SHOCKWAVE THERAPY FOR REFRACTORY ANGINA PECTORIS

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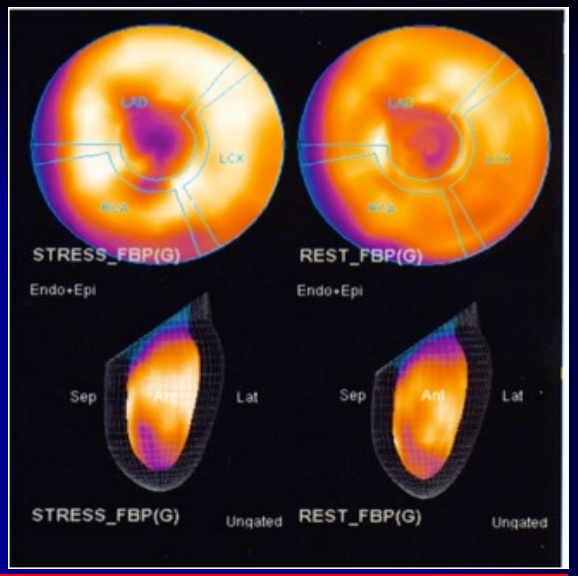
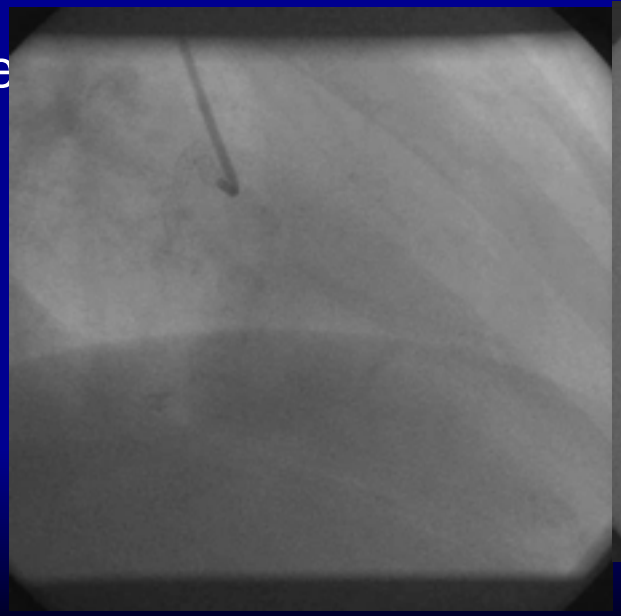
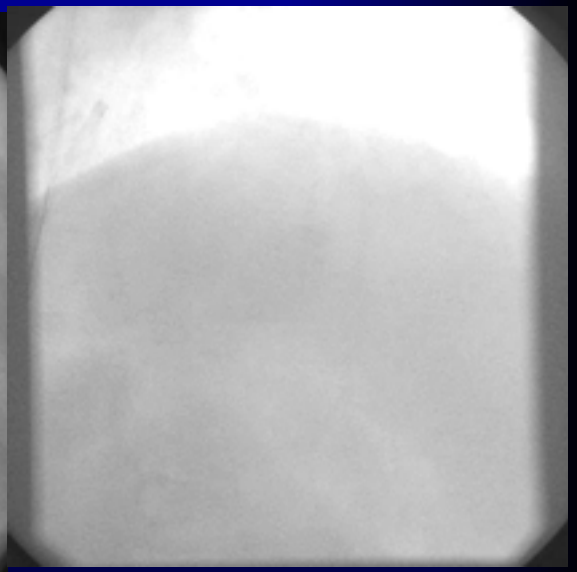
Ischemic area by SPECT



- O.C.83, Female
- Hypertension
- Previous MI stenting CX
- PCI or CABG not applicable
- CCS class III

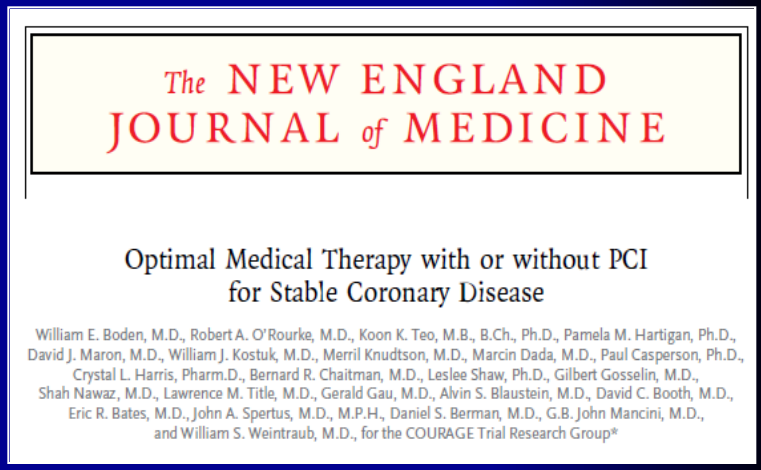
WHAT STRATEGY FOR THIS PATIENT?





Background

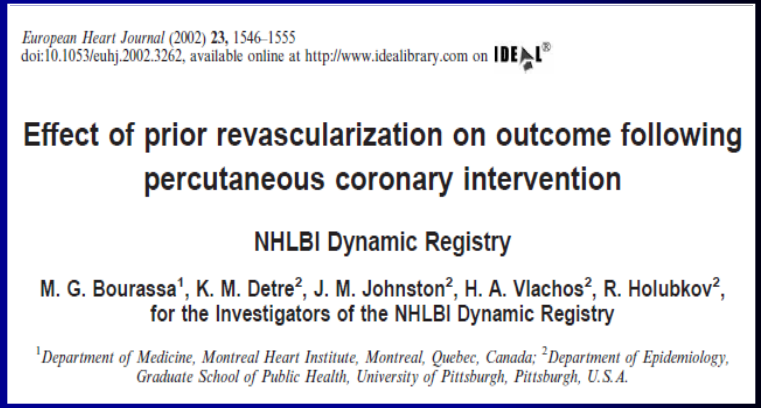
- The prevalence of patients with refractory angina not amenable to CABG or PCI is growing worldwide.
- The incidence is 30.000 – 50.000 new patients/year in Europe
- Therapeutic options for such patients are limited and invasive.



The NEW ENGLAND JOURNAL of MEDICINE

Optimal Medical Therapy with or without PCI for Stable Coronary Disease

William E. Boden, M.D., Robert A. O'Rourke, M.D., Koon K. Teo, M.B., B.Ch., Ph.D., Pamela M. Hartigan, Ph.D., David J. Maron, M.D., William J. Kostuk, M.D., Merril Knudtson, M.D., Marcin Dada, M.D., Paul Casperson, Ph.D., Crystal L. Harris, Pharm.D., Bernard R. Chaitman, M.D., Leslee Shaw, Ph.D., Gilbert Gosselin, M.D., Shah Nawaz, M.D., Lawrence M. Title, M.D., Gerald Gau, M.D., Alvin S. Blaustein, M.D., David C. Booth, M.D., Eric R. Bates, M.D., John A. Spertus, M.D., M.P.H., Daniel S. Berman, M.D., G.B. John Mancini, M.D., and William S. Weintraub, M.D., for the COURAGE Trial Research Group*



European Heart Journal (2002) **23**, 1546–1555
doi:10.1053/euhj.2002.3262, available online at http://www.idealibrary.com on IDEAL®

Effect of prior revascularization on outcome following percutaneous coronary intervention

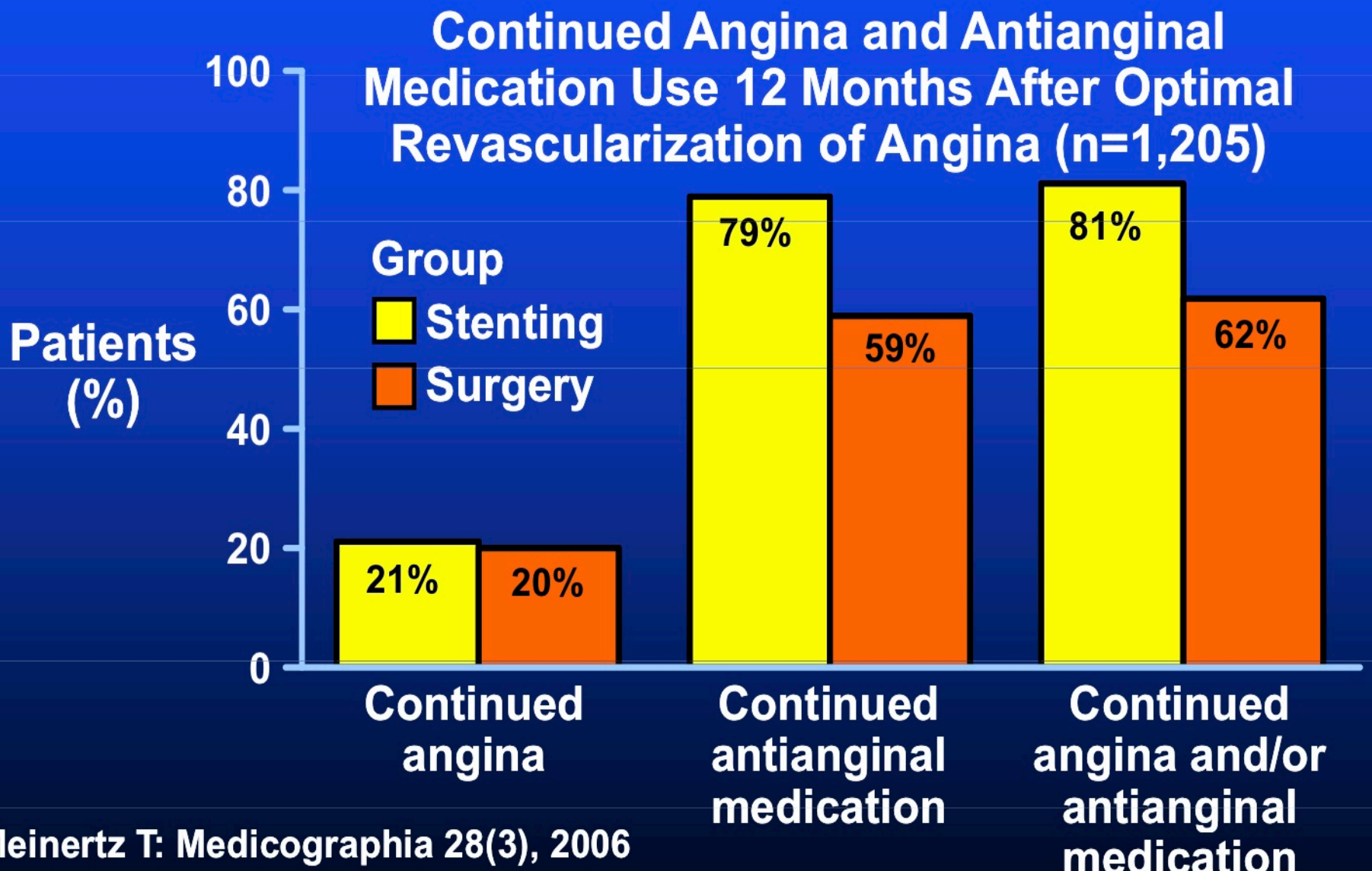
NHLBI Dynamic Registry

M. G. Bourassa[1], K. M. Detre[2], J. M. Johnston[2], H. A. Vlachos[2], R. Holubkov[2], for the Investigators of the NHLBI Dynamic Registry

[1]*Department of Medicine, Montreal Heart Institute, Montreal, Quebec, Canada;* [2]*Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, U.S.A.*

