

SILENT MYOCARDIAL ISCHEMIA HISTORY

Since Heberden –
“angina pectoris” pain in the chest, a sole and
sine qua non condition for suspecting and
diagnosing myocardial ischemia
both if acute (acute MI)
or chronic (chronic AP)

איסכמיה שקטה - פרספקטיבה היסטורית והשיבות קלינית

הרצאה בקורס למתמחים בקרדיולוגיה
קיסריה, 8 בספטמבר 2004

MYOCARDIAL ISCHEMIA WHY SILENT? The “old” concepts.

Droste *et al.* 1983:
* Patients with silent ischemia have a
reduced pain perception
Cohn *et al.* 1983:
* Less myocardium at jeopardy?
Falcone *et al.* 1998:
* Decreased sensibility to pain in silent
ischemia patients

SILENT INFARCTION & ISCHEMIA HISTORY

Herrick 1912: Acute MI can be without pain
Master 1940: Exercise test can be positive without
chest pain
Phibbs *et al.* 1968: On exercise testing, 10% truly
silent, ie., not even dyspnea
Ellestad *et al.* 1968: On exercise testing >50% had
no pain
Kannel *et al.* 1970's: Unrecognized (silent)
myocardial infarction
Stern *et al.* 1973: Silent ischemic episodes on Holter
monitorings

SILENT MYOCARDIAL ISCHEMIA New concepts

Mazzone *et al.* JACC 2001:
* A different biochemical inflammatory system
activation is present in patients with silent
ischemia, who have an increased production of
inflammatory cytokines.
* These data suggest that the immune and
inflammatory system activation maybe crucial for
developing anginal symptoms.
* Without this, ischemia may remain silent.

SILENT MYOCARDIAL ISCHEMIA New concepts

Rosen *et al.* Ann Inter Med 1996:
*PET studies showed the frontal cortical activation is
necessary for the sensation of pain.
*In silent ischemia patients, this cortical activation
was significantly limited to the right frontal
region, the ventral cingulate cortex and the left
temporal pole.
* “Silent ischemia – a central problem”

SILENT MYOCARDIAL ISCHEMIA NEW CONCEPTS

Hinderliter *et al.* JACC (abstr) 2003

In patients with daily-life ischemic ST depression episodes on 48-hour Holter monitoring:

both the flow-mediated endothelium dependent and the nitroglycerin-induced endothelium independent vasodilatation were impaired.

SILENT MYOCARDIAL ISCHEMIA NEW CONCEPTS

Ikonomidis *et al.* JACC 2001 (abstr.):

- *The cytokine levels are high in patients with silent daily life episodes on Holter, inducing increased platelet activation.
- *The increased thrombin generation is observed only in the silent, but not in the mixed (silent + angiotonic) patients.
- * Aspirin reduces the increased thrombin generation, possibly due to its anticoagulant and antiinflammatory effects.

SILENT MYOCARDIAL ISCHEMIA INDUCED BY MENTAL STRESS

Sheps *et al.* Circulation 2002

In the PIMI study:

In 196 patients with coronary artery disease and exercise-induced ischemia:

- * New or worsened wall motion abnormalities during speech test – predicted death.
- * The presence of pain (or its absence) during the test had no influence on prognosis.

SILENT MYOCARDIAL ISCHEMIA DIAGNOSIS

Elhendy *et al.* Circulation, 2002:

Dobutamine stress SPECT imaging:

“Do not interpret the absence of angina in patients with reversible perfusion abnormalities as a predictor of a benign outcome: the risk of cardiac death or MI was similar with or without pain.”

SILENT MYOCARDIAL ISCHEMIA IN ASYMPTOMATIC PERSONS

Rywik *et al.* Circulation 2002:

In the BLSA study:

“well educated” “friendly” “comfortable” volunteers
Among the 1,448 who had exercised tests:

- * 472 had ST depression,
- * None had pain during the test.
- * The ST depression of >1mm independently predicted future coronary events.

SILENT MYOCARDIAL ISCHEMIA On exercise testing

Laukannen *et al.* JACC 2001:

- * Silent ischemia on exercise testing was a most powerful predictor of IHD in asymptomatic men, who presented with any of the standard coronary risk factors.
- Jones *et al.* JACC 2003 (abstr.)
- * In >10,000 patients with 2.6 years of follow-up, pre-test anginal symptoms were not predictive of risk for death.

SILENT MYOCARDIAL ISCHEMIA IN DIABETICS

Rutter *et al.* JACC 2002:

In 86 asymptomatic type 2 diabetics:

- * Silent ischemia during treadmill testing was the strongest independent predictor for future cardiac events.
- Next predictor was the presence of micro-albuminuria.

SILENT MYOCARDIAL ISCHEMIA IN DIABETICS

In asymptomatic diabetics the frequency of abnormal thallium scans was:

27%, in Wackers *et al.* JACC 2003 (abstr.)

25% in Rajagopalan *et al.* JACC 2003(abstr.)

SILENT MYOCARDIAL ISCHEMIA EARLY DETECTION

Blumenthal *et al.* Circulation, 2003:

Among 734 asymptomatic healthy persons, yet a brother or sister had premature coronary heart disease:

- * 153 had an abnormal thallium scintigram and 105 had a subsequent coronary arteriogram: 95% had coronary arteriosclerosis
- * These persons would benefit most from preventive therapy.

SILENT MYOCARDIAL ISCHEMIA IN DIABETICS

In asymptomatic diabetics:

Anand *et al.* JACC 2004 (abstr)

26% had positive coronary calcium score on EBT. Of them 40% had silent ischemia on perfusion imaging.

Sultan, *et al.* Diabetes Care, 2004

20% had randomly performed positive technetium sestamibi test.

