Exercise and ventricular ectopy: Relationship to coronary artery disease

Neil L. Coplan, M.D., and Gilbert W. Gleim, Ph.D. *New York, N.Y.*

Ventricular ectopy is a common finding during exercise testing. Ventricular premature depolarizations (VPDs) occur during exercise in patients with many different types of cardiac disease, including ischemic heart disease,[1-4] cardiomyopathy,[4] and mitral valve prolapse.[5,6] In addition, exercise-related ventricular ectopy (EVE) has been noted to occur in subjects with no clinical evidence of cardiac disease.[7-10] This report reviews the clinical significance of detecting EVE, with particular reference to ischemic heart disease.

EVE and diagnosis. EVE has been reported to occur in a large number of subjects without cardiac disease (Table I). For example, McHenry et al.[1] noted that 16% of subjects without angiographic evidence of significant coronary artery disease had EVE. This reduces the predictive value of EVE for the diagnosis of cardiac disease, especially in a population with a low pre-test probability of disease, where testing will result in a large number of false positive responses. The results from this table also show that EVE is not present in the large majority of patients with coronary artery disease, indicating that EVE in general is an insensitive diagnostic parameter.

However, some types of EVE tend to occur more commonly in patients with ischemic heart disease and may have more clinical significance. McHenry et al. noted that 53 of 57 patients with coronary disease and EVE began having VPDs before attaining an exercise heart rate of 130 bpm; compared to this, only 12 of 23 patients without coronary disease had EVE at this point in exercise.[1] In addition, patients with coronary artery disease have a higher incidence of frequent and complex ventricular ectopy (i.e., couplets, triplets, etc.), although the large majority of patients with coronary artery disease have neither frequent nor complex ventricular ectopy.[1,3,11]

EVE may be more useful for estimating severity of coronary artery disease.[1-3,12] Goldschlager et al.[2] found that patients with angina and EVE had a significantly higher incidence of two- or three-vessel disease and abnormal ventricular contraction patterns, and concluded that EVE may serve as an aid in detecting potentially high-risk patients. McHenry et al.[1] also found that a significantly higher percentage of patients with multivessel coronary artery disease had EVE when compared to those with lesser degrees of disease, although the predictive value of EVE for the equivalent of three-vessel coronary disease was only 32% (18 of 57). Of note, both McHenry et al.[1] and Goldschlager et al.[2] showed that suppression of ventricular ectopy during the final stages of exercise does not denote less extensive underlying disease.

Weiner et al.[13] found that 19% of 446 consecutive patients referred for cardiac catheterization for evaluation of known or suspected coronary artery disease had EVE, and that the frequency of both simple VPDs and complex ventricular arrhythmia increased in relation to the extent of the disease. The incidence of ventricular arrhythmia increased from 7% in those without coronary artery disease to 34% in those with left main coronary disease; 36 of 86 patients with EVE in this study had three-vessel or left main disease. The incidence of complex VPDs (which included repetitive forms and frequency >20 VPDs/min) increased from 2% in those without coronary artery disease to 16% in patients with left main coronary disease.

EVE and prognosis. EVE was shown by Califf et al.[11] to be of no prognostic value in patients who lacked angiographically significant coronary disease. The Coronary Artery Surgery Study[12] evaluated the significance of EVE in patients with stable coronary artery disease. As in other studies,[1-3] EVE was associated with more advanced coronary artery disease and lower mean ejection fraction. The 5-year

From the Nicholas Institute of Sports Medicine and Athletic Trauma, and the Division of Cardiology, Department of Medicine, Lenox Hill Hospital.

Received for publication Jan. 15, 1987; accepted May 5, 1987.

Reprint requests: Neil L. Coplan, M.D., Nicholas Institute of Sports Medicine, Lenox Hill Hospital, 130 E. 77th St., New York, NY 10021.

event-free survival (including death, myocardial infarction, arrhythmia, unstable angina, and heart failure), however, was not influenced by the presence or absence of EVE. Nair et al.[13,14] also showed no prognostic value for EVE.

In contrast, Udall and Ellestad[15] showed that complex ventricular arrhythmias during exercise were associated with an increased incidence of new coronary events at 2 years follow-up (especially when EVE was associated with ST depression during exercise). Califf et al.[11] found that among 620 patients with significant coronary artery disease, patients with paired complexes or nonsustained ventricular tachycardia during exercise had a lower 3-year survival rate (75%) than did patients with simple ventricular arrhythmia (83% survival) or no EVE (90% survival). EVE was determined to have independent prognostic value prior to cardiac catheterization, but its prognostic value was insignificant once the result of catheterization was known. The authors concluded that EVE serves as a marker for left ventricular (LV) dysfunction or coronary artery disease, and that increased mortality in patients with EVE is due to the presence of more extensive underlying disease.