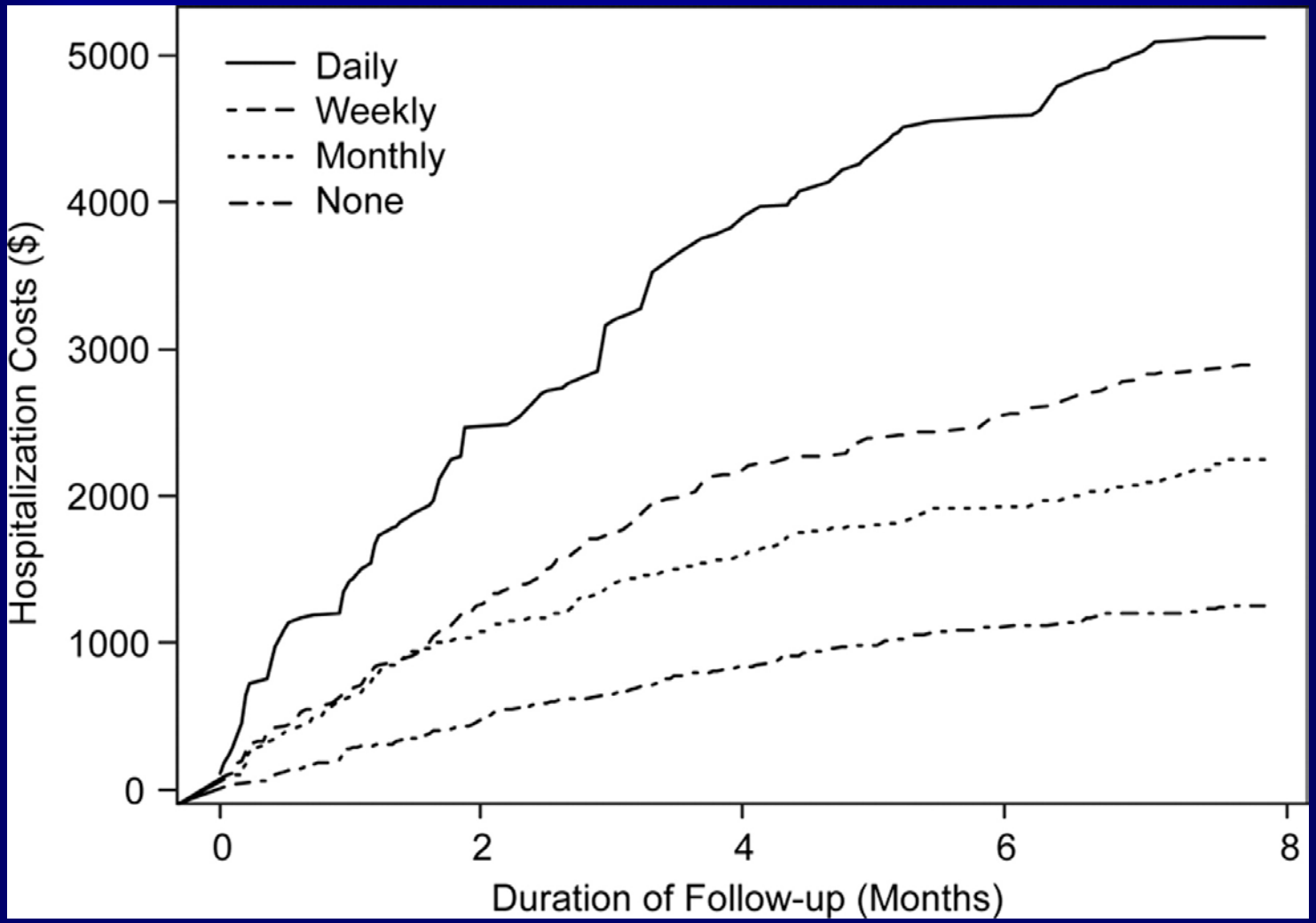
-Effect of prior revascularization on outcome following percutaneous coronary intervention. NHLBI Dynamic Registry. M.G Bourassaa, K.M Detreb,f1, J.M Johnstonb, H.A Vlachosb and R Holubkovb. European Heart Journal (2002) 23, 1546–1555
-Optimal medical therapy with or without PCI for stable coronary disease. COURAGE Trial Research Group. N Engl J Med. 2007 Apr 12 ;356 (15) :1503-16

Prevalence of Refractory Angina and Antianginal Medication Use



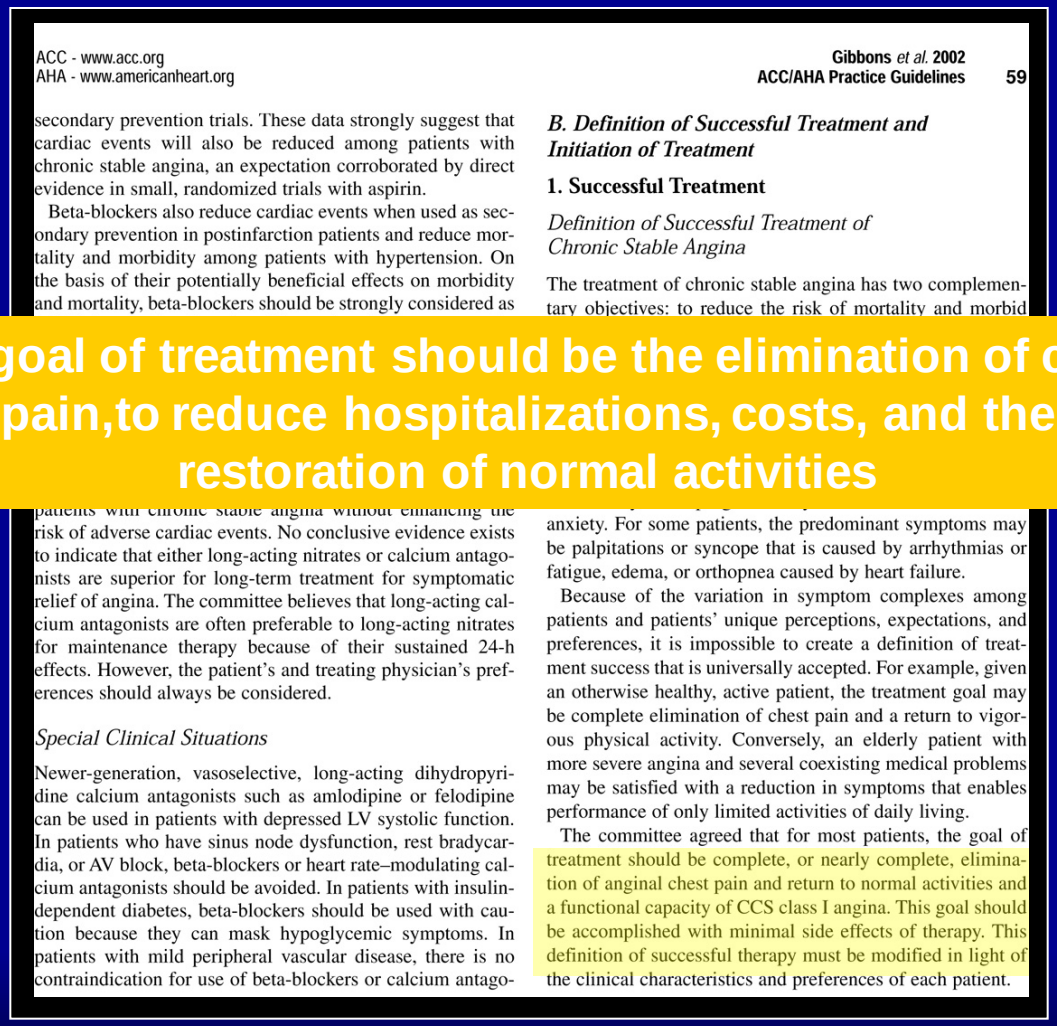
Meinertz T: Medicographia 28(3), 2006

Hospitalization Costs based on the frequency of angina attacks



Arnold S V et al. Circ Cardiovasc Qual Outcomes 2009;2:344-353

ACC/AHA guidelines on the management of chronic stable angina



secondary prevention trials. These data strongly suggest that cardiac events will also be reduced among patients with chronic stable angina, an expectation corroborated by direct evidence in small, randomized trials with aspirin.

Beta-blockers also reduce cardiac events when used as secondary prevention in postinfarction patients and reduce mortality and morbidity among patients with hypertension. On the basis of their potentially beneficial effects on morbidity and mortality, beta-blockers should be strongly considered as

patients with chronic stable angina without enhancing the risk of adverse cardiac events. No conclusive evidence exists to indicate that either long-acting nitrates or calcium antagonists are superior for long-term treatment for symptomatic relief of angina. The committee believes that long-acting calcium antagonists are often preferable to long-acting nitrates for maintenance therapy because of their sustained 24-h effects. However, the patient's and treating physician's preferences should always be considered.

Special Clinical Situations

Newer-generation, vasoselective, long-acting dihydropyridine calcium antagonists such as amlodipine or felodipine can be used in patients with depressed LV systolic function. In patients who have sinus node dysfunction, rest bradycardia, or AV block, beta-blockers or heart rate–modulating calcium antagonists should be avoided. In patients with insulin-dependent diabetes, beta-blockers should be used with caution because they can mask hypoglycemic symptoms. In patients with mild peripheral vascular disease, there is no contraindication for use of beta-blockers or calcium antago-

The goal of treatment should be the elimination of chest pain,to reduce hospitalizations, costs, and the restoration of normal activities

B. Definition of Successful Treatment and Initiation of Treatment

1. Successful Treatment

Definition of Successful Treatment of Chronic Stable Angina

The treatment of chronic stable angina has two complementary objectives: to reduce the risk of mortality and morbid

anxiety. For some patients, the predominant symptoms may be palpitations or syncope that is caused by arrhythmias or fatigue, edema, or orthopnea caused by heart failure.

Because of the variation in symptom complexes among patients and patients' unique perceptions, expectations, and preferences, it is impossible to create a definition of treatment success that is universally accepted. For example, given an otherwise healthy, active patient, the treatment goal may be complete elimination of chest pain and a return to vigorous physical activity. Conversely, an elderly patient with more severe angina and several coexisting medical problems may be satisfied with a reduction in symptoms that enables performance of only limited activities of daily living.

The committee agreed that for most patients, the goal of treatment should be complete, or nearly complete, elimination of anginal chest pain and return to normal activities and a functional capacity of CCS class I angina. This goal should be accomplished with minimal side effects of therapy. This definition of successful therapy must be modified in light of the clinical characteristics and preferences of each patient.

Gibbons RJ, et al. *ACC/AHA 2002 Guideline Update for the Management of Patients with Chronic Stable Angina*

CABG

Angioplasty

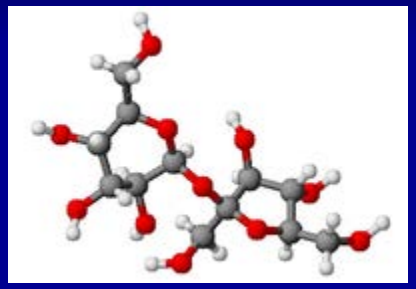
Anti-anginals
Medication

CAD Treatment
Options

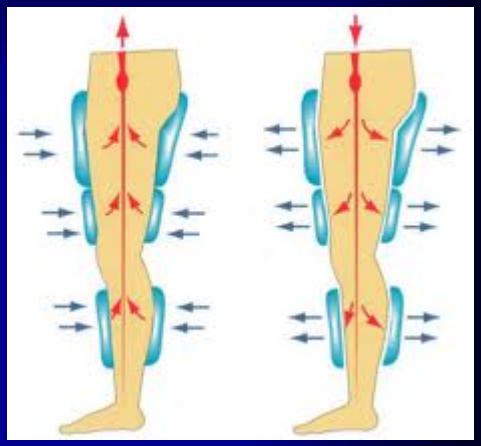
?

REFRACTORY ANGINA

Laser revascularization

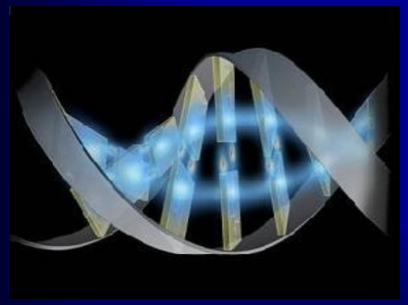


New drugs

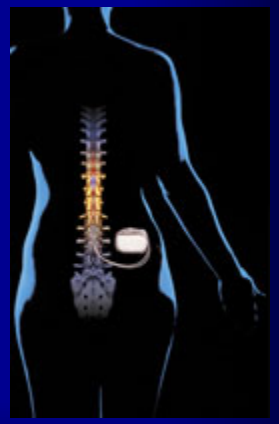


External counterpulsation

ESMR



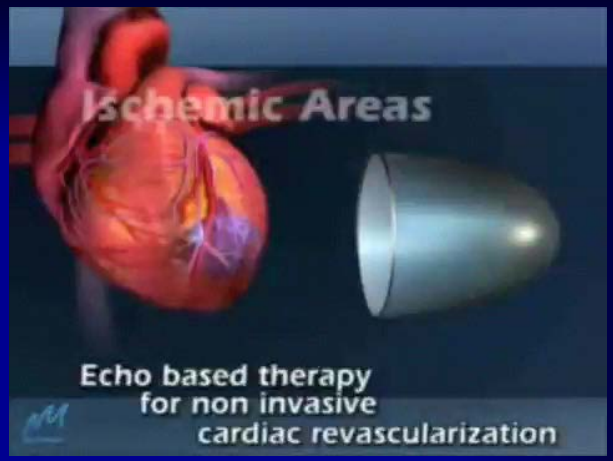
Gene therapy

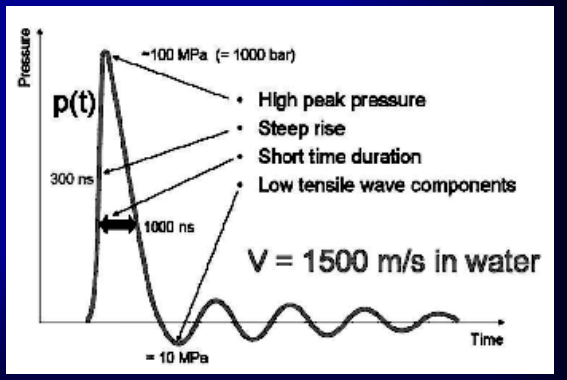


Spinal cord stimulation

ESMR Therapy
Extracorporeal Shockwave Myocardial Revascularization

- Shockwaves are special acoustic waves that can be focused on a selected area inside the body.
- Shockwaves have been used in urology and in the treatment of some orthopedic settings.
- In-vitro and animal studies demonstrated the increase of angiogenic factors after low intensity shockwaves treatment.
- The effect is precise and controlled.