SILENT MYOCARDIAL ISCHEMIA DURING MYOCARDIAL INFARCTION

Kannel 1998:

- * In spite of the increased awareness and improved diagnosis of silent coronary disease over the years, the incidence of unrecognized myocardial infarctions has so far not decreased.

SILENT MYOCARDIAL ISCHEMIA DYSPNEA vs. PAIN

Bergeron *et al.* JACC 2004

Over 3,000 pts with positive exercise echo:

15% had dyspnea only

67% had chest pain only

18% had both

- * Those with dyspnea only, had a higher likelihood of more future cardiac events than those with pain only.

SILENT MYOCARDIAL ISCHEMIA DO WE NEED THERAPY?

The ACIP study, Sharaf *et al.* JACC 1997

- * In silent ambulatory ischemic patients multivessel disease, severe proximal stenoses, complex plaques were frequently observed.
- These may explain the adverse outcome and the need for risk factor modifications in these patients.

SILENT MYOCARDIAL ISCHEMIA DURING ACUTE CORONARY SYNDROMES

Stern *et al.* Am J Geriatr Cardiol. 2004.

- * With advancing age the frequency of patients with ACS who are painless or have atypical symptoms only, increases:

<65 years	14%
65-74 years	21%
>75 years	32%
- * The painless/atypical symptom patients had an increased 7 day, 30 day and 1 year mortality

SILENT MYOCARDIAL ISCHEMIA THERAPY

Andrews *et al.* Circulation 1997:

Silent ischemic episodes were resolved by lowering of LDL cholesterol with statins, in 13 of 20 patients treated for 6 months reduction was observed.

SILENT PLAQUES/PLAQUE RUPTURES

- * Tuzcu *et al.* Circulation 2001
Atheromata in the coronary arteries may remain silent for decades, as demonstrated by consecutive IVUS studies.
- * Nissen, JACC, 2003
Most episodes of plaque rupture are silent; thus a metabolic approach should guide management.

SILENT MYOCARDIAL ISCHEMIA THERAPY

Deanfield *et al.* JACC 2002:

The CAPE II trial:

- When transient ischemia was detected on Holter monitoring, (irrespective of the presence or absence of pain) Amlodipine, alone or with Atenolol, produced superior ischemia reduction.

SILENT MYOCARDIAL ISCHEMIA THERAPY

The CAPTURE study, Patients after PTCA, Klotzwick *et al.* Circulation 1998:

Abciximab reduced the frequency of recurrent ischemic episodes on Holter. Recurrent ischemic episodes predicted MI or death.

SILENT MYOCARDIAL ISCHEMIA NEW THERAPIES (2)

- *ACE- inhibitors improve flow-mediated vasodilatation, counteract thrombosis, LDL oxidation, proliferation of vascular smooth muscle cells, etc.
Khalil *et al.* JACC 2001
- *Aspirin helps by its antiinflammatory effects
Ikonomidis *et al.* JACC 2001 (abstr.)

SILENT MYOCARDIAL ISCHEMIA NEW THERAPIES (1)

Aimed not to alleviate symptoms (which are none), but to improve outcome.

- * Amlodipine is slowing coronary arteriosclerosis
Pitt *et al.* Circulation 2002 (abstr.)
Vaughan *et al.* JACC 2000
- * Statins induce plaque stability, improve endothelial function, reverse coagulation and platelet abnormalities
Anderson *et al.* JACC 2000

Cont'd

SILENT MYOCARDIAL ISCHEMIA

Bergmann & Giedd's Editorial Comment on Zellweger's article: JACC July 2003
"Silent Ischemia: Unsafe at Any Time"

SILENT MYOCARDIAL ISCHEMIA AFTER SUCCESSFUL PCI AND STENTING

ZELLWEGER *et al.* JACC July 2003

Study in 356 patients: of the 81 patients with residual target vessel ischemia on perfusion scan, 62% were silent (no anginal symptoms)

Critical event rate was:

- 17% - no ischemia
- 32% - silent ischemia
- 51% - symptomatic ischemia

SILENT MYOCARDIAL ISCHEMIA Risks of Death

Framingham Heart Study
Fox *et al.* Circulation 2004

- Cohorts from 1950-1999
- 20% of nonsudden cardiac deaths
- 48% of sudden cardiac deaths
- were in subjects free of antecedent clinically detected coronary heart disease

SILENT MYOCARDIAL ISCHEMIA NEW TESTS

- *PET scanning – for metabolic changes
 - *Computed tomography–for coronary calcium
Hoff *et al.* JACC 2003
 - *Combined PET - CT technique
Namdor, JACC 2003
 - *MRI for assesment of subclinical disease – Fayad *et al.* Review in Circulation 2002
 - *Ischemia-modified albumin - de Filippi, Kontos, JACC 2003 (abstr.)
- Will they close the "detection gap" ?
Are they cost-effective ?

SILENT MYOCARDIAL ISCHEMIA CONCLUSIONS IN 2004 (2)

- Testing for the asymptomatic patient should be “judiciously” applied, and mainly for individuals with risk factors (ACC-AHA Guidelines).
- There are good prospects, that with the newly introduced cardiac therapies, the course of ischemic heart disease, even if asymptomatic, can be improved.

SILENT MYOCARDIAL ISCHEMIA CONCLUSIONS IN 2004 (1)

- We have new data now on the deleterious effect of silent ischemia.
- We have better ways now to detect such silent (hidden, preclinical or occult) coronary artery disease.

Cont'd

... ונסיים עם סיימון וגרפנקל

The Sounds of Silence

"Hear my words that I might teach you...
... Silence as a cancer grows"

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