

**THE CORRELATION OF SILENT ISCHEMIA IN POST
INFARCTION PATIENTS TO THE PROGNOSTIC
DETERMINANTS OF CORONARY ARTERY DISEASE**

Thesis

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**This Work is Dedicated
To My Wife**



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INTRODUCTION

The cardinal manifestation of coronary artery disease traditionally has been considered to be the patient's description of chest pain and related symptoms. It is now clear, however, that such subjective complaints provide limited information relative to the presence of transient ischemia myocardial (Quyyumi et al., 1985) and an individual patient's prognosis (Gottlieb et al., 1986). One reason for this dilemma is that transient ischemia is not always painful. In fact recent studies indicate that silent myocardial ischemia may be the most common form of myocardial ischemia that occur during daily life in patients with most if not all, forms of coronary disease.

Asymptomatic subjects with proven coronary artery disease, including those with no previous manifestations of coronary heart disease and those with previous myocardial infarction, have silent ischemic episodes during daily activity. Patients with all forms of angina stable effort and unstable rest angina and those with coronary artery spasm have very frequent episodes of silent myocardial ischemia during ordinary activity.

This article indicates that silent ischemia had definite prognostic implication in both symptomatic and asymptomatic

patients with coronary artery disease. Patients surviving an acute myocardial infarction are at a particular high risk if they show evidence of myocardial disease. At present, many noninvasive diagnostic modalities are available for evaluation of symptomatic and silent myocardial ischemia in such patients. Because as many as 30% of patients may become asymptomatic after myocardial infarction, physicians must be aggressive in evaluating their patients for the presence of silent myocardial ischemia. The presence of silent ischemia would help identify those patients at high risk of postinfarction complications. Future use of currently available therapeutic modalities directed toward treatment of total ischemic burden on the myocardium may help to lower morbidity and mortality in this patient by reducing the risk of subsequent cardiac events.

For this purpose we studied the clinical features, risk factors, ambulatory 24-hour Holter monitoring, stress ECG (electrocardiogram) and coronary angiographic data in patients with postinfarction silent ischemia versus those without ambulatory ST-segment changes during daily activities.

The aim of this work is to evaluate silent myocardial ischemia in patients with previous myocardial infarction and assessment of the relation of ambulatory ischemia detected by 24-hour Holter monitoring to known predictors of severity of

coronary artery disease on exercise stress testing and coronary angiography. This study is trying to formulate a future working plane for the stratification and management of this important sector of postinfarction patients an almost everyday cardiology practice.

PART I
REVIEW OF LITERATURE

SILENT MYOCARDIAL ISCHEMIA AND SCOPE OF THE PROBLEM

Coronary heart disease continues to be the most common cause of death and a major cause of disability despite major advances in diagnosis and treatment. Apparently healthy subjects who are totally asymptomatic or patients who seem to be doing well with controlled angina often present with acute myocardial infarction or sudden death. Some developments over the past decade have led to the suggestion that episodes of transient myocardial ischemia may link all of these varied clinical presentations.

Several hundred thousand apparently healthy people die each year because of ischemic heart disease, seemingly without warning. In these individuals, the heart's "warning system" dysfunctions or fails to be activated by an acute ischemic episodes. It is now recognized that such clinically silent myocardial ischemic episodes also occur in many patients with ischemic heart disease who do not die or have myocardial infarction (**Schaag and Pepine 1977**). This possibility had been suggested for years by autopsy findings of severe coronary artery disease in individuals who died of other causes (**Mason 1963**).

Review of the sequence of events known to occur during an ischemic episode reveals that the early portion of all ischemic episodes, manifested by profound biochemical, mechanical, and electrical alterations, is silent. Apparently, most ischemic episodes marked by objective alterations never evolve to a painful or symptomatic phase.

Accordingly silent myocardial ischemia may be defined as objective evidence for myocardial ischemia in the absence of angina or equivalent symptoms. Other terms used to describe this syndrome include asymptomatic, painless, and clinically unrecognized myocardial ischemia.