The prognostic significance of EVE following myocardial infarction is uncertain. Granath et al.[16] showed that patients with ventricular arrhythmia during an exercise test 9 weeks after myocardial infarction had significantly increased mortality when compared to those without EVE. Theroux et al.[17] noted that patients with EVE during a post MI exercise test had an increased risk for sudden death, but the risk was not as great as that associated with detection of ST depression. Weld et al.[18] found a significant and independent association between EVE and 1-year mortality following myocardial infarction, with the mortality rate in patients with EVE and an exercise duration of less than 6 months being considerably higher than that of patients with EVE and better exercise tolerance (14% vs 26%). In contrast, other investigators[19-21] have not noted that EVE following myocardial infarction is useful for defining a group at increased risk for cardiac mortality.

Mechanism underlying EVE. EVE may result from increased sympathetic activity, the development of myocardial ischemia, left ventricular dysfunction, electrolyte abnormalities, or drug effect.[22,23] Combinations of factors may be present, making it difficult to isolate what is causing the arrhythmia.

Does EVE occur primarily as a consequence of myocardial ischemia in patients with coronary artery disease? Tilkian et al.[24] found no significant change in the frequency or severity of EVE after coronary artery bypass surgery. The authors noted that patients with all grafts patent showed a tendency toward more frequent and higher grades of arrhythmia, and postulated that the arrhythmogenic action of catecholamines may have contributed to the development of EVE. Weiner et al.[3] found that patients without preoperative wall motion abnormalities had complete resolution of EVE if ischemia was abolished on a postoperative exercise stress test. EVE that persisted post coronary artery bypass surgery correlated with severity of preoperative wall motion abnormality and the presence of postoperative ischemic ST depression during exercise testing.

Table I. Frequency of exercise-related ventricular ectopy in subjects studied with coronary angiography

Study (reference)	*CAD (no.)*	*%EVE*	*no CAD (no.)*	*%EVE*
McHenry et al.[1]	197	23	141	16
Weiner et al.[3]	335	23	111	7
Califf et al.[11]	620	27	973	16
Sami et al.[12]	1241	10.5	245	6.5

CAD = coronary artery disease; %EVE = percentage of group with exercise-related ventricular ectopy.

Management of EVE. There have been no long-term studies evaluating whether EVE should be treated. The absence of strong data that EVE is an independent risk factor for future cardiac events is a factor that argues against treatment specifically aimed at eliminating the arrhythmia, especially in a clinically normal population. Jelinek et al.[25] showed that suppression of exercise-induced ventricular arrhythmia with antiarrhythmic therapy is frequently difficult and only partially effective, with side effects from medication developing in many patients. It seems reasonable at present to recommend that therapy in asymptomatic patients without sustained ventricular arrhythmia should be directed toward treating the underlying dysfunction (i.e., myocardial ischemia, heart failure) rather than using primary antiarrhythmic therapy designed to suppress ventricular ectopy.

Conclusions. EVE is an insensitive and nonspecific indicator of heart disease. Subjects with no apparent heart disease commonly have EVE, but frequent and complex VPDs are unusual in this population. Certain characteristics, such as EVE that begins at a low heart rate and the appearance of complex/frequent VPDs, increase the probability of underlying cardiac disease. However, the mortality of patients with coronary artery disease have neither

frequent nor complex EVE. Suppression of EVE during exercise does not necessarily imply the absence of underlying heart disease.

In patients with a strong likelihood of having coronary artery disease, EVE tends to reflect the extent of disease and wall motion abnormality. Prognosis is related to the nature and degree of the underlying disease, and management should be directed toward measures such as improving LV performance and reducing myocardial ischemia.

