sion on ECG and a planar thallium (TL) perfusion defect during maximal treadmill testing was a potent independent predictor of future coronary events (CE) over a mean follow-up of 4.7 years in 407 asymptomatic volunteers aged 40–96 years (mean = 60) from the Baltimore Longitudinal Study of Aging (Circulation 1990;81:428). To determine the longer term prognostic significance of SI in this population, we examined the incidence and predictors of CE over a mean follow-up of 9.2 years. A total of 61 CE developed (32 cases of new angina pectoris, 17 non-fatal myocardial infarctions, 12 cardiac deaths). Events occurred in 15% of subjects with both negative ECG and TL responses, 30% of those with either a positive ECG or TL result, and 48% of those in whom both tests were positive ($p < 0.001$). By proportional hazards analysis, older age (relative risk [RR] = 2.3 per 15 year increment), male gender (RR = 2.2), hypertension (RR = 2.5), shorter exercise duration (RR = 0.91 per minute), and a concordant positive ECG and TL response (RR = 2.5) were significant independent predictors of CE. Hard CE, i.e. myocardial infarction or cardiac death, were predicted by older age (RR = 3.1), male gender (RR = 2.8), current smoking (RR = 3.0), plasma cholesterol (RR = 1.01 per mg/dl), fasting plasma glucose (RR = 1.01 per mg/dl) and a concordant positive ECG and TL (RR = 3.4). Thus, at a mean follow-up of over 9 years, exercise-induced SI remains a potent predictor of future CE in apparently healthy volunteers, independent of conventional risk factors.

2:15

716-2 Myocardial Ischemia Induced by Mental Stress Predicts a Poorer Prognosis in Patients with Coronary Artery Disease

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Although it is clear that mental distress elicits myocardial ischemia, the relationship of mental stress-induced myocardial ischemia (MSI) to prognosis in patients with CAD is unknown. 130 CAD patients with stable angina underwent a series of mental stress and exercise tests using radionuclide ventriculography and standard 12-lead ECG, then were followed for one year. Myocardial ischemia was defined as a new wall-motion abnormality, ejection fraction (EF) decrease >5%, or ST-segment depression ≥0.1 mV from baseline. Cardiac events (CE) were defined as CABG, PTCA, unstable angina admission requiring angiography (UA), nonfatal myocardial infarction (NMI), and cardiac death.

Of the 130 patients, 50% had both MSI and exercise-induced ischemia (ESI), 18% experienced MSI alone, and 18% had ESI alone. Of the 117 patients achieving one-year follow-up, 20 suffered various CE: 19 had UA, 9 had PTCA, 4 had CABG, 2 had NMI, and 1 died. Logistic regression analyses were performed to examine the possible relationships among age, baseline systolic blood pressure (SBP), baseline EF, MSI, ESI and CE. Results showed that baseline SBP and MSI, but not ESI, were univariable predictors of CE (see Table). Multivariable logistic models were then used, with age, baseline SBP, and baseline EF as covariables, to determine if the addition of either MSI or ESI provided prognostic information in predicting CE. MSI was independently predictive of CE after adjustment for the covariables.

Univariable	X^2	p Value
Age	0.49	0.48
Baseline SBP	5.32	0.02
Baseline EF	0.001	0.97
MSI	4.77	0.03
ESI	0.48	0.49

In *conclusion*, MSI may have greater prognostic potential than ESI for a specific population of CAD patients.

2:30

716-3 Prognostic Significance of Transient Ischemic Episodes; Response to Treatment Shows Improved Prognosis. Results of the TIBBS-follow-up

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TIBBS is a multi-center trial in which patients with stable angina pectoris and a positive exercise ECG were selected for randomized medical treatment when they showed transient ischemic episodes (TIE) on 48-h-ambulatory ECG monitoring (AECG). The follow-up study at 1 year investigates the implications for the prognosis of the patients.

Of 621 patients screened on the basis of history of stable angina pectoris and positive exercise ECG, 565 had technically sufficient 48-h-AECG, and 193 showed 0 or 1 TIE (1 mm, 1 min, 1 min. apart) 152 showed 2–6 TIE, 153 showed >6 TIE. Follow-up at one year was >90% complete. Physicians in charge of the patients were unaware of the results of AECG.

Patients with 0–1 TIE had less cardiac events (death, AMI, CABG, PTCA, hospitalisation for unstable A.p.) at one year (11.9%) compared to patients with 2–6 TIE (+26.3%) or patients with >6 TIE (30.5%) ($p < 0.001$).

