Editorial Comment

Silent Ischemia, Ventricular Arrhythmia and Sudden Cardiac Death*

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Sudden cardiac death continues to be the most frequent cause of mortality in patients with coronary artery disease despite the many recent advances in the management of ischemic heart disease. Many studies have reported that ventricular arrhythmia, particularly runs of nonsustained ventricular tachycardia documented on ambulatory electrocardiographic (ECG) monitoring, is an independent risk factor for sudden death. In most cases, sudden death is the result of sustained ventricular tachycardia (1,2).

Silent ischemia, ventricular arrhythmia and sudden death. There are substantial animal data showing that ventricular tachyarrhythmias are often provoked by acute ischemia (3). These data are supported by clinical observations of an increased incidence of such arrhythmias in association with acute myocardial infarction (4) or during transient ischemia such as occurs with coronary vasospasm (5). However, the vast majority of patients who die suddenly do not have symptoms of active ischemia immediately before the event, and their sudden death does not usually occur during physical activity, when silent or symptomatic ischemia is likely to be present (6). It has been suggested (7) that in such patients the ventricular tachyarrhythmia is the result of silent or asymptomatic ischemia. The supporting evidence has been largely circumstantial, derived from a few studies (8,9) that noted a relation between the occurrence and perhaps the complexity of ventricular arrhythmia and symptomatic or asymptomatic ST segment depression, an indicator of ischemia, in some patients with coronary artery disease. However, these data are not conclusive because it has also been reported (10) that ischemia-related arrhythmia occurs only in patients who have ventricular premature beats in baseline studies, and whose ischemic episodes are not usually associated with complex or repetitive arrhythmias. Other suggestive, but not conclusive, data come from the observation (11) of a circadian pattern of silent ischemia, with the greatest frequency of asymptomatic ST depression occurring between 6 AM and 12 PM. A circadian pattern of sudden death, with an increased incidence during the same hours, has also been observed (12). Additional support comes from the finding (7) that many survivors of sudden cardiac death have asymptomatic ST segment changes during exercise in association with new or worsening wall motion abnormalities indicating silent ischemia. Finally, patients with coronary artery disease, particularly those with three vessel disease, who have silent ischemia have more cardiac events and a higher mortality rate than do those with symptomatic ischemia (13). Unfortunately, these observations do not necessarily imply a causal relation among silent ischemia, ventricular arrhythmia and sudden death but may reflect only an irrelevant association.

The present study. In contrast to this evidence, a few studies (14) have found no relation between silent ischemia and ventricular arrhythmia. This was also the conclusion of Hausmann et al. (15) in their report in this issue of the Journal. In their study 97 patients with documented coronary artery disease underwent ambulatory ECG monitoring to establish the presence of ventricular arrhythmia as well as ST segment shifts. Symptoms accompanied 118 (21%) of the 573 ischemic episodes and the remaining 455 episodes were asymptomatic. Ventricular arrhythmia was observed in only 5% of the ischemic episodes, which involved 10% of patients. Even in these 10% of patients, only 30% of the ischemic episodes (82% of which were silent) were associated with ventricular arrhythmia. The percent of episodes of asymptomatic ST segment depression was the same in patients with and without ischemia-related ventricular arrhythmias. As in previous studies, the majority (60%) of all ischemic episodes occurred between 6 AM and 12 PM.

The results of this study support the conclusion that silent ischemia plays only a limited role in provoking ventricular arrhythmias and perhaps sudden cardiac death, because ischemia-related arrhythmia was documented in only a small number of patients and in association with only a minority of episodes of ST segment depression. However, there are a number of caveats. Only 46% of the patients in this study had ≥2 days of ambulatory ECG monitoring, and the daily reproducibility of ventricular arrhythmia was not commented on. In the remaining patients who had only 1 day of monitoring, variability of arrhythmia cannot be established. Left ventricular ejection fraction averaged 61%, and it was <40% in only three patients. It is possible that there is a relation between silent ischemia and ventricular arrhythmia in patients with left ventricular dysfunction and congestive heart failure, but this cannot be established from this study.

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An important concern is the definition of ischemia-mediated arrhythmia, which in contrast to previous studies included arrhythmias occurring within 5 min preceding an ischemic episode. This presents a problem because the time course of ST segment depression in relation to the development of ischemia is uncertain, and it is not clear that arrhythmia that occurs before ST segment depression is the result of ischemia.

Prognostic significance. A more basic concern is whether the development of spontaneous ventricular arrhythmia during either silent or symptomatic ischemia is of prognostic importance. It is certainly possible that such arrhythmia is only an associated finding in patients with coronary artery disease and is not mediated or induced by active ischemia. A more important question is whether ventricular arrhythmia occurring during overt or silent ischemia is causally related to the precipitation of ventricular tachycardia or fibrillation and sudden cardiac death, but neither this study nor others have addressed this issue. An important area of research is how best to clinically assess the electrical stability of the myocardium and its ability to generate and sustain a ventricular tachyarrhythmia whether or not ischemia is present. It is unlikely that ventricular premature beats or even isolated runs of nonsustained ventricular tachyarrhythmias are markers for such instability, because their presence and frequency are highly variable in patients with heart disease. They are perhaps only an associated epiphenomenon in such patients.

Clinical implications. The lack of association between silent or overt ischemia, ventricular arrhythmia and, probably, sudden cardiac death is not unexpected. Studies of survivors of sudden death have generally not observed any relation between the onset of ventricular tachyarrhythmia and physical exertion (6). Most often, sudden death occurs during relative inactivity and without preceding symptoms of angina. The majority of studies in which patients were wearing an ambulatory ECG monitor when sudden death occurred have not demonstrated ST segment changes before the onset of ventricular tachyarrhythmia (16). During exercise testing there is no definite association between symptomatic or asymptomatic ST segment changes and ventricular arrhythmia (17). Moreover, sustained ventricular tachyarrhythmia rarely occurs during exercise testing in patients with known coronary artery disease, even when ST segment depression is present (18,19).

The absence of definite evidence that silent ischemia plays an important role in the genesis of ventricular arrhythmia and sudden death does not necessarily mean that no relation exists. A causal link may be present in some patients, but there have been no studies in which adequate techniques have been used to clearly establish such a relation. Some measure for evaluating underlying electrical instability with and without ischemia is necessary. Further investigation, perhaps utilizing electrophysiologic testing or newer ECG signal processing techniques, might provide these important data, establishing a link that is now elusive.

References