REFERENCES

1. McHenry PL, Morris SN, Kavalier M, Jordan JW. Comparative study of exercise-induced ventricular arrhythmias in normal subjects and patients with documented coronary artery disease. Am J Cardiol 1976;37:609-616.
2. Goldschlager N, Cake D, Cohn K. Exercise-induced ventricular arrhythmias in patients with coronary artery disease: Their relation to angiographic findings. Am J Cardiol 1973; 31:434-440.
3. Weiner DA, Levine SR, Klein MD, Ryan TJ. Ventricular arrhythmias during exercise testing: Mechanism, response to bypass surgery, and prognostic significance. Am J Cardiol 1984;53:1553-1557.
4. Helfant RH, Pine R, Kabde V, Banka VS. Exercise-related ventricular premature complexes in coronary heart disease: Correlations with ischemia and angiographic severity. Ann Intern Med 1974;80:589-592.
5. Swartz MH, Teichholtz LE, Donoso E. Mitral valve prolapse: A review of associated arrhythmias. Am J Med 1977;62:377-389.
6. Sloman G, Wang M, Walker J. Arrhythmias on exercise in patients with abnormality of the posterior leaflet of the mitral valve. Am Heart J 1972;83:312-317.
7. Froelicher VF, Thomas MM, Pillow C, Lancaster MC. Epidemiologic study of asymptomatic men screened by maximal treadmill testing for latent coronary artery disease. Am J Cardiol 1974;34:770-776.
8. McHenry PL, Fisch C, Jordan JW, Corya BR. Cardiac arrhythmias observed during maximal treadmill exercise testing in clinically normal men. Am J Cardiol 1972;29:331-336.
9. Faris JV, McHenry PL, Jordan JW, Morris SN. Prevalence and reproducibility of exercise-induced ventricular arrhythmias during maximal exercise testing in normal men. Am J Cardiol 1976;37:617-622.
10. Ekbloom B, Hartley LH, Day WC. Occurrence and reproducibility of exercise-induced ventricular ectopy in normal subjects. Am J Cardiol 1979;43:35-37.
11. Califf RM, McKinnis EA, McNeer JF, Harrell FE, Lee KL, Pryor DB, Waugh RA, Harris PJ, Rosati RA, Wagner GS. Prognostic value of ventricular arrhythmias associated with treadmill exercise testing in patients studied with cardiac catheterization for suspected ischemic heart disease. J Am Coll Cardiol 1983;2:1060-1067.
12. Sami M, Chairman B, Fisher L, Holmes D, Fray D, Alderman E. Significance of exercise-induced ventricular arrhythmia in stable coronary artery disease: a Coronary Artery Surgery Study project. Am J Cardiol 1984;54:1182-1187.
13. Nair CK, Aronow WS, Sketch MH, Pagano T, Lynch JD, Mooss AN, Esterbrooks D, Runco V, Ryschol K. Diagnostic and prognostic significance of exercise-induced premature ventricular complexes in men and women: A four year follow-up. J Am Coll Cardiol 1983;1:1201-1206.
14. Nair CK, Thomson W, Aronow WS, Pagano T, Ryschon K, Sketch MH. Prognostic significance of exercise-induced complex ventricular arrhythmias in coronary artery disease with normal and abnormal left ventricular ejection fraction. Am J Cardiol 1984;54:1136-1138.
15. Udall JA, Ellestad M. Predictive implications of ventricular premature contractions associated with treadmill stress testing. Circulation 1977;56:985-989.
16. Granath A, Sodermark S, Winge T, Volpe U, Zetterquist S. Early work load tests for evaluation of long-term prognosis of acute myocardial infarction. Br Heart J 1977;39:758-763.
17. Theroux P, Waters DD, Halphen C, Debaisieux J, Mizgala H. Prognostic value of exercise testing soon after myocardial infarction. N Engl J Med 1979;301:341-345.
18. Weld FM, Chu K, Bigger JT, Rolnitzky LM. Risk stratification with low-level exercise testing 2 weeks after acute myocardial infarction. Circulation 1981;64:306-314.
19. Davidson DM, DeBusk RF. Prognostic value of a single exercise test 3 weeks after uncomplicated myocardial infarction. Circulation 1980;61:236-232.
20. DeBusk RF, Haskell W. Symptom-limited vs heart rate limited exercise testing soon after myocardial infarction. Circulation 1980;61:738-743.
21. Starling MR, Crawford MH, Kennedy GT, O'Rourke RA. Exercise testing early after myocardial infarction: Predictive value for subsequent unstable angina and death. Am J Cardiol 1980;46:909-914.
22. Sung RJ, Shen EN, Morady F, Scheinman MM, Hess D, Botvinick EH. Electrophysiologic mechanism of exercise-induced sustained ventricular tachycardia. Am J Cardiol 1983;51:525-530.
23. DeMaria AN, Vera Z, Amsterdam EA, Mason DT, Massumi RA. Disturbances of cardiac rhythm and conduction induced by exercise. Am J Cardiol 1974;33:732-736.
24. Tilkian AG, Pfeifer JF, Barry WH, Lipton MJ, Hultgren HN. The effect of coronary bypass surgery on exercise-induced ventricular arrhythmias. Am Heart J 1976;92:707-714.
25. Jelinek MV, Lohrbauer L, Lown B. Antiarrhythmic drug therapy for sporadic ventricular arrhythmias. Circulation 1974;49:659-666.