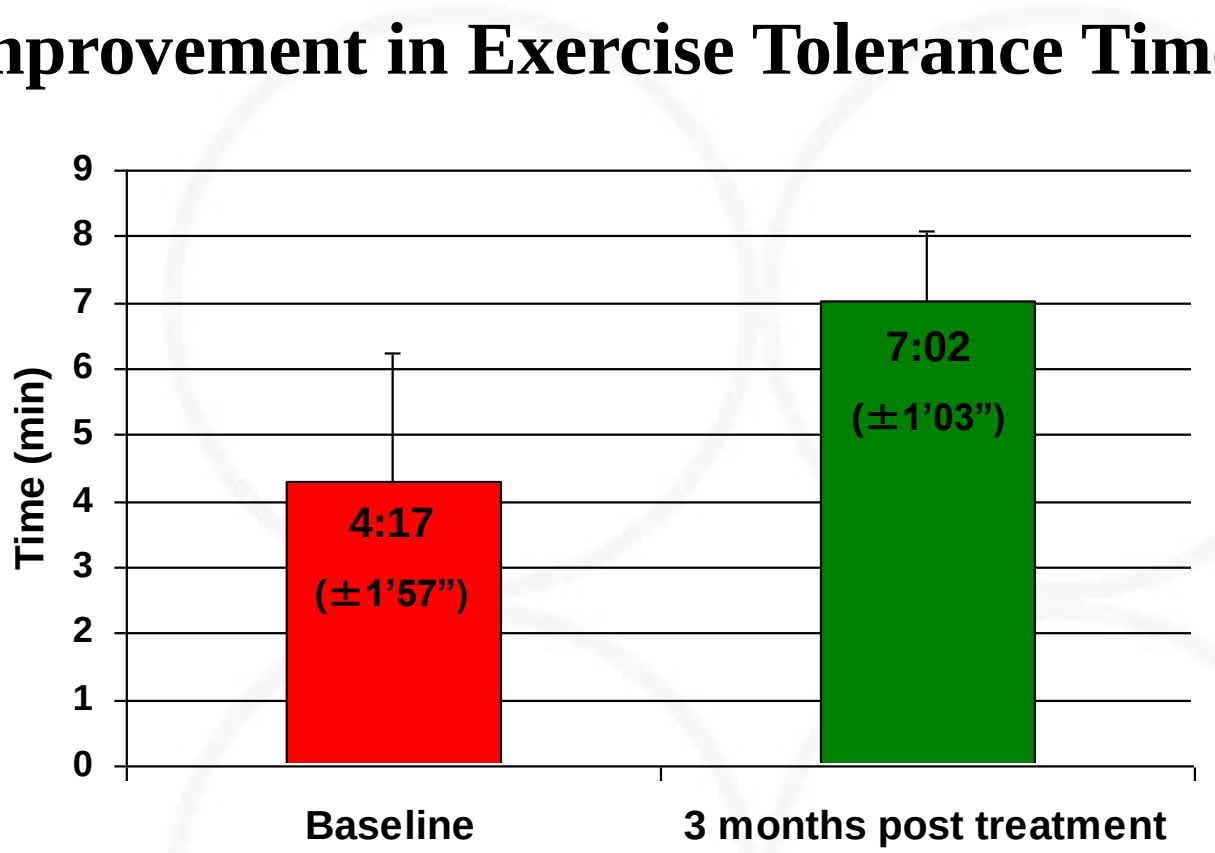
Results (3 months FU): CCS Class

No patient remained at CCS class IV



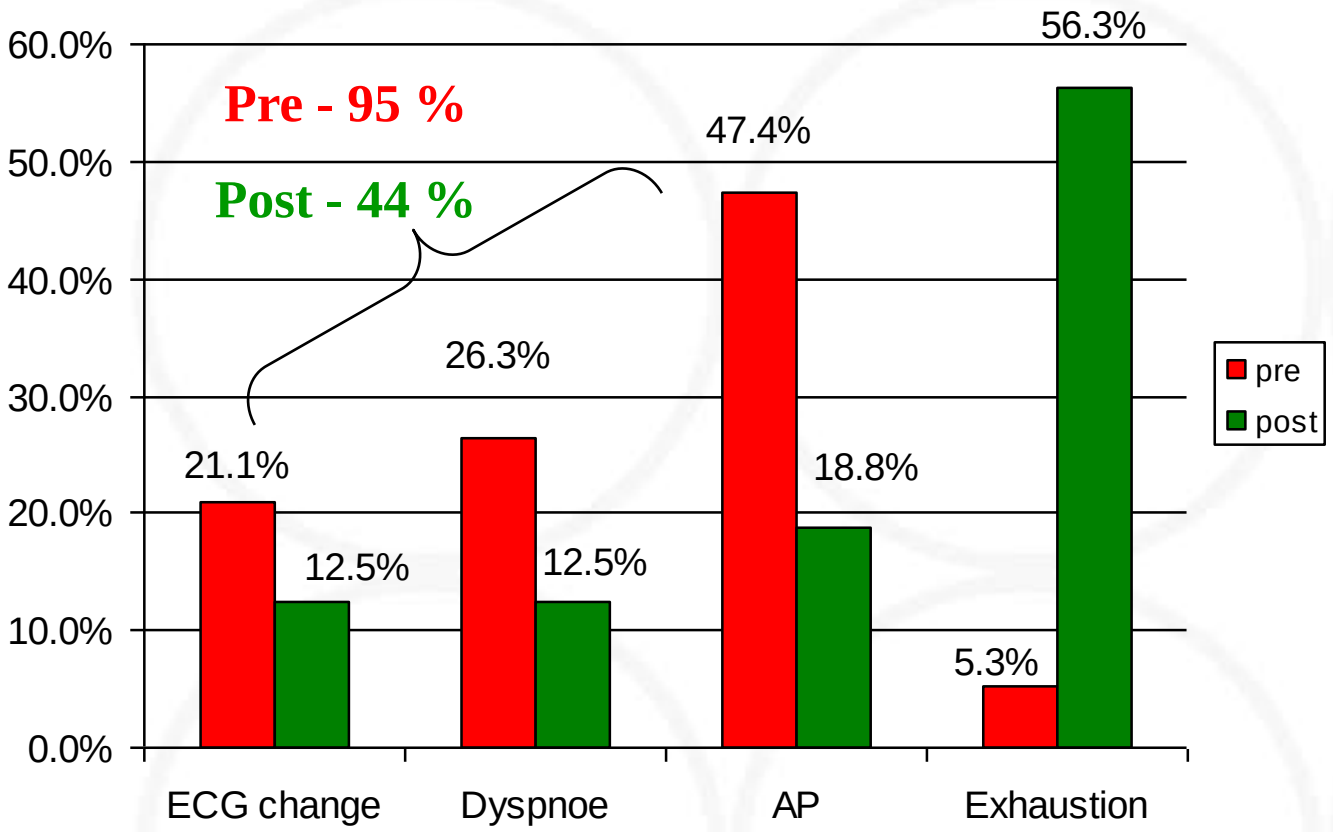
P<0.05; n=25

Results (3 months FU): Exercise Time



P<0.05; n=25

