Symptoms Other Than Chest Pain May Be Important in the Diagnosis of “Silent Ischemia,” or “The Sounds of Silence”

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“Silence like a cancer grows.”
Paul Simon, ©1964

Case presentation: In 2001, on routine testing, a 58-year-old man with a family history of heart disease had an above-normal cholesterol level and high blood pressure. His medical recommendation was to eat fewer fast foods and to take anticholesterol medication, which was stopped when his cholesterol level became lower. His blood pressure problem was treated successfully. His stress test was successful, and he started to exercise 2 to 3 times per week, in addition to adopting the South Beach Diet. The patient did not complain about chest pain, and there was no recommendation for any further cardiac diagnostic testing. Acute shortness of breath and mild chest pain in 2004 prompted a coronary angiogram, which necessitated a triple-bypass surgery. The patient later expressed his opinion that people with family history, high cholesterol, and high blood pressure ought to consider an angiogram even if they don’t have symptoms.

Background
It is estimated that in the United States today, between 2 and 3 million people with stable coronary artery disease (CAD) have evidence of asymptomatic ischemia. It is accepted that ~20% of the nonsudden cardiac deaths and nearly half of the sudden cardiac deaths occur with preexisting but undiagnosed CAD. An important objective of contemporary clinical cardioiology, therefore, should be the uncovering of the silent and therefore unsuspected disease, with the hope of reducing thereby the incidence of cardiovascular events or even death in susceptible individuals. With this in mind, the American Heart Association Prevention V Conference proposed the use of office-based testing and additional noninvasive procedures in selected patients.

It has become accepted that the presence of 1 or more of the classic risk factors of CAD, even without typical chest pain, and conversely, typical chest pain even without risk factors necessitates cardiac evaluation. There is concern, however, about those relatively younger people who do not have diagnosed risk factors and who do not present with chest pain. Are there other subjective manifestations that can or may be a symptom for subclinical coronary atherosclerosis inducing myocardial ischemia? Are there expressions other than pain that are imperative to call to the attention of the patient, of the primary care physician, and even more so, of the clinical cardiologist regarding the possibility of the presence of silent myocardial ischemia, requiring further testing?

Dyspnea
Shortness of breath is frequently considered by a physician as not being a serious warning sign; it could be passed off as undue physical exertion, emotional arousal, or even as the result of a lung condition possibly induced by smoking. A direct connection between dyspnea and an ischemic myocardium is not fully recognized, and most frequently, this symptom is considered related to heart failure. Dyspnea alone, without chest pain, as a clear sign of a positive exercise test was described in 1968 by Phibbs and coworkers, who found this symptom alone in 25.6% of patients at the time of an ECG-positive exercise test, whereas classic anginal pain was experienced by only 17.3% of the examinees. In a large series of patients referred for evaluation of dyspnea, with ischemia on exercise echocardiography versus 19% who had chest pain. During a 3-year follow-up, death and

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(Circulation. 2005;111:e435-e437.)
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Circulation is available at http://www.circulationaha.org

DOI: 10.1161/CIRCULATIONAHA.105.550723
nonfatal infarction occurred significantly more often in patients with dyspnea than in those without. Hyperventilation may also be a “sound of silence,” because it was included among the atypical symptoms evaluated in an elderly population for angiographic CAD and was not different from typical anginal pain for predicting the presence of CAD in either gender.5

Breathlessness alone can be the presenting symptom even for acute coronary syndrome and was found to be present in 26% of patients in the EuroHeart data set.6 Brieger and coworkers7 found that among the 8.4% of the patients who presented without chest pain, nearly half of them had dyspnea only. The patients with dyspnea or with other painless presentations of unstable angina had greater morbidity and a higher mortality. We8 have shown that atypical manifestations of the acute coronary syndrome, including dyspnea, become significantly more frequent with advancing age.

Dyspnea in the Diabetic Patient
Diabetic patients with shortness of breath as the predominant symptom had a significantly worse outcome and a higher likelihood of ischemic abnormalities on perfusion single-photon emission computed tomography (SPECT) than those who had typical angina pectoris or who were asymptomatic.9 Di Carli and Hachamovitch10 discussed the dilemma of screening for occult CAD among asymptomatic diabetic patients and stressed the excellent yield of abnormal SPECT findings in the setting of dyspnea. Exertional dyspnea, however, is less specific for the diagnosis of ischemia in patients with chronic kidney disease, as pointed out by Gupta and coworkers,11 because it may be secondary to anemia, volume overload, and several other factors associated with renal failure.

