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Editorial Comment

Silent Myocardial Ischemia: Practical Application of Evolving Concepts*

EZRA A. AMSTERDAM, MD, FACC
Davis, California

Recent investigations have considerably increased our understanding of the challenging problem of silent myocardial ischemia. Its documentation and prevalence have been demonstrated and its prognostic significance in certain groups of patients with coronary artery disease has been recognized. It has been shown that silent ischemia is common throughout the entire spectrum of coronary artery disease, including stable angina (1), unstable angina (2), myocardial infarction (3) and occult coronary disease in apparently healthy, asymptomatic individuals (4). In addition to electrocardiographic (ECG) evidence of silent ischemia during exercise testing (5) and ambulatory monitoring (6), objective evidence of this phenomenon in patients with coronary disease has been provided by transient myocardial perfusion defects (7) and left ventricular wall motion abnormalities (8) unassociated with symptoms.

Prognostic significance of silent ischemia. Appreciation of the prognostic implications of silent myocardial ischemia has provided a rationale for its application in the management of certain subgroups of patients with coronary artery disease. Silent ischemia is recognized as a risk factor for coronary disease in totally asymptomatic persons (4) and this recognition has helped guide the individualized approach to patients in this group (9). The impact of silent ischemia on prognosis has been most clearly documented by postinfarction exercise testing in patients with recent myocardial infarction. Such testing has shown that impaired survival is related to ischemia irrespective of the presence or absence of associated symptoms (10). These findings are now widely applied to risk stratification and management of patients after myocardial infarction. Subsequent studies (2) have implicated silent ischemia as a risk factor for future coronary events in patients with unstable angina. Most recently, the initial report of Stern and Tzivoni (11), suggesting the prognostic importance of silent ischemia in patients with stable angina, has been extended by several studies indicating that silent ischemia detected in this group by exercise stress (12) or ambulatory monitoring (13,14) is associated with extensive coronary artery disease (12,13) and an increased rate of coronary events (14).

The present study. In this issue of the Journal, Mulcahy and colleagues (15) address aspects of silent ischemia that are less well defined and have stimulated controversy: 1) the relation between treadmill exercise testing and ambulatory ECG monitoring in the detection of ischemia; and 2) the mechanisms of symptomatic versus asymptomatic ischemia. In their carefully performed study of 277 patients with documented coronary disease, Mulcahy et al. found that >90% of ischemic episodes detected by ambulatory ECG monitoring occurred in patients with a positive exercist test, which was also strongly correlated with both the frequency and the duration of ischemic episodes on ambulatory ECG monitoring that were silent or symptomatic in patients who were and were not receiving antianginal therapy. On the basis of these results, the authors conclude that "there is little indication to perform ambulatory ST segment monitoring in patients with a negative exercise test, except in patients who have a history suggestive of coronary artery spasm." The authors agree with previous findings that ischemia during ambulatory ECG monitoring is associated with a lower heart rate than is ischemia with exercise (16), but they proffer alternatives to the frequently proposed hypothesis of coronary flow reduction (16) as the basis for silent ischemia.

Role of exercise testing versus ambulatory ECG monitoring. Mulcahy et al. (15) extend data from previous studies indicating that the great majority of patients with ischemia detected during ambulatory ECG monitoring can be identified by ischemia on exercise testing (6,16–18). These studies also show that, except in patients with coronary spasm, ischemia on ambulatory monitoring is distinctly unusual when exercise does not induce ischemia or when ischemia is present only on maximal exertion. Indeed, <10% of patients with ischemia would have been missed by Mulcahy's group if only exercise testing had been utilized, and an even smaller proportion would have been missed had those with coronary spasm been excluded. The study of Mulcahy et al. is the largest to compare exercise testing and ambulatory monitoring and they have demonstrated the applicability of their findings in terms of multiple clinical variables. The strong correlation between ischemia during exercise testing and that during daily activities supports their view that increased coronary vasomotor tone may be overemphasized as a singular mechanism for ischemia during the latter

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From the Division of Cardiovascular Medicine, University of California, Davis, Medical Center, Davis, California.

Address for reprints: Ezra A. Amsterdam, MD, University of California, Davis, Medical Center, Division of Cardiovascular Medicine, 4301 X Street, Room 2050 POB, Sacramento, California 95817.

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circumstances, despite consistent demonstration of a lower heart rate during ischemia detected by ambulatory monitoring compared with exercise. Alternative explanations include an increase in other hemodynamic variables that could augment myocardial oxygen demand (19) and methodologic factors such as failure to detect the precise heart rate at the onset of ischemia during exercise stress. However, it is noteworthy that the heart rate-pressure product is lower during nonexertional stress-induced ischemia than during exercise (20) and positron emission tomographic findings are consistent with reduction of myocardial perfusion during nonexertional ischemia (21). Further elucidation of the mechanisms of ischemia during daily activity and the significance of the heart rate differential in relation to exercise-induced ischemia must await sophisticated studies with the capacity to monitor multiple determinants of myocardial oxygen demand and to assess coronary flow in larger numbers of patients.

Conclusions. Although in most instances ambulatory ECG monitoring adds little to the data obtained from exercise testing in the detection of ischemia, it may provide important additional information. Thus, in patients with stable coronary artery disease and a positive exercise test, prolonged cumulative ischemia on ambulatory monitoring has recently identified extensive coronary disease (13) and an adverse prognosis (14). In addition, the value of ambulatory ECG monitoring is established in determining the relation of ischemia to specific activities, the frequency and total duration of ischemia, the effect of therapy on total ischemic activity and the probability of coronary artery spasm. Although further investigation is needed to clarify the indications for several of the many applications of ambulatory ECG monitoring in assessing ischemia, current studies are providing a rational basis for its more optimal utilization in patients with coronary artery disease.

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