Results (3 months FU):
Termination of Exercise Test



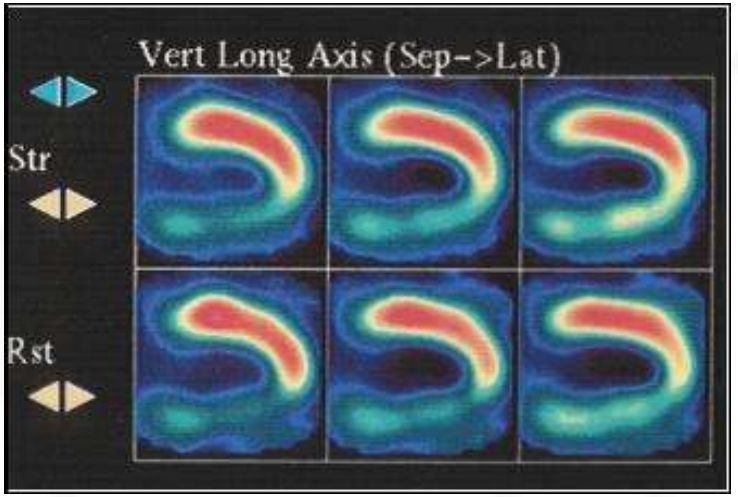
P<0.05; n=25

Results (3 months FU): SPECT Results

- **GHJ, 50, male**
- **3 vessels Disease**
- **Hypertension**
- **CABG**
- **PTCA**