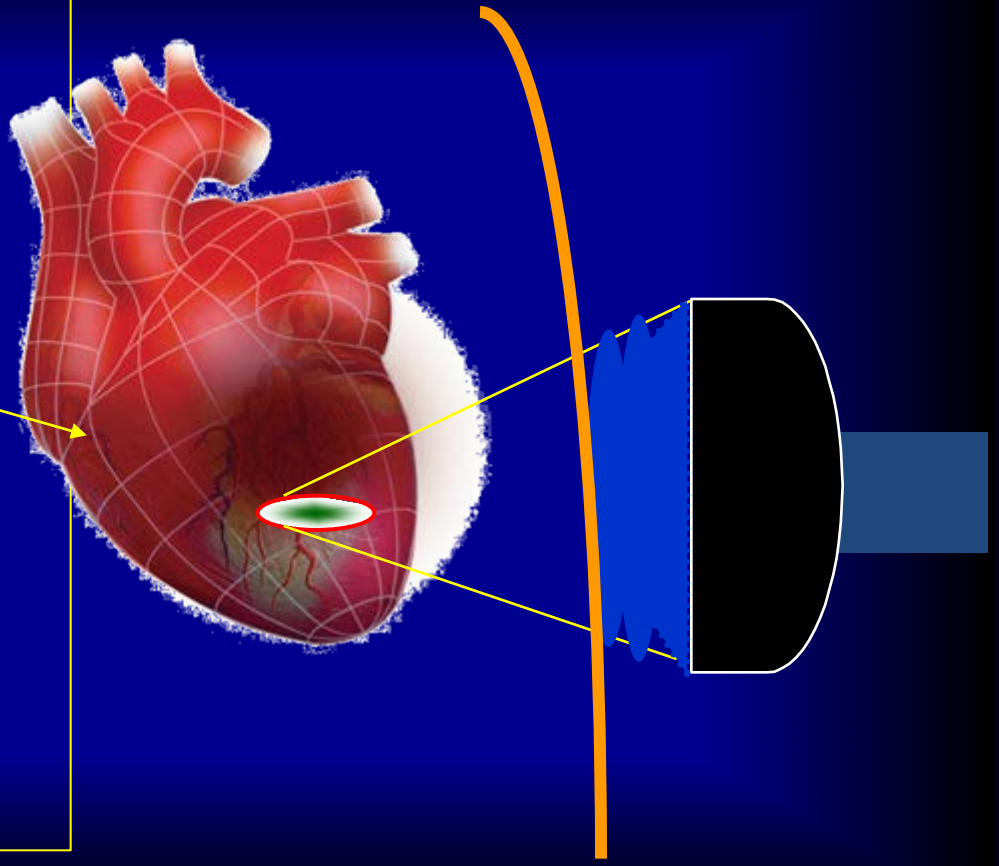




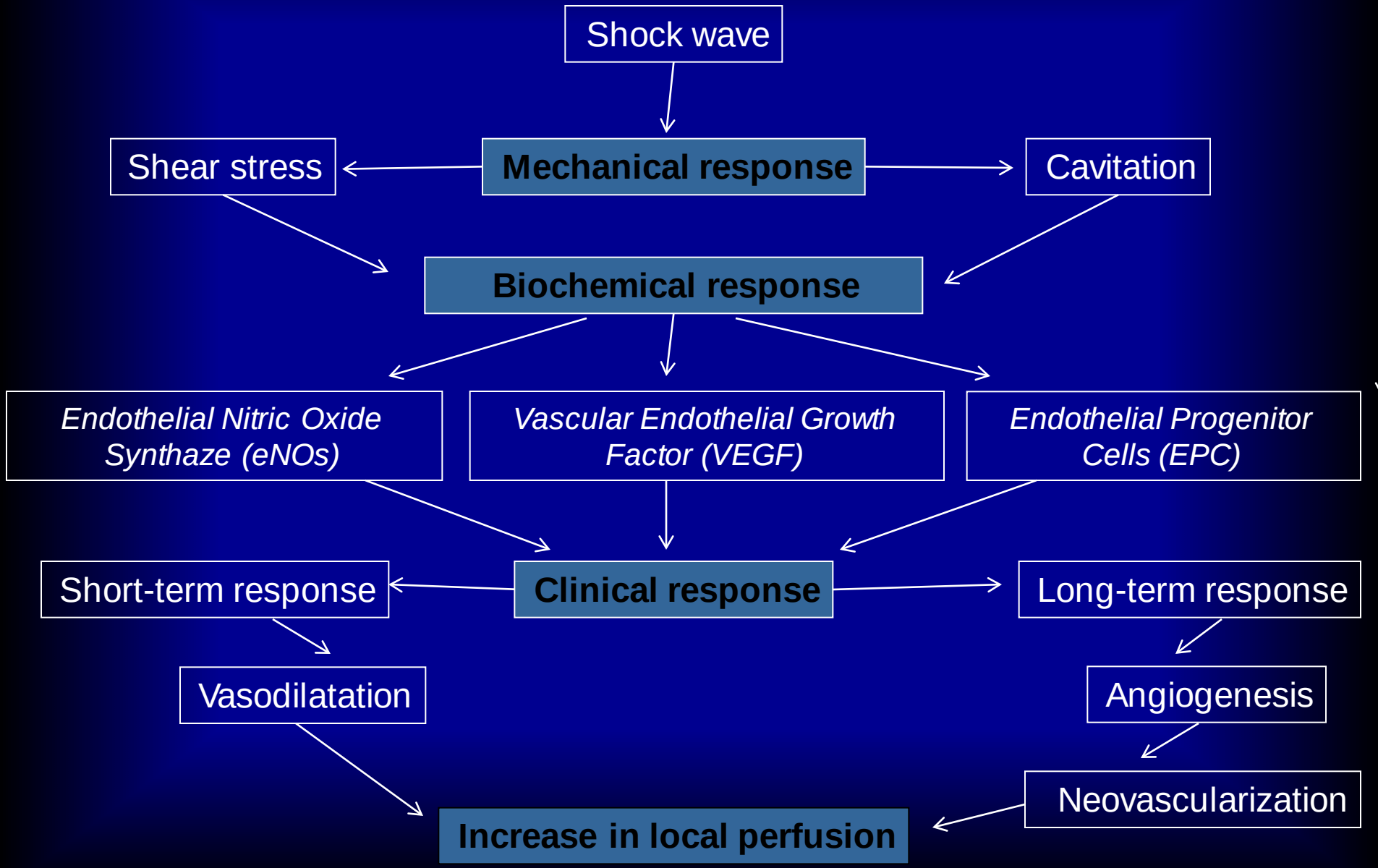
Main Physiological Effects

Short Term Effect: Local Vasodilatation

Long Term Effect: Angiogenesis



Low-energy shock waves



Aim

Analyze the benefits of ESMR, assessing the myocardial perfusion and the symptoms in patients suffering from chronic refractory angina

METHOD
PATIENT SELECTION

Inclusion criteria

- Reversible ischemia and/or hibernation shown by SPECT
- Functional Classification of Angina: CCS II-IV
- PCI / CABG not more applicable.
- Stable Angina pectoris (dyspnea) > 3 months
- Optimal medical therapy for at least 6 weeks prior to enrollment.

METHOD
PATIENT SELECTION

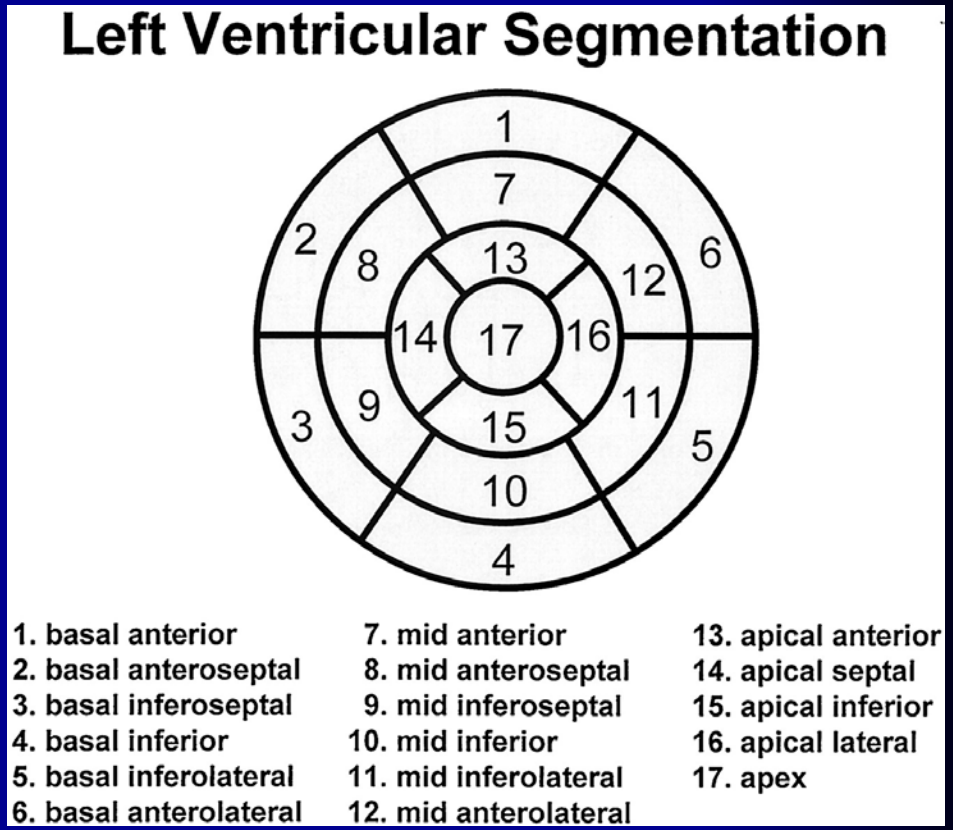
Exclusion criteria

- Acute MI < 3 months prior to treatment
- Patient with intraventricular thrombus
- Decompensated congestive heart failure
- Severe valvular heart disease
- Severe COPD
- Active endocarditis, myocarditis or pericarditis.
- Pregnancy
- Malignancy

