available regarding the prognostic importance of SI in the elderly. Therefore, we prospectively evaluated the prognostic significance of SI during Holter monitoring (HM) in elderly pts (≥65 years) with stable angina and proved CAD. The findings were then compared to those observed in a similar but younger (<65 yrs age) group of pts with stable CAD. All pts underwent maximal exercise treadmill test (ETT) and HM for 24–48 hours, while receiving their usual antianginal drugs. Pts were followed every 3 months and all fatal and nonfatal events were recorded. The study population consisted of two groups: pts < 65 (Gr 1) and pts ≥ 65 (Gr 2) years old. The two groups were similar in their clinical characteristics, risk factors for CAD, antianginal drugs, and angiographic findings. Compared to Gr 1, the Gr 2 pts had a significantly earlier onset of ischemia ($p < 0.01$) and achieved a significantly greater peak systolic blood pressure ($p < 0.02$) during ETT. Kaplan-Meier survival analysis revealed a significant difference in the outcome of the two groups. The Gr 1 pts with SI during HM had a nonsignificant increase in mortality (2/16, 12.5% vs. 1/19, 5.3%) compared to pts without SI. In contrast, elderly (Gr 2) pts with SI during HM had an eightfold increase in the risk of cardiac death (7/23, 30.4% mortality vs. 1/28, 3.6%, $p = 0.009$) compared to elderly pts without SI. Multivariate Cox regression analysis of clinical variables, angiographic findings, ETT parameters, and ischemia during HM, revealed the presence of SI on HM as the most powerful and independent predictor ($p = 0.006$) of cardiac death in the elderly.

Conclusion: The findings of our study clearly demonstrated that in the elderly pts, silent ischemia during daily life is associated with poor prognosis and a significantly increased risk of cardiac death. The adverse outcome associated with SI was noted despite antianginal drug therapy effective in controlling symptoms suggesting the need for more aggressive therapeutic interventions.

1015-71 Lower Adenosine Levels During Early Ischemia: Cause of Increased Injury in the Aging Heart?

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Myocardial injury following ischemia and reperfusion is increased in the aging heart, including in the aging 24 mo Fischer 344 rat (mean survival 29 mo) compared to the Fischer 344 adult (6 mo). Adenosine (ADO) has been increasingly appreciated as a cardioprotective agent in myocardial ischemia. We hypothesized that a potential mechanism of the increased injury in the aging heart is decreased production of ADO in response to ischemia. Isolated buffer perfused (glucose 5 mM — insulin 5 μ/l) hearts from aging and adult Fischer 344 rats were subjected to stop-flow ischemia for either 2, 5, 10, 15 or 25 min after a 15 min equilibration phase. ADO and hypoxanthine (HX) were measured by HPLC. Tissue total adenylates, ATP, glycogen and lactate were measured.

	Pre-ischemia (n = 5)	Ischemia 2 min (n = 5)	5 min (n = 6)	10 min (n = 6)	15 min (n = 5)	25 min (n = 5)
ADO 6 mo	0.2 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	2.2 ± 0.2	3.7 ± 0.6	4.5 ± 0.3
24 mo	0.2 ± 0.1	0.5 ± 0.1	0.3 ± 0.1*	1.1 ± 0.3*	2.1 ± 0.3*	3.5 ± 0.4
HX 6 mo	2.0 ± 0.2	1.6 ± 0.2	2.3 ± 0.3	2.2 ± 0.1	2.5 ± 0.2	2.8 ± 0.2
24 mo	1.9 ± 0.2	1.4 ± 0.1	1.4 ± 0.2*	2.1 ± 0.2	2.2 ± 0.8	3.5 ± 0.3

(Mean ± SE, nmol/mg protein), *$p < 0.05$ vs 6 mo

ADO levels were 50% lower in the aging heart at 5 and 10 min, remained depressed at 15 min and had not fully equalized to adult levels by 25 min of ischemia. HX was decreased at 5 min, consistent with decreased ADO production at that time. The change in total adenylate pool was similar in both groups. The decrease in tissue glycogen and increase in lactate were similar during ischemia in both groups, suggesting comparable glycolytic activity. ATP levels were decreased in aging hearts at 5 min (11.1 ± 2.3 vs 18.7 ± 1.9 nmol/mg protein), but reached levels similar to adult hearts as ischemia progressed.

Thus, decreased ADO levels during early ischemia may reflect reduced production of ADO in the aging heart, and increase the susceptibility of the aging heart to damage during ischemia and reperfusion.

1015-72 Elevated Plasma Homocysteine: An Important Independent Risk Factor for Coronary Artery Disease in the Elderly

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Background: High plasma homocysteine (HCY) concentration is an established risk factor for premature vascular disease which can be reduced using vitamin therapy. The role of increased homocysteine as a coronary risk factor in the elderly, however, remains uncertain.