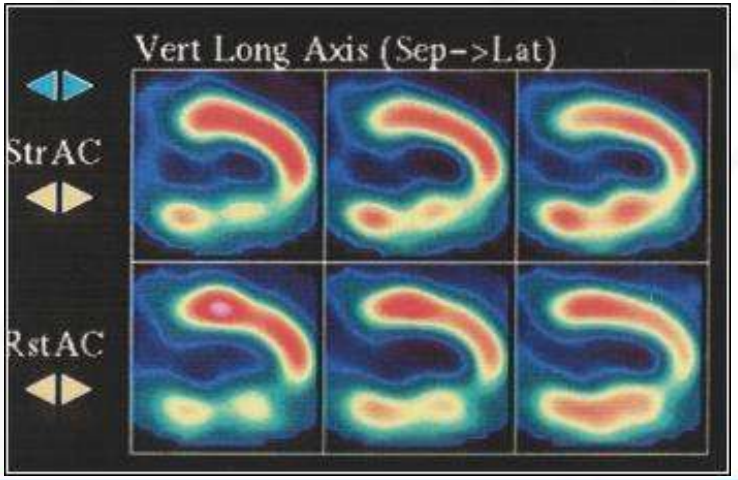
Pre

CCS class III
100 w



Post

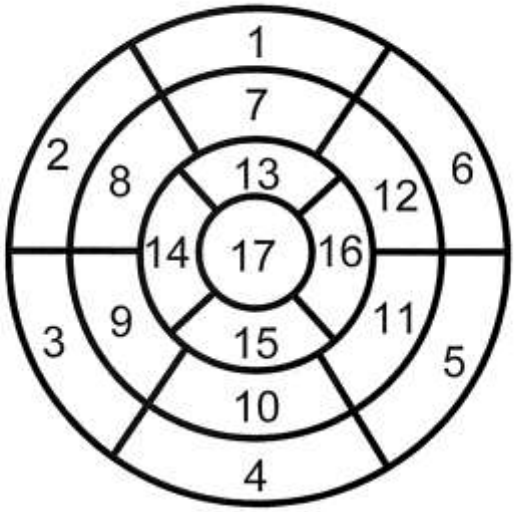
CCS class III
125 w



Blinded SPECT analysis

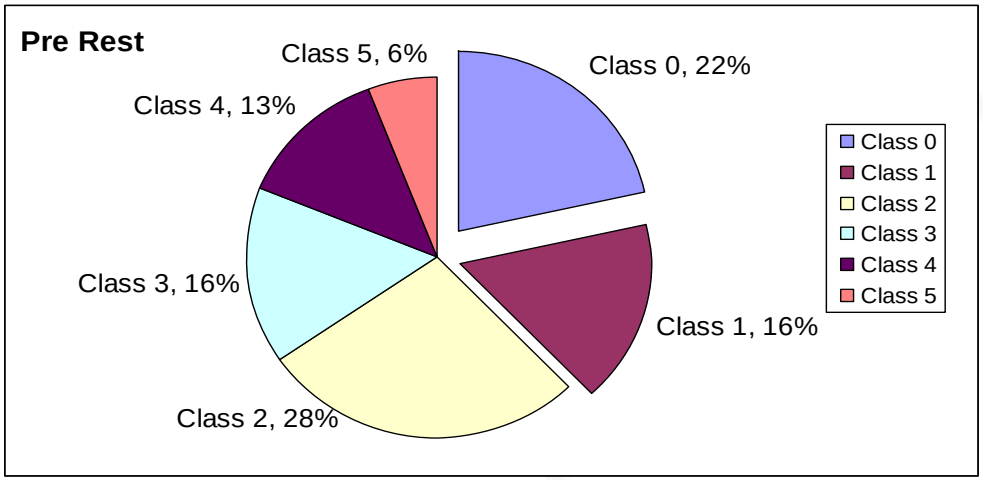
- SPECT study performed during Rest and Stress pre and post treatment (4 studies per patient)
- 17 segments model
- 0-5 grading for perfusion for each segment at Rest and at Stress
  - Class 0 : normal perfusion
  - Class 5 : no perfusion