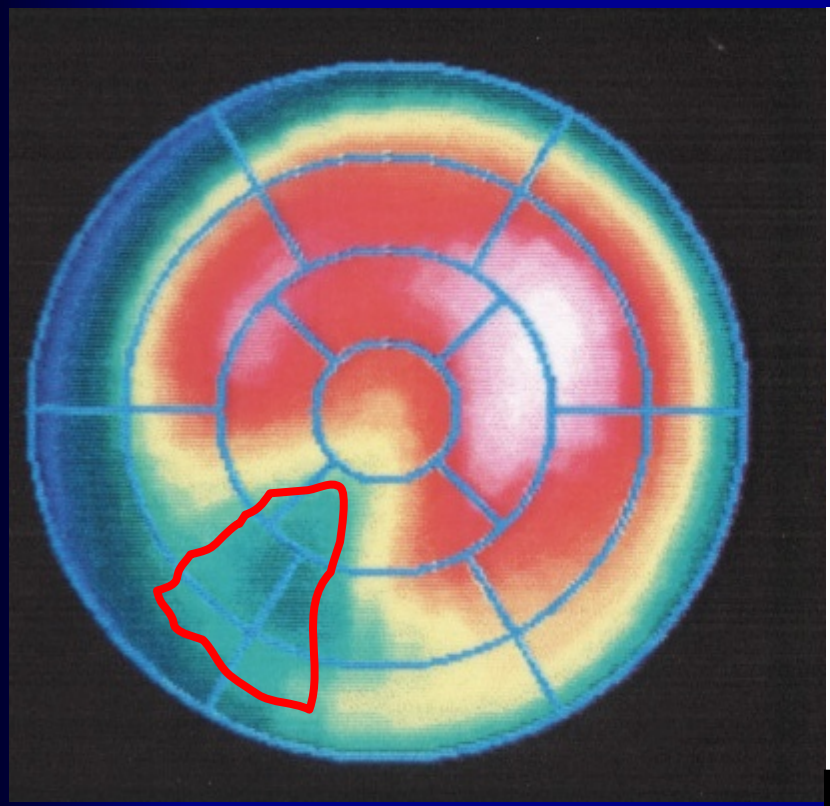
METHOD
Treatment Protocol

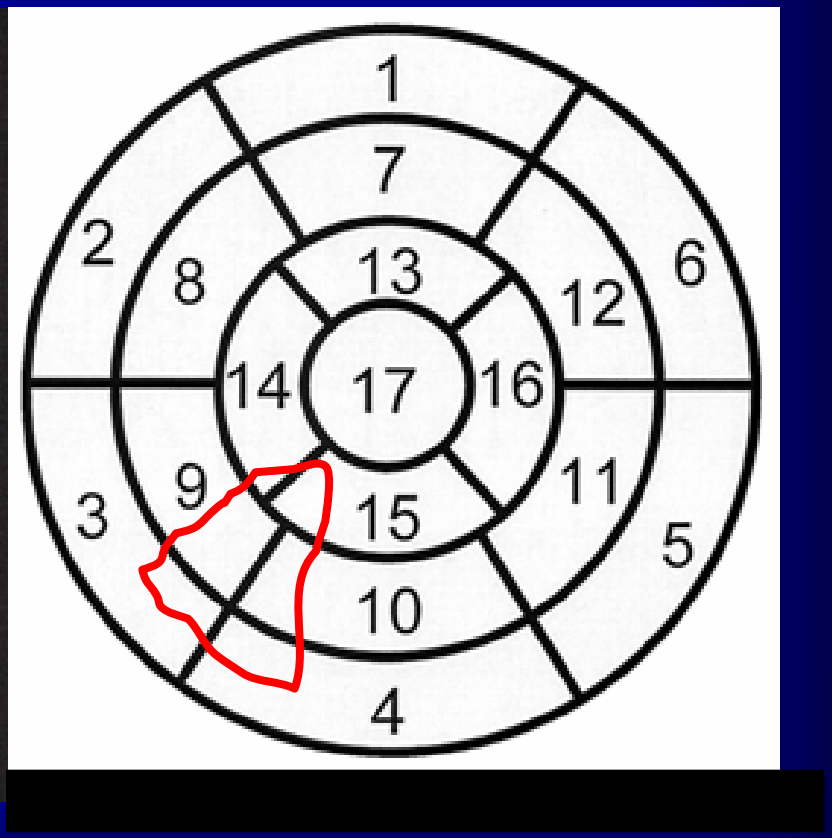
SPECT

- SPECT study performed during Rest and Stress pre and post treatment (4 studies for 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
- Summed Stress Score and Summed Rest Score



