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)

SILENT MYOCARDIAL ISCHEMIA

New concepts

Mazzon 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.

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. 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.

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 + anginotic) 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.

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.

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 microalbuminuria.

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

* 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, Klootwisk 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 (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

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
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
  de Filippi, Kontos, JACC 2003 (abstr.)
  Will they close the "detection gap"?
  Are they cost-effective?

* Computed tomography – for coronary calcium
  Hoff et al. JACC 2003

* Combined PET-CT technique
  Namdor, JACC 2003

* MRI for assessment of subclinical disease – Fayad et al. Review in Circulation 2002

Bergmann & Giedd’s Editorial Comment on Zellweger’s article: JACC July 2003
“Silent Ischemia: Unsafe at Any Time”
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.