- Blinded analysis. Observer was not aware of study date

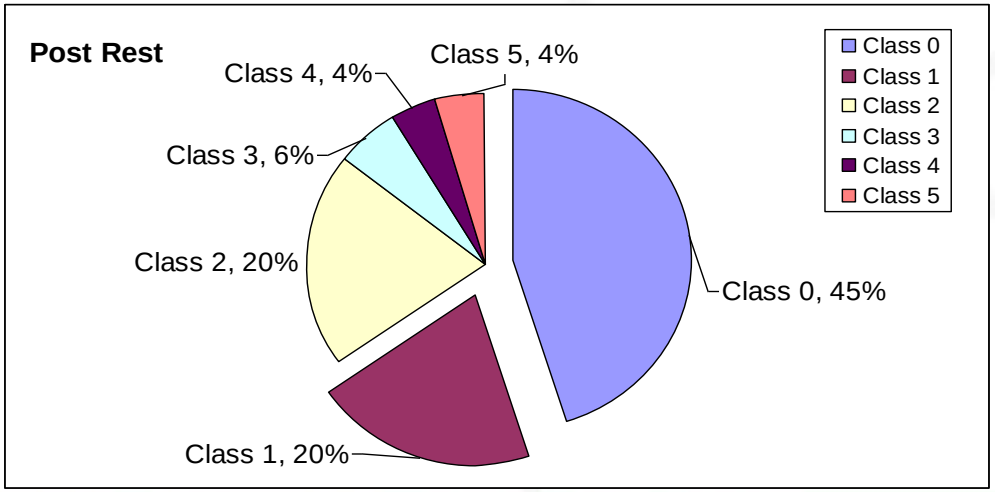
Left Ventricular Segmentation



1. basal anterior
2. basal anteroseptal
3. basal inferoseptal
4. basal inferior
5. basal inferolateral
6. basal anterolateral
7. mid anterior
8. mid anteroseptal
9. mid inferoseptal
10. mid inferior
11. mid inferolateral
12. mid anterolateral
13. apical anterior
14. apical septal
15. apical inferior
16. apical lateral
17. apex