Of 268 randomized patients, those 90 patients who had shown response to medical treatment with 100% reduction of TIE during the 8-week active phase of TIBBS (treatment with Bisoprolol 10 mg/20 mg o.d. vs. Nifedipin slow release 2 × 20/2 × 40 mg b.i.d.) had better prognosis: 17.8% events compared to 30.6% events in patients with less or no reduction of TIE ($p < 0.025$). Patients who responded with 50% reduction of TIE showed only a trend towards reduced risk of events: 23.3% vs 30.9% ($p < 0.117$).

Conclusion: AECG in patients with stable angina pectoris and positive exercise ECG selects patients with increased risk of cardiac events. Patients who do not respond to medical treatment with reduction of TIE are at further increased risk.

2:45

716-4 Placebo Treatment Reduces Both the Number of Ischemic Episodes and Duration of Ambulatory Silent Myocardial Ischemia in Patients with Stable Angina Pectoris

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Ambulatory silent myocardial ischemia occurs frequently in patients with stable exertional angina pectoris. It is widely accepted that a medication has antiischemic effects if it reduces either the number or the duration of silent myocardial ischemic episodes in comparison to pretreatment values. Effect of monotherapy with placebo on silent myocardial ischemia in 33 patients who took part in a parallel group investigational drug study and were assigned to the placebo arm of the study form the basis of this investigation. After discontinuation of all antianginal medications patients received two weeks of single blind placebo treatment followed by four weeks of double blind placebo treatment. Ambulatory holter monitoring was performed for 48 hours after two weeks of single blind placebo treatment and again after 4 weeks of double blind placebo treatment. The median value of silent myocardial ischemia attack rate during single blind placebo treatment was 7.2 episodes per 48 hours and decreased during double blind placebo treatment to a median rate of 3.1 episodes per 48 hours ($P < 0.004$; 95% CI, −5.41, −1.0). Similarly the duration of silent myocardial ischemic episodes decreased by a median of 16.1 minutes per 48 hours ($P < 0.001$; 95% CI, −35.7, −6.2 minutes) during double blind placebo treatment from a median value of 24.8 minutes per 48 hours during single blind placebo treatment. *Conclusion:* placebo monotherapy had a marked influence on ambulatory silent myocardial ischemia and reduced both the duration and number of silent myocardial ischemic episodes in patients with stable angina pectoris. These findings have important implications for interpretation of studies in which the effects of active treatment on silent myocardial ischemia are compared to baseline pretreatment values.

3:00

716-5 Treatment of Silent Ischemia in Unstable Angina: A Randomized Comparison of Sustained-release Verapamil Versus Metoprolol

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Silent ischemia is a frequent finding in pts with unstable angina (UA) which portends a poor prognosis. We compared the efficacy of sustained-release verapamil and metoprolol (M) in the treatment of silent ischemia and studied whether detection of silent ischemia was related to unfavourable outcomes irrespective of treatments. Consecutive pts with UA were randomized to therapy with verapamil or metoprolol and all received nitrates, heparin and aspirin by protocol. ST shift (≥1 mm, 60–80 msec after J point and separated by ≥1 min from other episodes) was detected on 72 hr Holter monitoring (leads AVF, V_2, V_5).

There were 37 pts in the verapamil (218 ± 89 mg/day) and 40 pts in the metoprolol (88 ± 24 mg/day) group. The two groups were similar in baseline characteristics. Recurrent angina episodes were more frequent in the verapamil group (29 vs 12, $p = 0.05$). Overall 26 (34%) pts had 100 episodes of ST shift, 75% ST↓, 95% silent. Comparing the verapamil vs metoprolol group, there was no difference in the frequency (51 vs 49 episodes, $p = 0.9$) and duration (23 ± 48 min vs 18 ± 50 min, $p = 0.6$) of ST shift episodes. 20 in-hospital unfavourable outcomes (5-MI, 15-urgent revascularization) were distributed equally between verapamil and metoprolol pts. However, pts with unfavourable outcomes irrespective of treatment more often had ST shift (50% vs 28%, $p = 0.07$), and with longer duration (40 ± 69 vs 13 ± 38 min, $p = 0.03$). Pts with ST shift ≥60 min had a 60% probability of unfavourable outcome compared with 33% for ST shift between 1–59 min and 20% for pts without ST shift ($p = 0.04$).