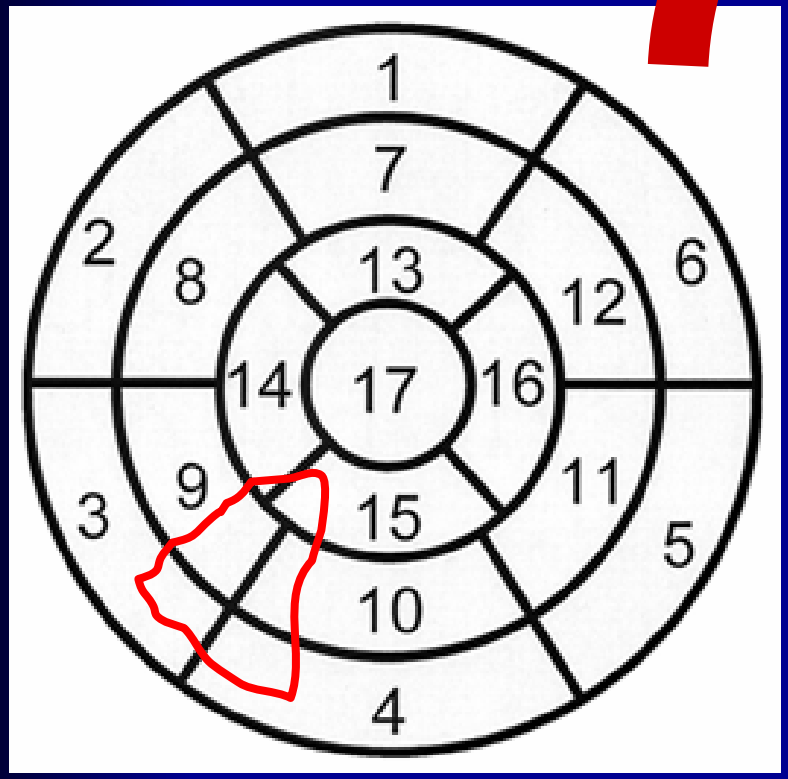
METHOD
Myocardial ischemia detection



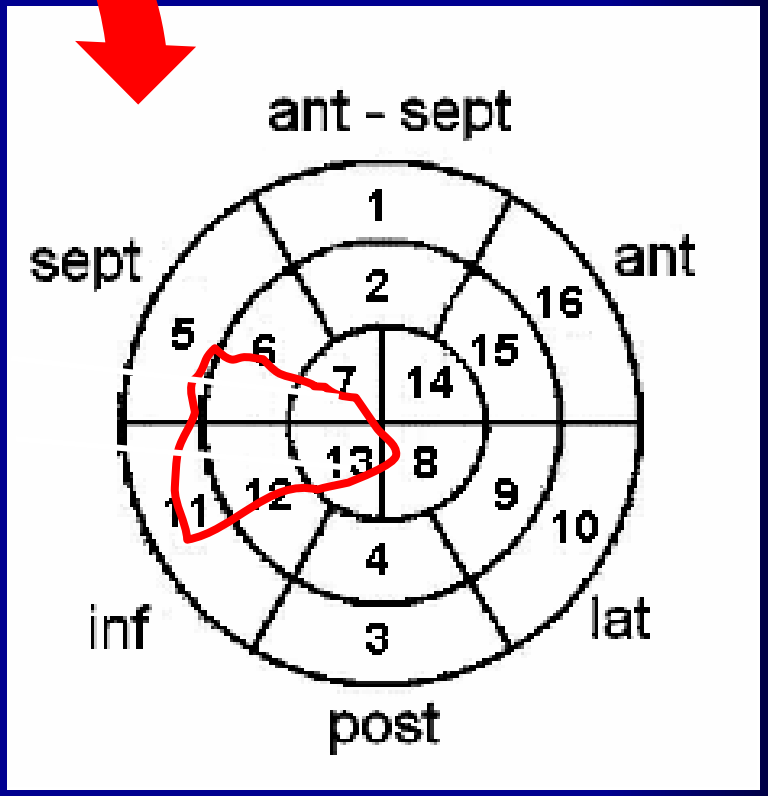


Myocardial ischemia detection

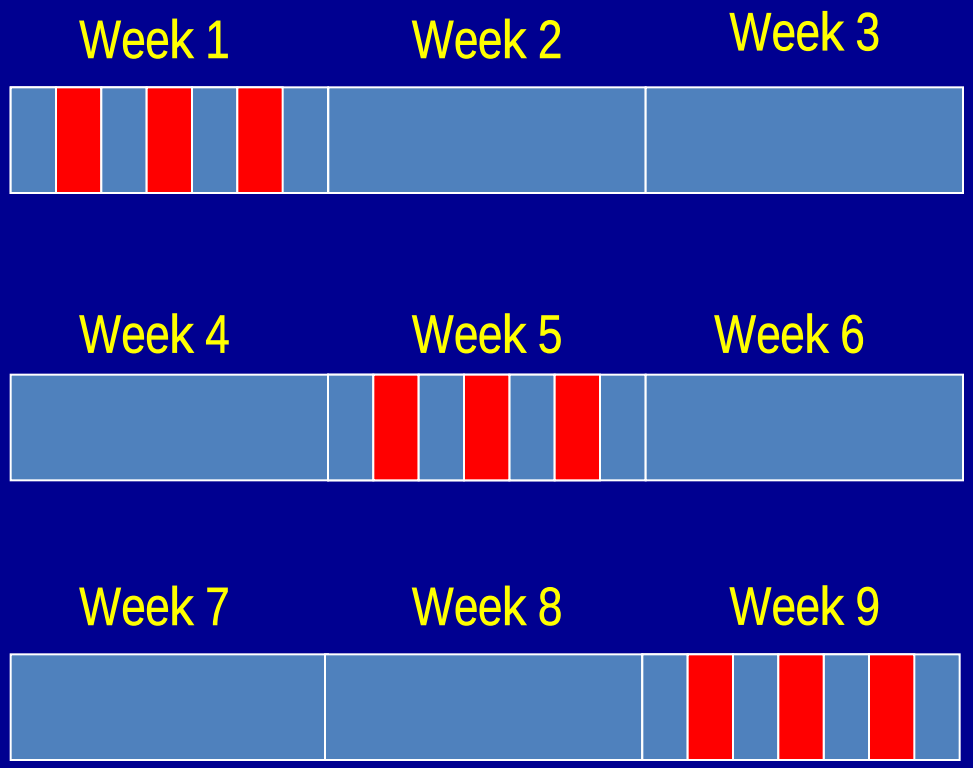
SPECT



ECHO

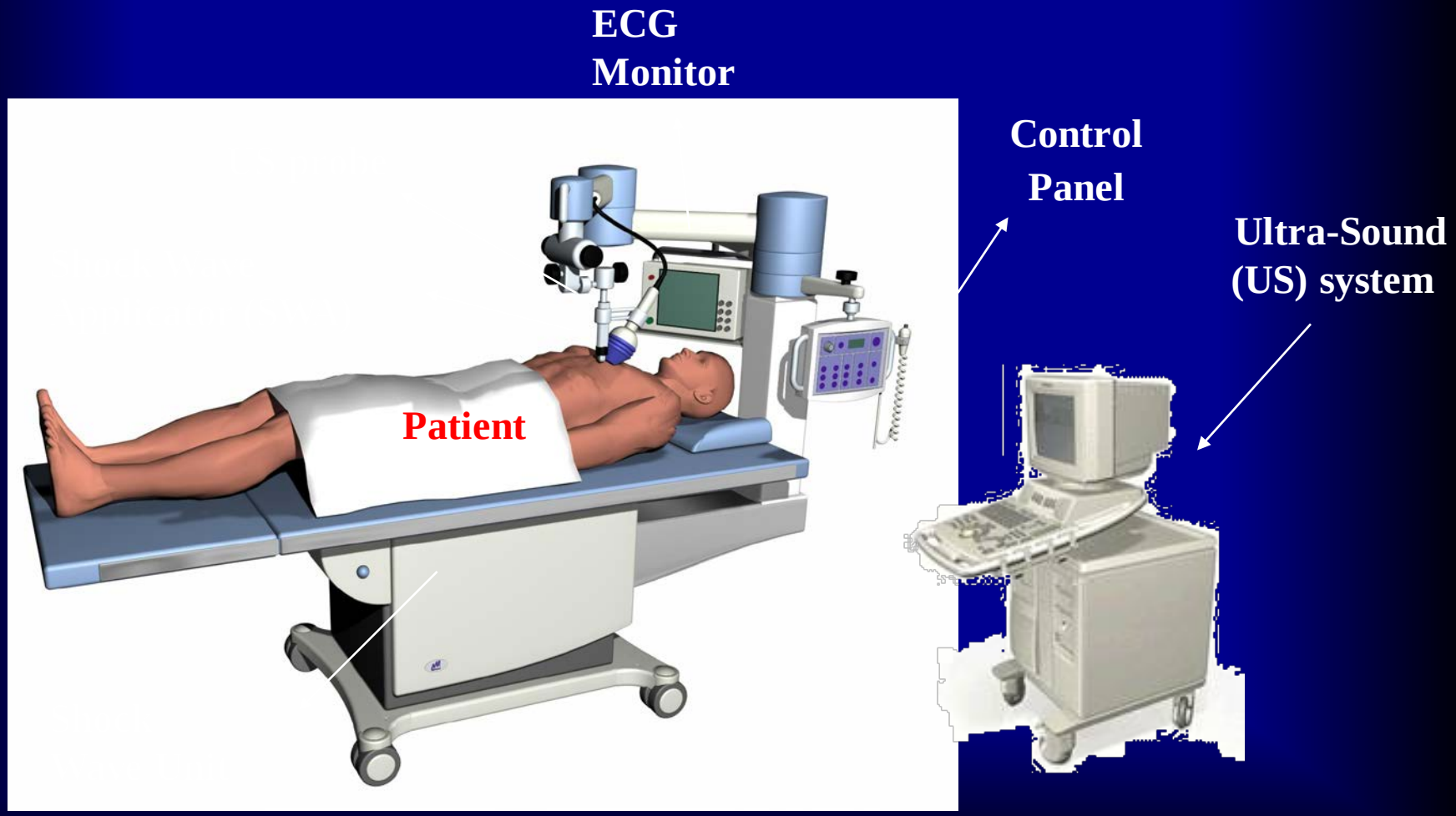


METHOD
Treatment Protocol

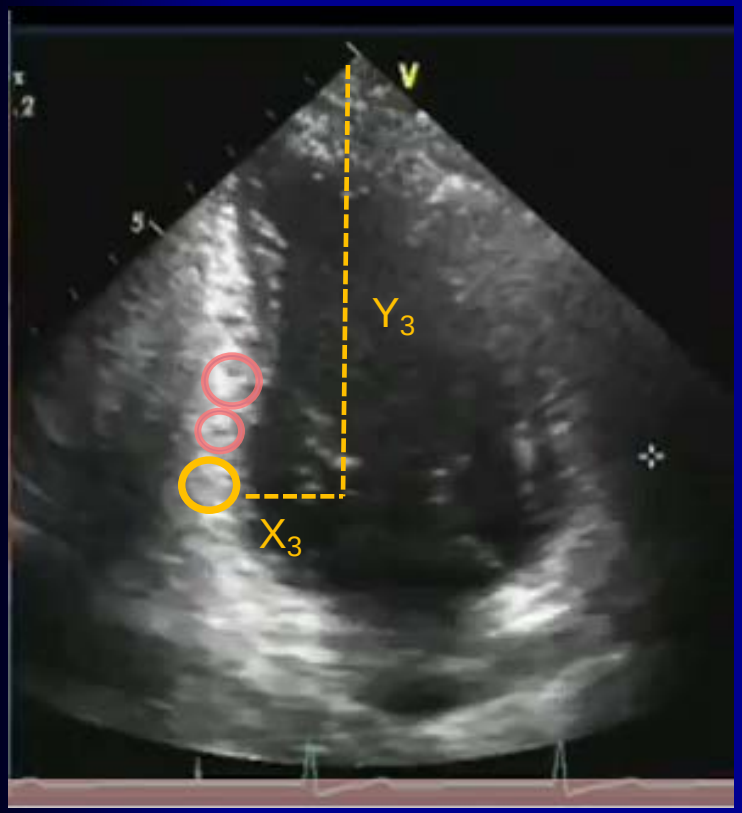


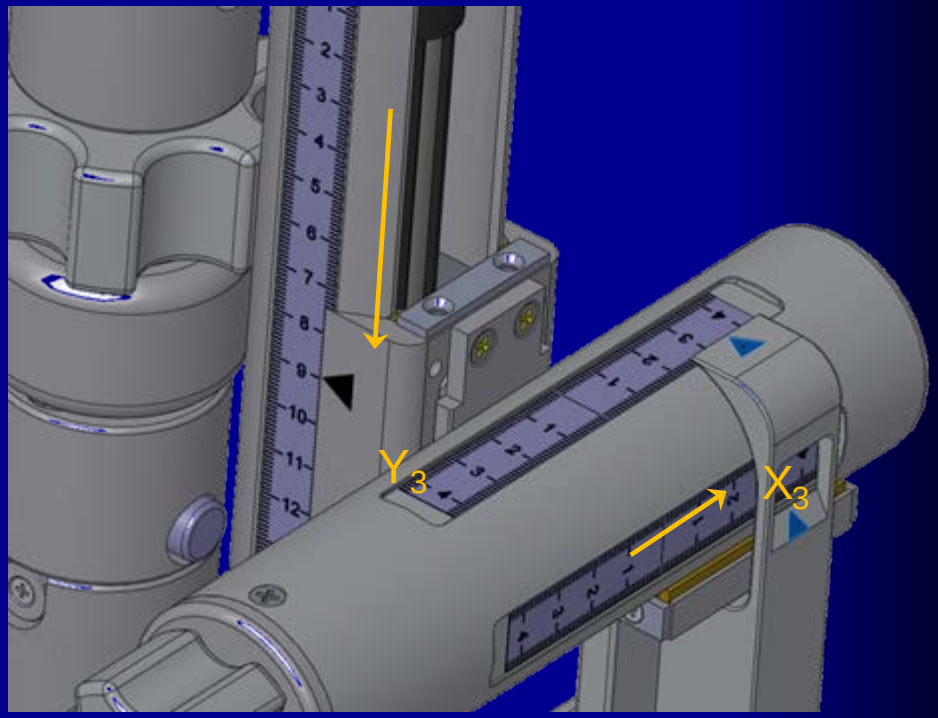
3 treatments per week at 5-10 ischemic zones, 100 shocks per zone, 0.09 mj/mm^2

Cardiospec System Components



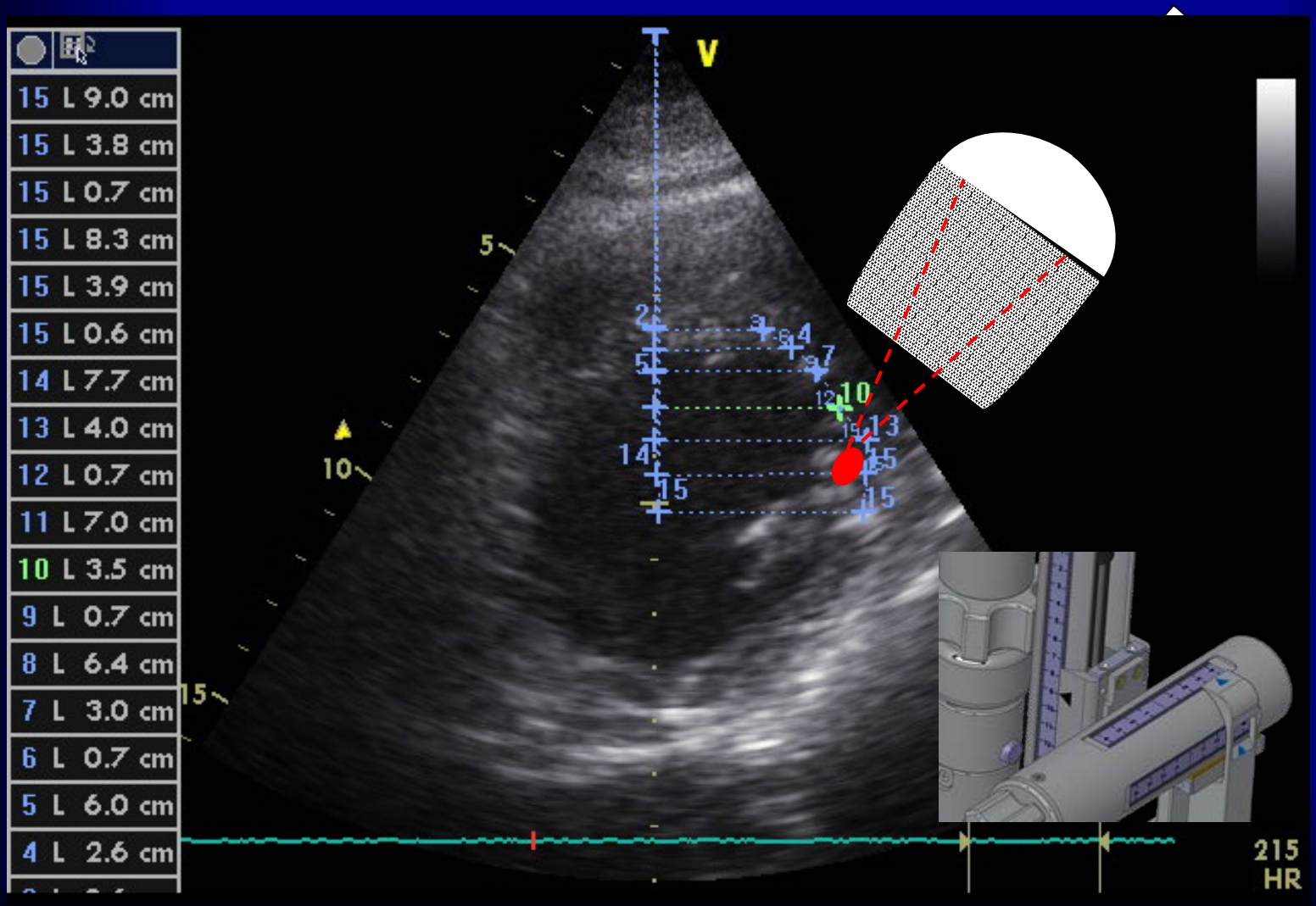
ECHO treatment: Regions of interest





- Locate the first sub-segment on the ultrasound image
- Determine its position as X_3Y_3 coordinates.
- Adjust position of the SWA for treating the first sub-segment on the horizontal scale for X_3 value and on the vertical scale for Y_3 value

ECHO treatment: Regions of interest



METHOD
Primary End-Points

- **CCS class improvement at 3 - 6 -12 months**

(CCS: Canadian Cardiovascular Society Functional Classification of Angina)

- **SPECT perfusion improvement at 6 months**

(Summed Rest Score-Summed Stress Score)

METHOD
Secondary End-Points

- Reduction in extra nitrogliceryne consumption
- Reduction in hospitalization
- Improvement of LV ejection fraction (ECHO)

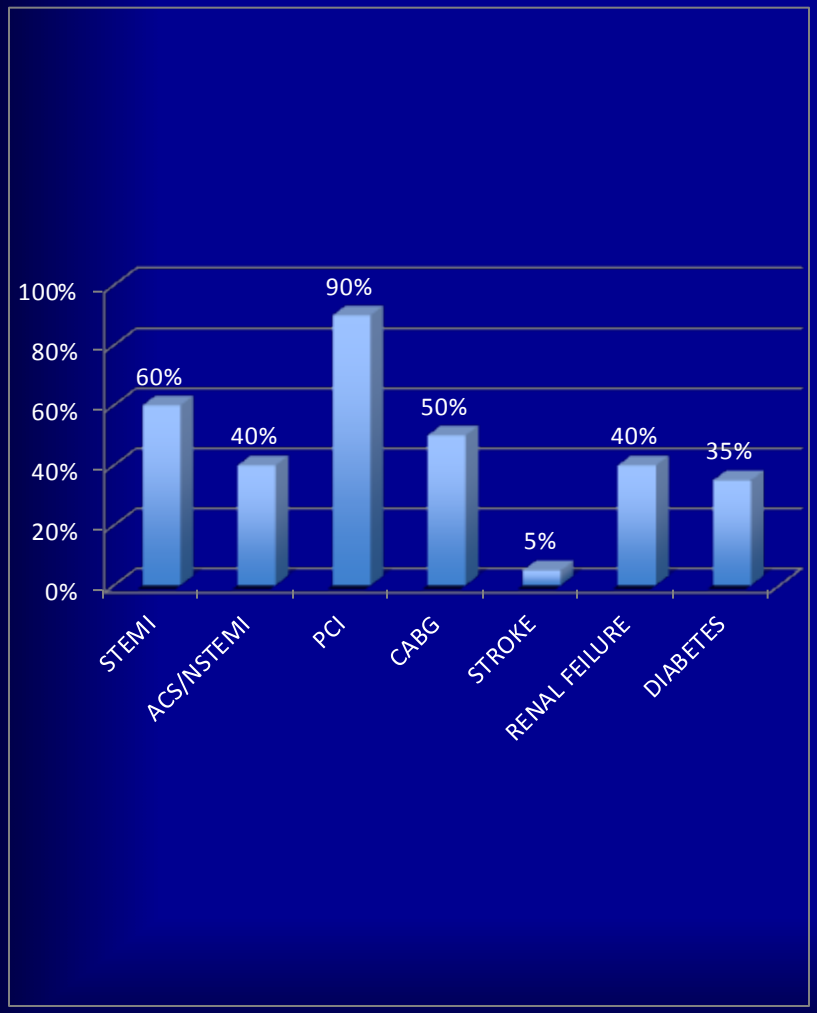
Follow up

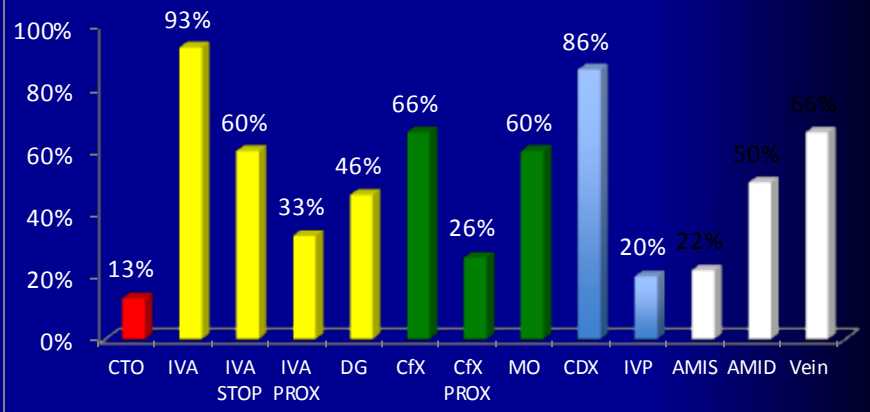
- Clinical assessment at 1-3-6-12 months
- SPECT at 6 months
- Echocardiography at 6 months