Results (3 months FU): SPECT at Rest





38% 65%

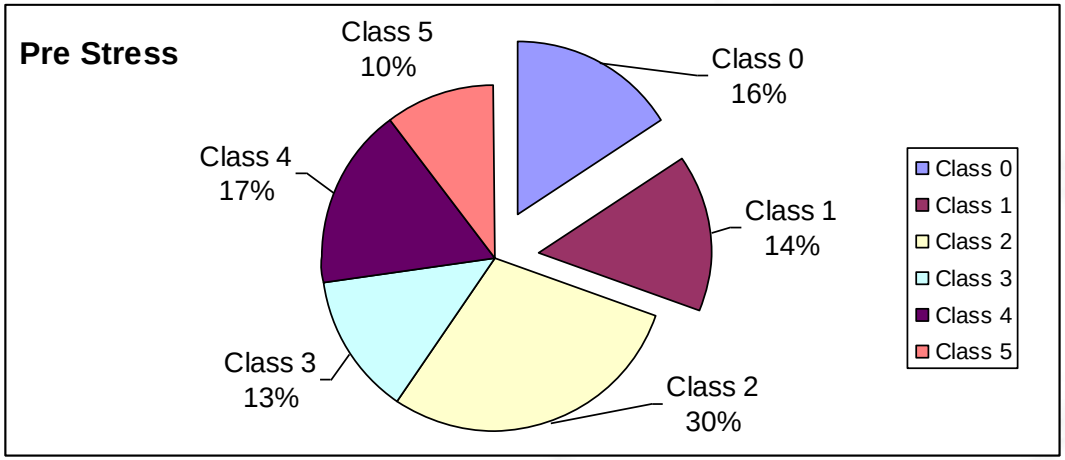
Class	Pre Rest	Post Rest	Change
Class 0	22%	45%	107%
Class 1	16%	20%	27%
Class 2	28%	20%	-26%
Class 3	16%	6%	-64%
Class 4	13%	4%	-67%
Class 5	6%	4%	-25%

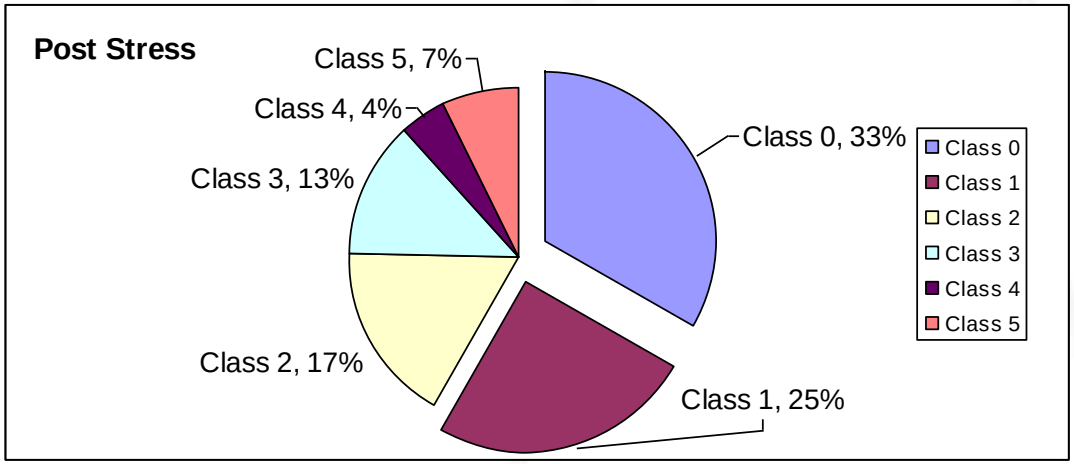
19% 8%

Pre → Post

P<0.05

Results (3 months FU): SPECT – Stress





30% 58%

Class	Pre Stress	Post Stress	Change
Class 0	16%	33%	109%
Class 1	14%	25%	70%
Class 2	29%	17%	-40%
Class 3	13%	13%	0%
Class 4	17%	4%	-75%
Class 5	10%	7%	-29%

27% 11%

Pre → Post

P<0.05

ESMR – Conclusions

Myocardial low-energy shockwave therapy is feasible and safe

In patients with severe coronary artery disease, refractory angia pectoris, and documented myocardial segments with reversible ischemia it can improve:

- Symptoms at rest and during exercise
- Myocardial perfusion shown by SPECT
- Quality of life shown by SAQ

WESTDEUTSCHES HERZZENTRUM ESSEN
KLINIK FÜR KARDIOLOGIE