Palpitations
A patient’s subjective feeling of rapid heartbeat, sometimes irregular, with a sense of trembling in the chest, experiencing what we call palpitations, may not be recognized by the physician as an indication of myocardial ischemia. This is despite the well-known notion that ischemia is a significant harbinger of cardiac arrhythmias, mainly of the ventricular variety,12 especially if a vasospastic mechanism is suspected to be the cause of silent myocardial ischemia.13 Ambulatory ECG monitoring has demonstrated an increase in arrhythmias during transient ischemic episodes14,15 and also that cardiac acceleration usually precedes and frequently continues during a transient silent episode.16 Tresch and Aronow17 stressed that cardiac arrhythmia may be a manifestation of myocardial ischemia in elderly patients. We know now that structural alterations occur in the transiently ischemic myocardium.18 Muscle fiber hypertrophy and increased interstitial nonmuscular tissue develop, especially in the endocardial layer, and the changed electrophysiological properties of the myocardium create an arrhythmia-prone milieu with life-threatening potential. Wit and coworkers19 demonstrated the marked influences of myocardial ischemia on the electrophysiological properties of the myocardial cell. Although this association between ischemia and arrhythmias appears obvious, there is no documentation that the perception of transient rapid or irregular heartbeats may be the sole expression of an otherwise silent ischemic episode.

Fatigue
A patient may complain of a sudden limitation in the ability to walk and of feeling “suddenly weak.” Braunwald20 considers fatigue to be “among the most common symptoms in patients with impaired cardiovascular function” and also “one of the most nonspecific of all symptoms.” He mentions, however, that fatigue may be a “possible” symptom that may precede or accompany an acute myocardial infarction. Thadani21 pointed out that the deterioration of the walking distance of a patient should call the attention of the physician to ischemia if associated with chest pain; without pain, however, this complaint will usually point to the diagnosis of heart failure. Fatigue in diabetic patients who are otherwise asymptomatic requires further testing for CAD, according to the American Diabetes Association recommendations.22 Despite the fact that coronary blood flow limitation that results in myocardial ischemia is evidently a good reason to feel “weak,” authoritative texts do not mention fatigue as a possible expression of a transient ischemic episode.

Erectile Dysfunction
This symptom may be a potential marker to identify diabetic patients who should be screened for silent CAD; the authors of a study on this subject23 also suggest that if silent CAD is suspected in diabetic patients, especially if additional cardiovascular risk factors are present, there is a need to perform an exercise ECG before treatment for erectile dysfunction is begun.

Genetics
Another important “sound” of harboring premature CAD may be perceived from careful listening to the family history of a person. A strong warning sign can be heard from the medical history of a patient’s parents, and the warning is even stronger if the doctor listens to the medical history of the patient’s siblings. Nasir and coworkers24 studied nearly 10,000 asymptomatic individuals, and the presence of premature coronary disease in a parent was associated in males with a 64% prevalence of CAD and an even higher prevalence (78%) if 1 sibling had the premature disease. The corresponding figures in females were 36% and 56%, respectively. This and other newly gained information may be additional instruments for the family risk score, applicable to population screening for identifying families at risk who are possibly amenable to intervention.25 One can only agree with O’Donnell26...
that even if genome-wide tests are available soon for genotyping or sequencing to identify disease-associated genetic variants, an accurate family history will likely still have an important role in clinical practice for risk prediction and prevention.

Guide for the Clinician

As the Prevention V Conference emphasized,4 risk assessment begins in the physician’s office. Whereas a patient may misunderstand the cause and significance of a vague or ambiguous cardiac sensation,27 the ear of the physician should not miss these “sounds” of ischemia, because this condition, if undiagnosed, will certainly prolong the occult period of the disease, possibly leading to serious consequences for the patient. Because many new diagnostic procedures are available today to diagnose CAD, they should be applied to a patient even in the absence of precordial pain if other symptoms are potentially suggestive of ischemia. These “sounds of silence” should be heard by us, even if they are only “whispered.” We should not miss using our advanced diagnostic and therapeutic possibilities and should not let silent ischemia “grow as cancer.”

Acknowledgments

The author thanks Dr Gilda Werman, Dr Robert Werman, and Liane Herman for their excellent editorial help.

References

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_Circulation._ 2005;111:e435-e437
doi: 10.1161/CIRCULATIONAHA.105.550723

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/111/24/e435

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