TREATED POPULATION

- 33 patients treated
- Age : 70,8 ± 10 (45-85)
- Male patients : 80%
- Angina CCS : mean 2,8
- Diabetic patients : 35%

Treated Population





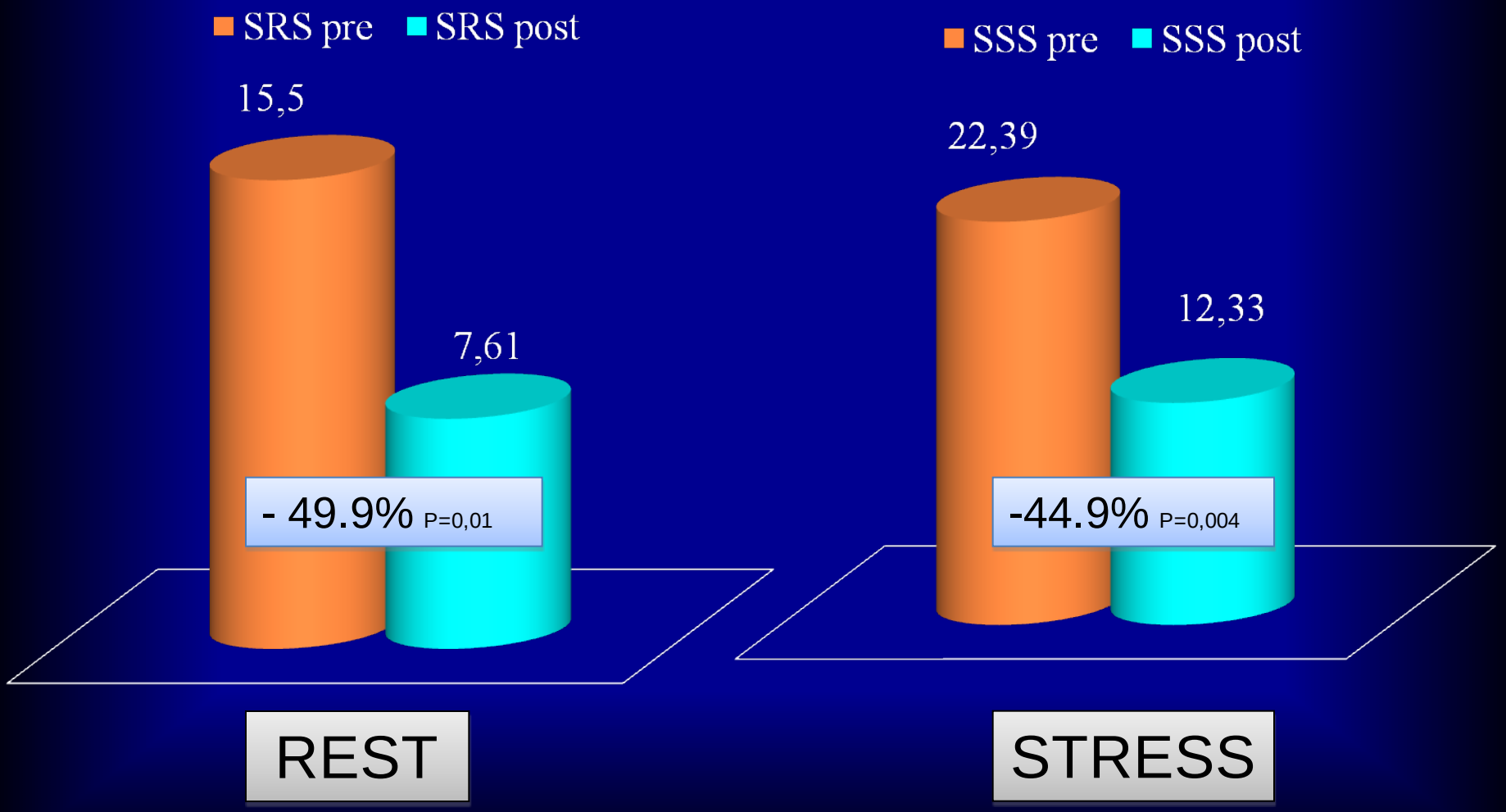
Results: follow-up

- **33 patients treated**
  - **5 patients will have a complete treatment in November**
  - **8 patients have a 3 months follow**
  - **18 patients underwent SPECT after 6 months , with a complete follow-up at > 1 year**
  - **2 patients drop-out: died**
    - **one sudden death 5 months after the treatment**
    - **one because of septic shock**

Results: Side effects

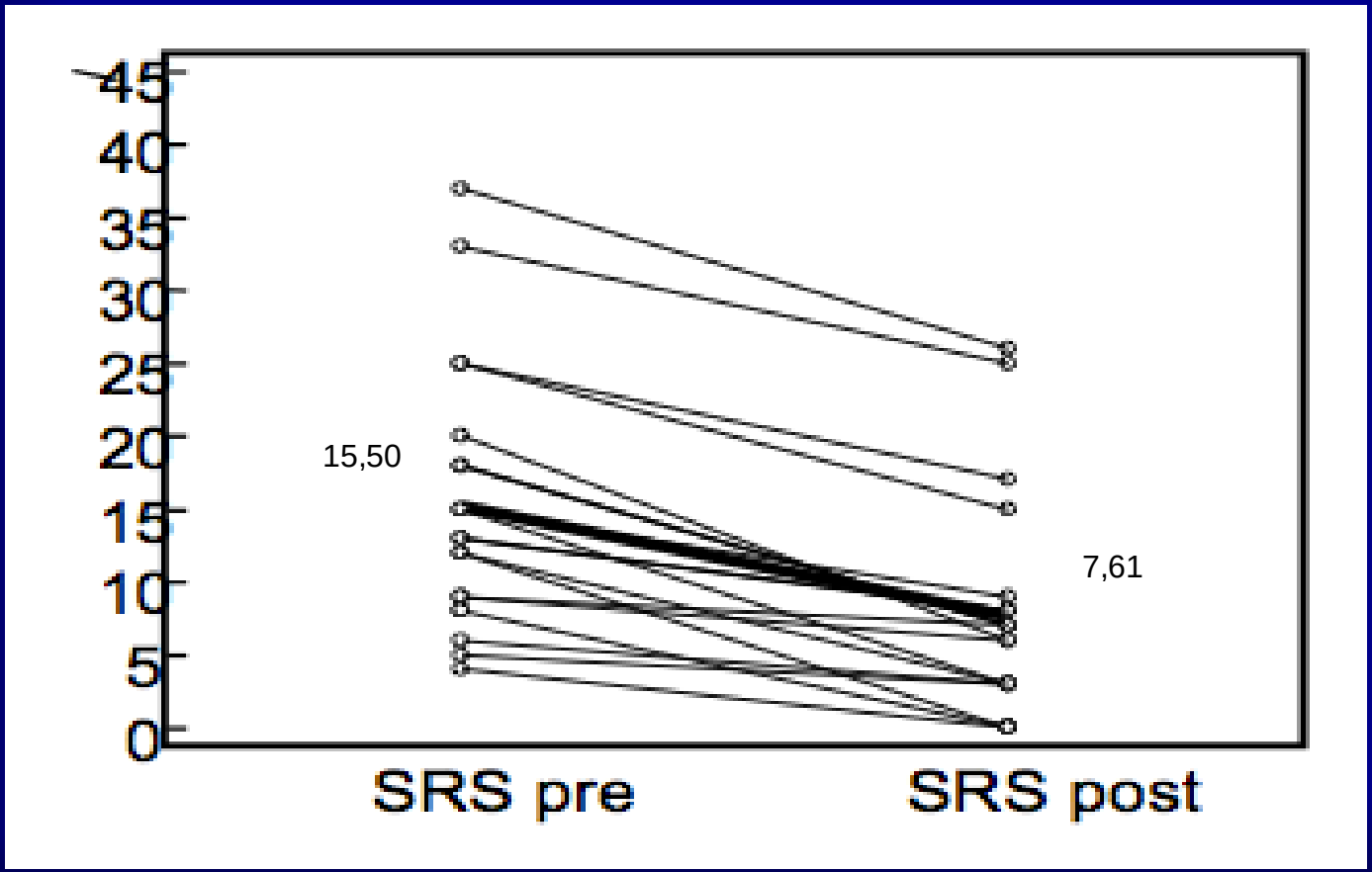
- No side effects recorded at any time:
  - No pericarditis
  - No local pain
  - No arrhytmyas
  - No skin damage
  - No costal-muscular pain
- All the patients completed the treatment