There are several areas that require qualification relative terminology. It is important to note that silent myocardial ischemia is not equivalent to asymptomatic coronary artery disease. For example, it is possible for a patient with prior myocardial infarction due to localized coronary artery disease to have neither angina nor objective evidence for ischemia because there is no area of potentially ischemic myocardium. Furthermore, silent myocardial ischemia is not analogous to an asymptomatic positive exercise test in an otherwise healthy person. The frequency of false-positive exercise test results in the generally healthy population is high, and most of these individuals do not have coronary artery disease (Froelicher et al., 1977).

Silent myocardial ischemia can be considered to occur in three general types of subjects according to **Cohn's study (1981)**. The patient who is totally asymptomatic but demonstrates silent myocardial ischemia is classified as type 1. One who has had a myocardial infarction but is now asymptomatic despite persistent ischemia is classified as type 2. A type 3 patient has both angina and silent myocardial ischemia. Estimating the prevalence of these clinical types provides important data to assess the significance of silent myocardial ischemia, as described in the following paragraphs.

In type 1 patients, the studies of Erikssen and Thaulow in Norway (1984) have been especially useful. These investigators screened 2,014 male office workers between the ages of 40 and 59. Eighty-six of the men had positive exercise tests, and 50 of 86 had coronary artery disease documented by coronary arteriography. In another large scale study, **Froelicher et al. (1976)** reported significant coronary artery disease (also defined by coronary arteriography) in 34 (2.4%) of 1,290 airmen. Another, smaller study reported an even higher (9.3%) in 129 male factory workers (**Langou et al., 1980**).

In type 2 patients, the exercise test has also proved valuable. Not all postinfarction patients are suitable for such testing because of concomitant angina, serious arrhythmias, or congestive heart failure. **Chen (1986)** reported that about 20%

of all the postinfarction patients who can exercise will have silent ischemia. The frequency of silent myocardial ischemia on Holter monitoring in patients who cannot exercise has been reported to be 18% (Gottlieb et al., 1986).

In type 3 patients, the Holter monitor has proved to be an effective way of documenting the frequency of out of hospital events. In several studies (Deanfield et al., 1983, Quyyumi et al., 1985, Tazivoni et al., 1986) from different centers in which patients with angina were monitored for 24 to 96 hours, the number with at least one episode of silent ischemia ranged from 30% to 100%. Patients with ischemic events had either totally silent ischemia or a combination of painful and silent events. Similarly, in two studies of patients with unstable angina, 29 of 43, (Gottlieb et al., 1986) and 37 of 70 (Nademanee et al., 1987) had silent ischemic events on their Holter recordings after their admitting complaints had been treated and their condition stabilized.

In conclusion silent myocardial ischemia represents a cardiovascular problem of substantial scope and magnitude. This problem is present in asymptomatic subjects as well as those with known coronary artery disease. Recognition of silent ischemia, in addition to symptomatic ischemia, provides a more complete picture of the ischemic process in any given patient with coronary heart disease. The reasons why silent

ischemia is silent and its prognostic significance and detection are only a few of the many questions remaining to be answered. This study will address selected aspects of this important growing concern.

POSSIBLE MECHANISMS RESPONSIBLE FOR SILENT MYOCARDIAL ISCHEMIA

The pathophysiologic mechanism of angina pectoris and why pain is present or absent during episodes of myocardial ischemia is not well understood. Two mechanisms are under investigation. One theory holds that there is a lesser amount of ischemic myocardium in painless episodes compared with painful ones. A second theory involves alteration in the patient's sensibility to pain, either centrally or peripherally.

The pathogenesis of myocardial ischemia has been recently reviewed in connection with the various angina syndromes and specifically with regard to silent myocardial ischemia (**Maseri and Louis, 1987 and Dehmer, 1987**). There are few aspects of the pathogenesis of ischemia in general that appear likely to provide insight into silent ischemia in particular. One is the formulation that the onset of myocardial ischemia initiates a sequence of manifestations. The appearance of any given manifestation in the sequence is dependent both on whether it occurs early or late in the sequence and on the duration or severity of the ischemia (**Cohn, 1986 and Hill and Pepine, 1986**). Because ECG changes and the development of angina are successively later manifestations, it is postulated that ischemia of sufficient degree to produce