Methods: We studied 228 patients with angiographically documented coronary disease (≥70% stenosis in at least one major epicardial vessel). These included 136 patients less than, and 92 greater than 65 years old. Patients were compared to 223 healthy controls 199 (<65) and 24 (>65). The presence of traditional risk factors including hypertension, smoking, hypercholesterolemia and diabetes mellitus were noted. Total fasting plasma homocysteine was measured in all subjects. A gender-adjusted threshold for a high homocysteine level was defined as the 80th percentile for healthy controls (corresponding to a level of 11.7 μmol/L in women and 13.6 μmol/L in men).

Results:

	Age < 65		Age > 65	
	Patients	Controls	Patients	Controls
Homocysteine	12.2 ± 4.0*	11.0 ± 3.4	14.2 ± 4.6*	11.9 ± 3.6
High HCY (%)	33*	20	50†	25
Odds Ratios	2.0*	NA	2.9*	NA
Confidence Interval	1.2–3.2	NA	1.0–8.3	NA

*$p < 0.01$ vs controls, †$p < 0.03$

Conclusions: Homocysteine concentrations are elevated in patients with coronary artery disease older than 65 years in age. A high value confers an independent three-fold risk for coronary disease in this patient group. Accordingly, intervention studies designed to reduce plasma homocysteine levels should not exclude the elderly.

1015-73 Relationship Between Homocyst(e)ine, Vitamin B12 and Cardiac Disease in the Elderly

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Elevated plasma homocyst(e)ine (HCS) is an independent risk factor for coronary artery disease (CAD) among middle aged adults. Moveover, HCS also increases with age. This study assessed plasma HCS among 384 elderly (ages 73 ± 7 y) patients undergoing coronary angiography. The degree of CAD was scored using proximal and diffuse (Freisenger) indices. Plasma HCS, serum Vitamin B12 and folate and left ventricular ejection fraction (LVEF) were measured and risk factors for CAD were recorded. There was no apparent correlation between plasma HCS and extent of CAD after adjusting for age. Nine percent of patients (pts) had Vitamin B12 deficiency (B12 def), ie. Vitamin B12. < 300 pg/ml as well as HCS > 16 nmol/ml. LVEF for the 32 B12 def pts = 40.5% was significantly less than for 326 non B12 def pts with LVEF = 50.6% ($p < 0.001$). Significance remained after adjusting for proximal and Freisenger indices, history of smoking, diabetes, previous myocardial infarction, age and sex. (Adjusted Difference of LVEF = 8.2, 95% CI 2.6–13.8). In conclusion we did not find a significant correlation between plasma HCS and extent of CAD as assessed angiographically using proximal and diffuse indices. The data demonstrate that B12 def pts (with elevated HCS levels) had significantly lower LVEF than non B12 def pts. Whether low LVEF results in malabsorption of Vitamin B12 and B12 def or, conversely, whether B12 def and its marker, ie, elevated HCS, depress LVEF, warrants further investigation.

1015-74 Ciradian Variation of Silent Myocardial Ischemia is Abolished by Propranolol

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A prospective study investigated whether there is a circadian variation of silent ischemia (SI) in elderly patients (pts) with heart disease before and after propranolol and no antiarrhythmic (AA) drug. Follow-up 24-hour ambulatory electrocardiograms were obtained at a median of 6 months (range 2 to 12) in 221 elderly pts, mean age 81 ± 8 years, with heart disease (64% with prior myocardial infarction and 36% with hypertensive heart disease) and complex ventricular arrhythmias randomized to propranolol 85 ± 28 mg daily (112 pts) or to no AA drug (109 pts). SI was diagnosed if horizontal or downsloping ST-segment depression ≥1.0 mm below the level at rest occurred after the J point, lasted ≥1.0 minute, and was unassociated with angina. If ST-segment depression at rest occurred, an additional 2.0 mm of ischemic ST-segment depression below the level at rest at 80 ms after the J point was needed. SI was present before no AA drug in 35 of 109 pts (32%) and after no AA drug in 39 of 109 pts (36%) (p not significant). SI was present before propranolol in 42 of 112 pts (38%) and after propranolol in 27 of 112 pts (24%) ($p < 0.001$). Double harmonic regression models showed a significant circadian variation of the maximal amount of SI before no AA drug ($p = 0.002$, $R^2 = 58\%$, adjusted $R^2 = 49\%$), after no AA drug ($p = 0.009$, $R^2 = 50\%$, adjusted $R^2 = 39\%$), before propranolol ($p = 0.003$, $R^2 = 56\%$, adjusted $R^2 = 46\%$),