Results – Perfusion SPECT

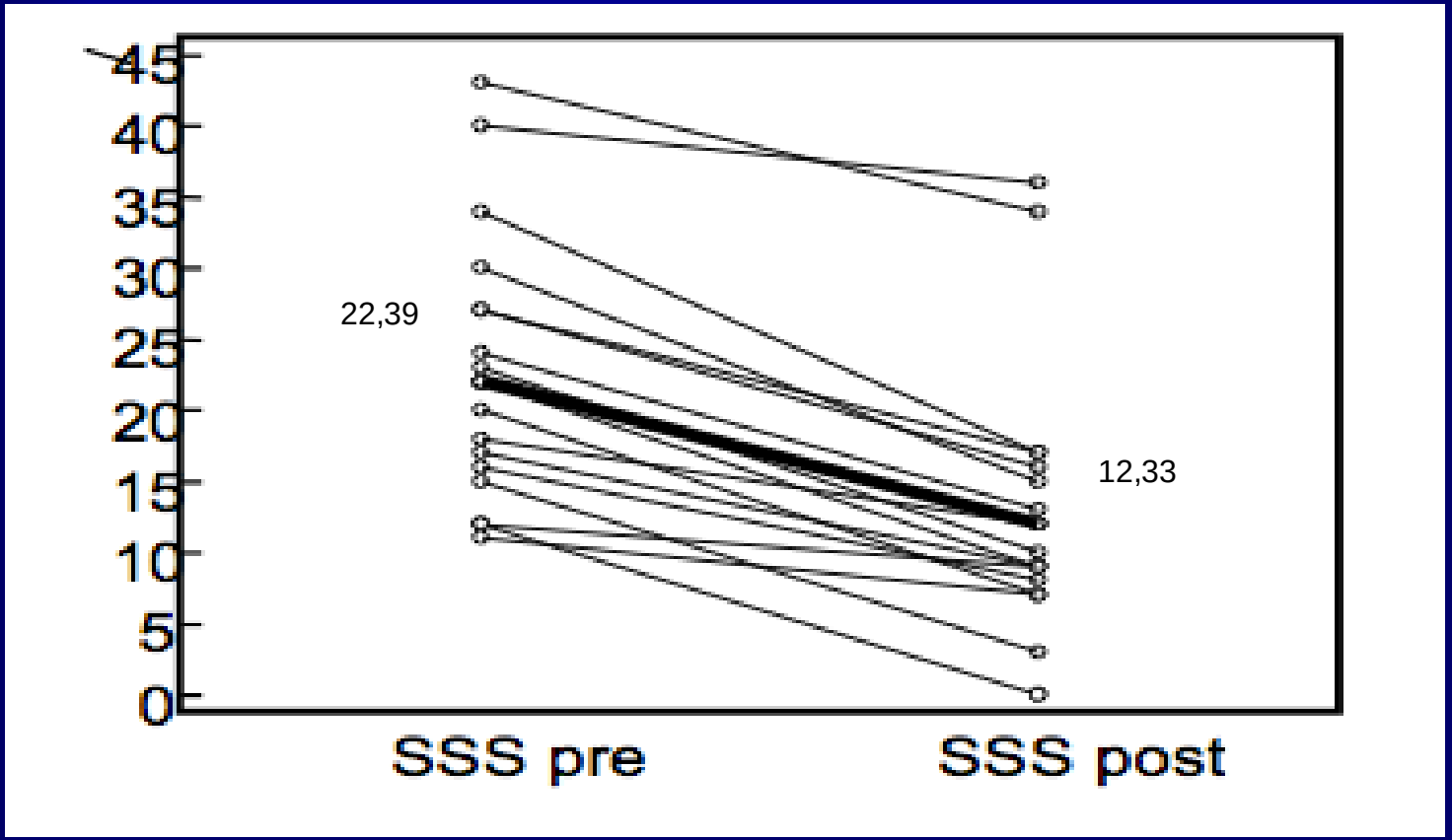


SSS= Summed Stress Score SRS= Summed Rest Score

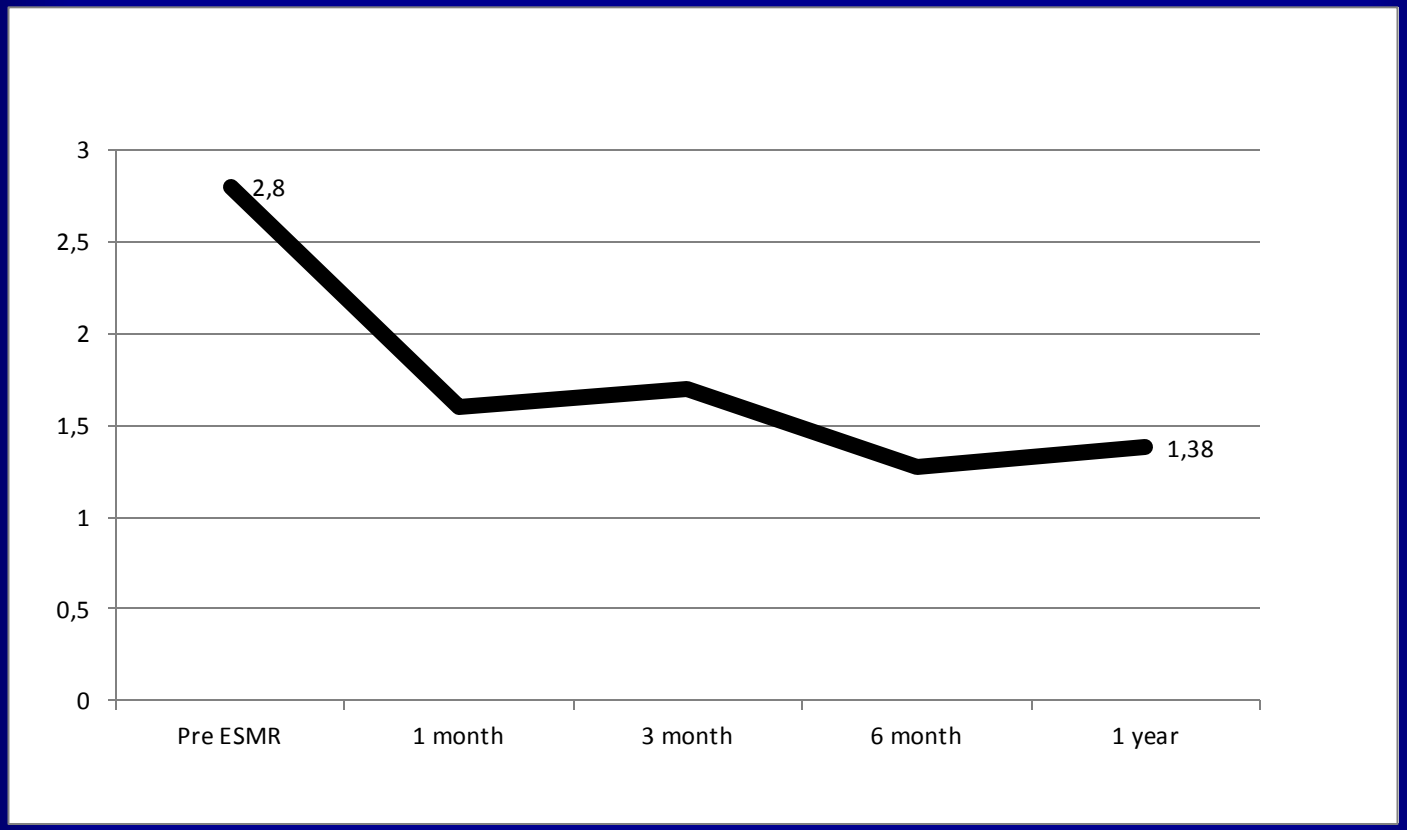
SPECT RESULTS
PRIMARY END-POINTS 6 months
Summed Rest Score (SRS) by SPECT



SPECT RESULTS
PRIMARY END-POINTS 6 months
Summed Stress Score (SSS) by SPECT

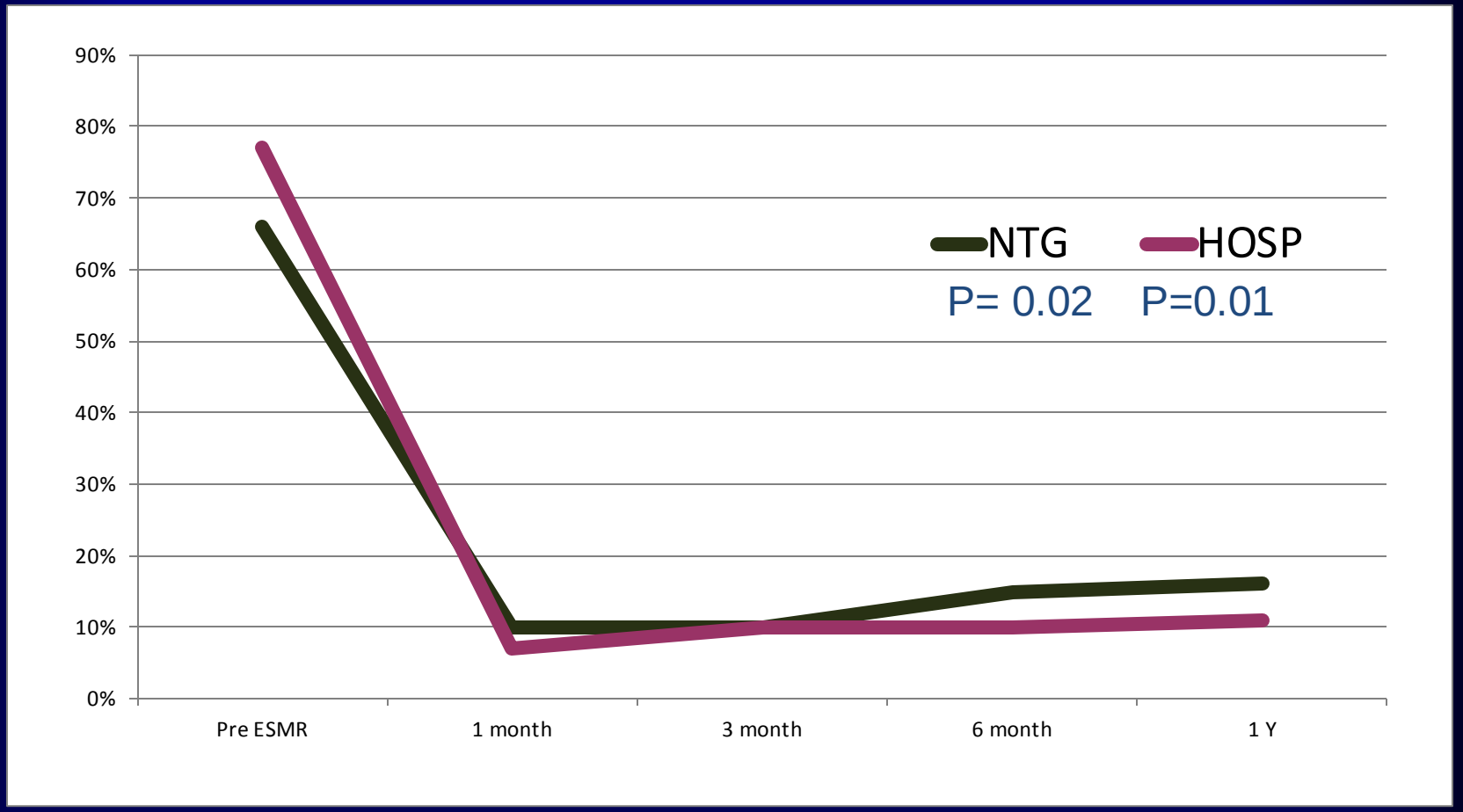


Results - Symptoms and CCS

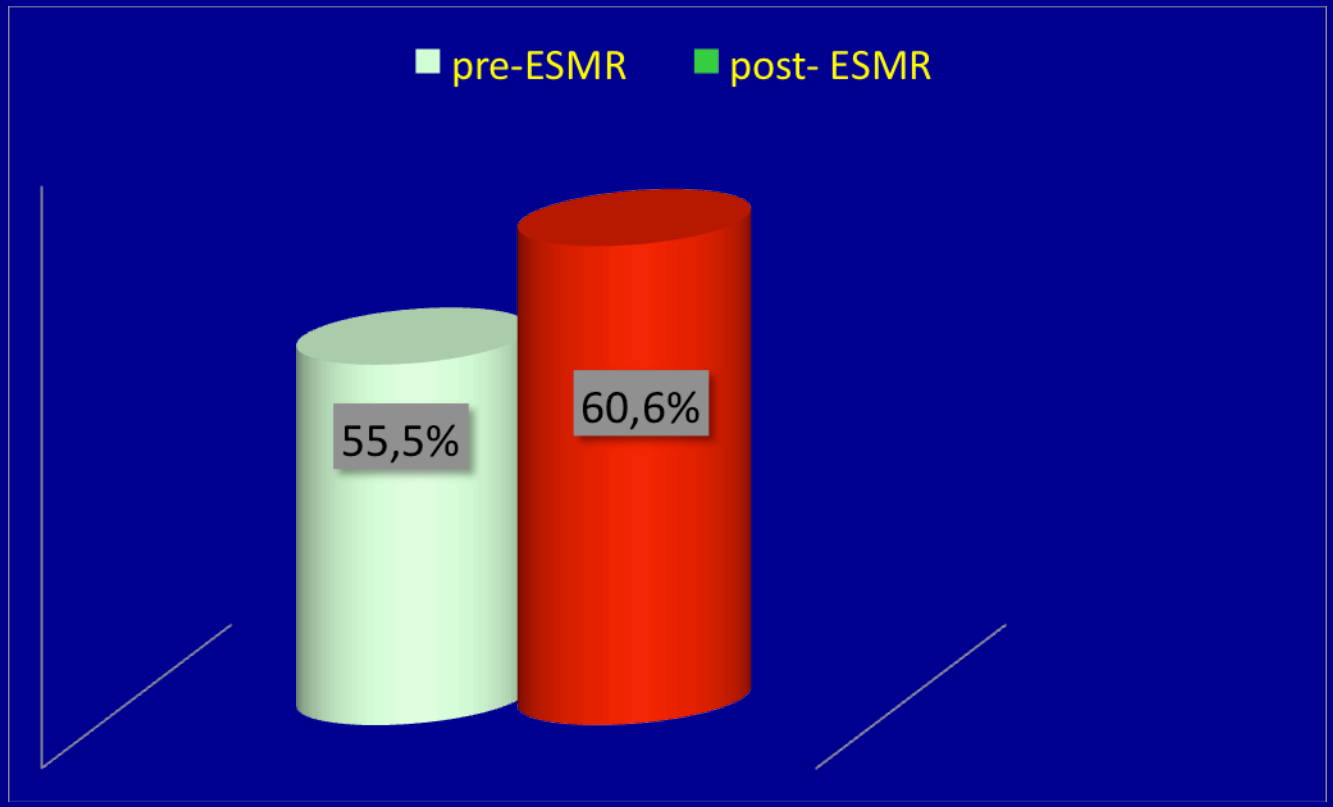


P=0.001

Results - NTG and Hospitalization



Results - LVEF



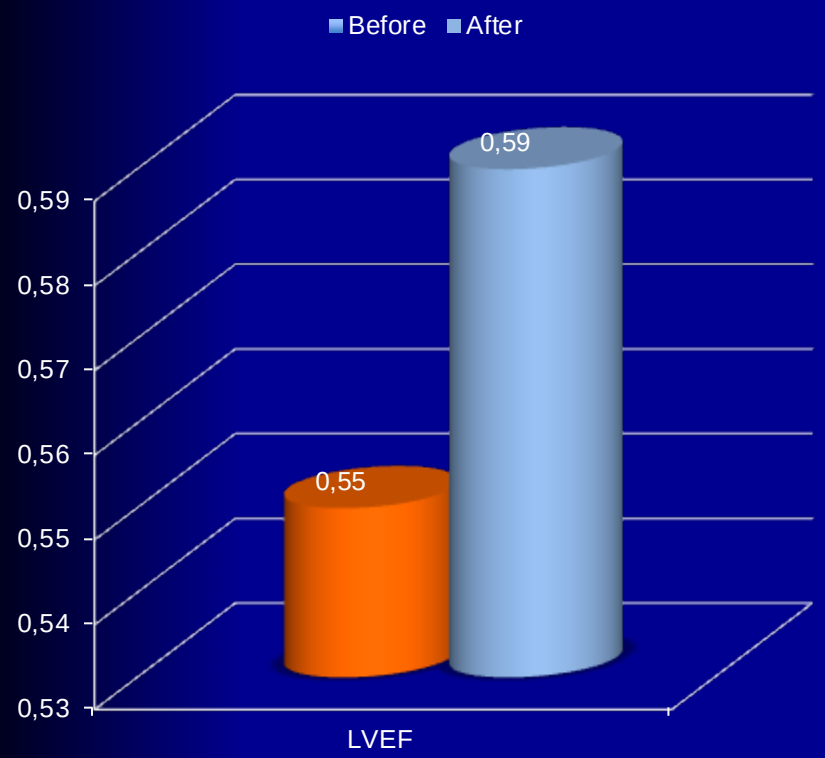
+ 8.4%

P=0.02

DIABETIC PATIENTS

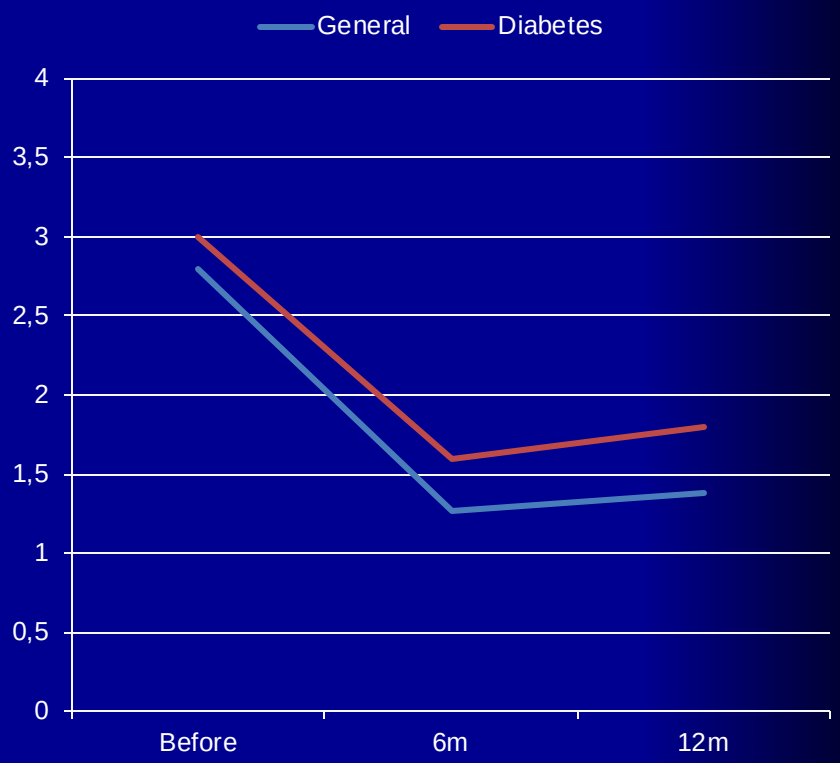
RESULTS in Diabetes

LVEF by ECHO



+7%

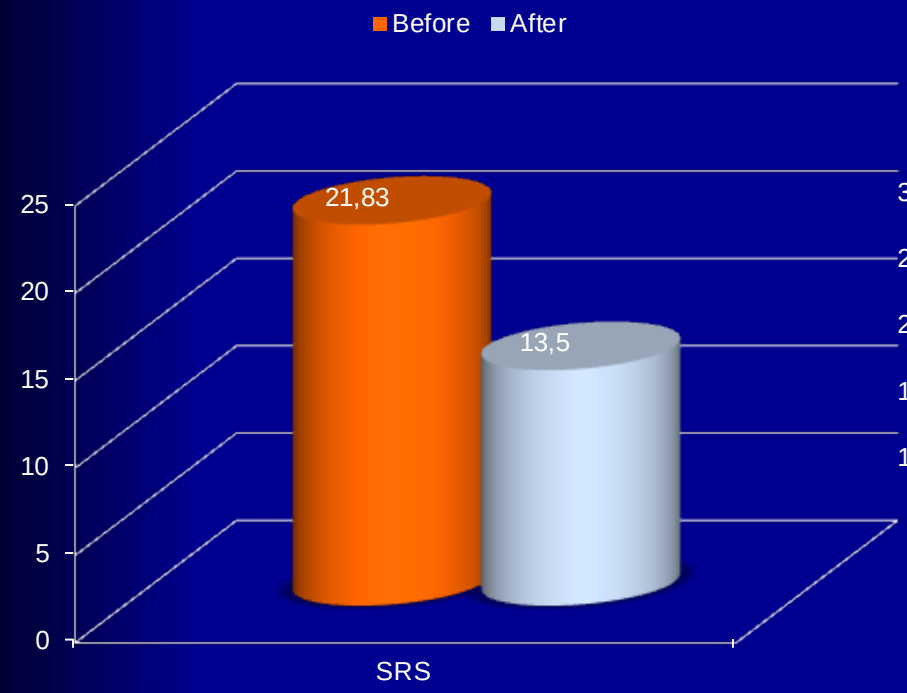
CCS Angina



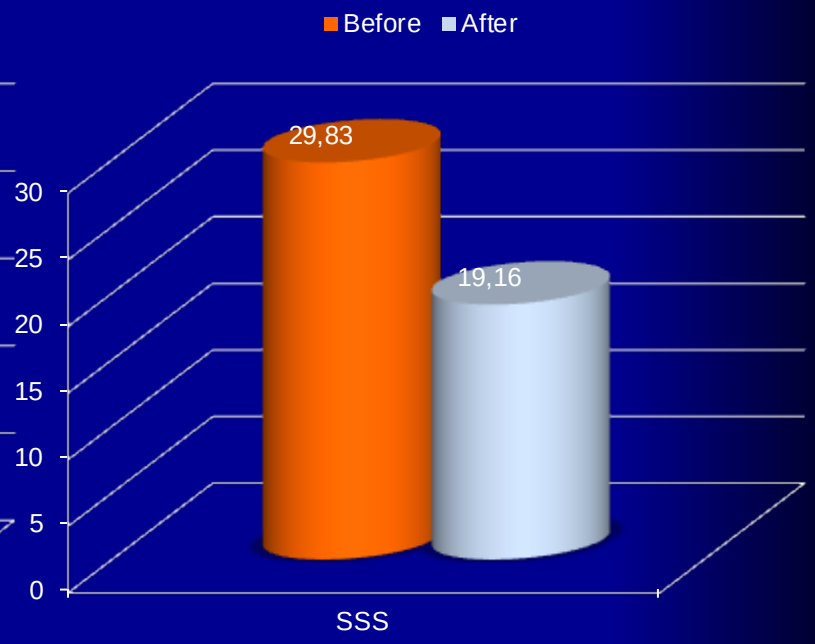
-6m:
P=0,003

-12m:
-P=0,052 ns

RESULTS in Diabetes
6 months
CHANGE SRS-SSS by SPECT



+38% SRS



+36% SSS

CONCLUSIONS

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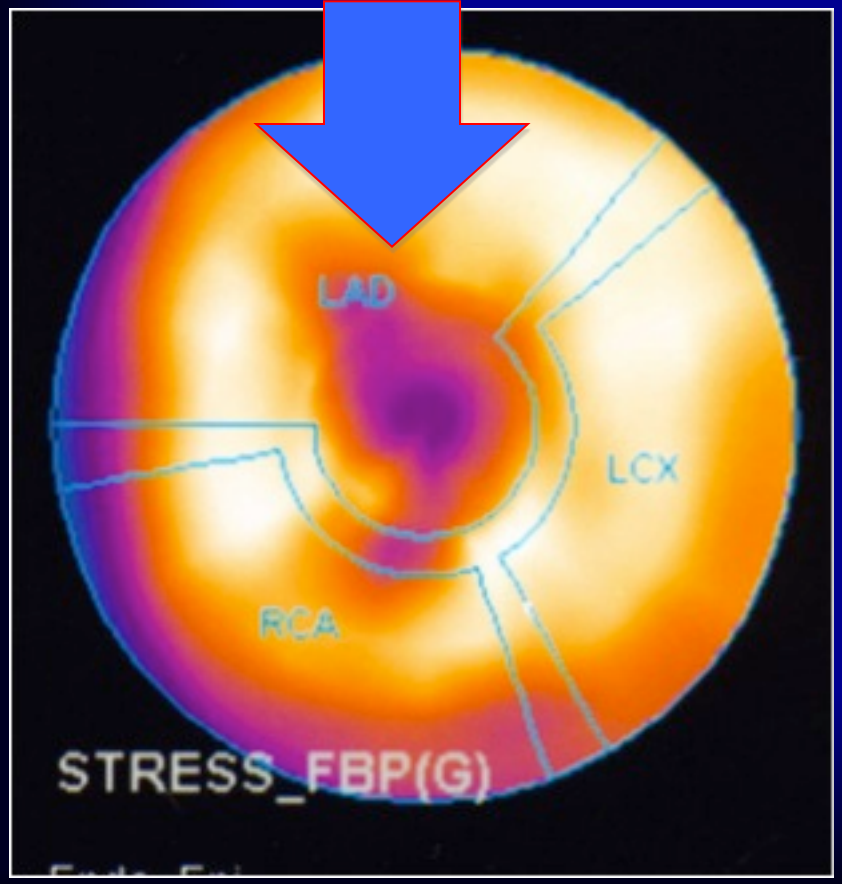
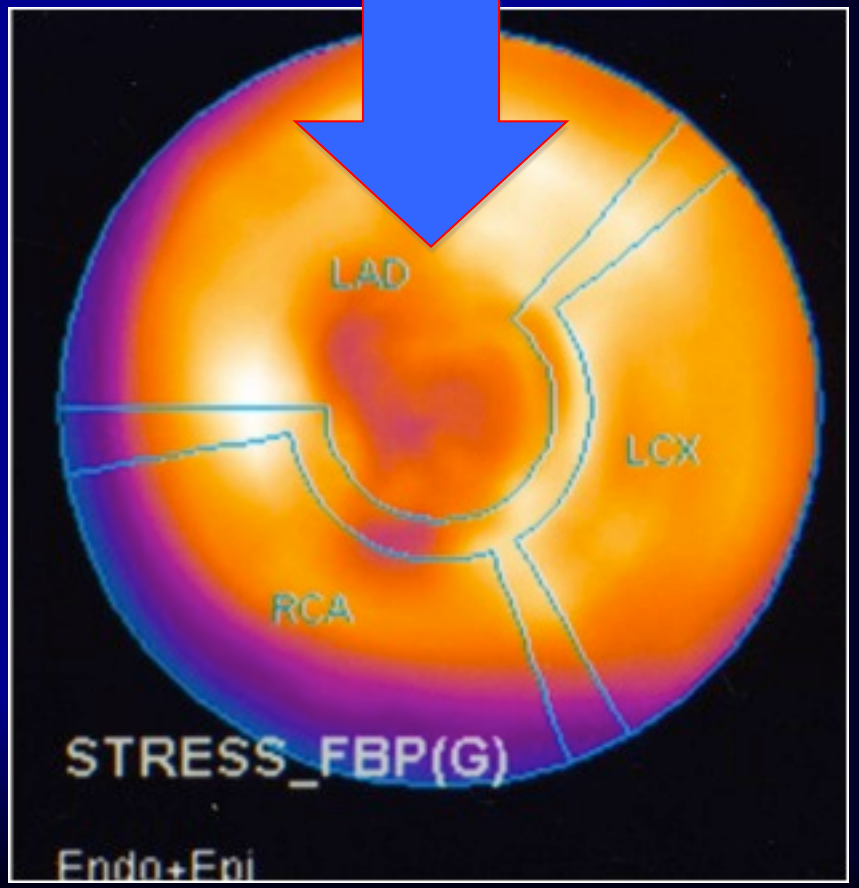
Before ESMR (CCS III)

After ESMR (CCS I)

WHAT STRATEGY FOR THIS PATIENT?





SUMMARY

- No side effects
- Improvement CCS class of angina:
  - + 55% 6 m, + 49% 2 Y (p=0,001)
- Improvement of perfusion shown by SPECT
  - + 49.9% SRS (p=0,01), +44.9% SSS (p=0.004)
- Improvement Local contractility and LVEF shown by ECHO

Take home message

1. ESMR is an effective and safe therapeutic option for patients suffering from refractory coronary artery disease that really improve the myocardial perfusion and the myocardial function.

2. ESMR treatment significantly improves symptoms and the need for further hospitalization without any adverse effect, but larger studies are necessary to confirm these findings.

3. All this in about 20 minutes, with no adverse psychological consequences for patients.

4. The evidence of the clinical benefit is detectable at the 1st month.

5. The clinical benefit is very stable at 2 years of F U.

6. There isn't any contraindication.

THANKS FOR YOUR ATTENTION

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