

Ventricular Arrhythmias, Part I: Prevalence, Significance, And Indications For Treatment

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Abstract: Evaluation and treatment of patients with ventricular arrhythmias are full of pitfalls for the unwary. In this series of articles we discuss how to recognize and avoid these pitfalls and present our

Evaluation and management of patients with ventricular arrhythmias are two of the most difficult tasks faced by the family physician. Which patients should be treated? How aggressively should treatment be pursued, particularly for patients who develop adverse reactions to antiarrhythmic medications? Is treatment really effective? Does it prolong life? Considering the high cost of Holter monitoring, exercise stress testing, and echocardiography, what constitutes a medically appropriate yet cost-effective workup of patients with ventricular arrhythmias? How should such patients be followed? Who should be referred? What are the end points of therapy? And finally, how can one judge if the treatment chosen is successful?

Definitive answers to many of these questions remain elusive. Yet, clinical decisions must be made. If this is done without adequate forethought or awareness of potential problems, the treating physician may encounter a number of pitfalls (Table 1). The purpose of this article is to address these pitfalls within the limits of our medical knowledge and to present an approach that has served us well in the evaluation and management of patients with ventricular arrhythmias.

Prevalence of Premature Ventricular Contractions in the General Population

Premature ventricular contractions (PVCs) occur quite commonly in the general population. They

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approach to management. The prevalence and clinical significance of ventricular arrhythmias and indications for treatment are addressed in this initial installment. (JABFP 1988; 1:135-42.)

are found in up to 50 percent of otherwise healthy, asymptomatic adults.^{1,2} Their frequency increases with age, and it is well accepted that a majority of adults more than 60 years of age have some ventricular ectopy during 24 hours of monitoring. However, in the absence of underlying heart disease, complex forms of ventricular ectopy (i.e., multiform PVCs, ventricular couplets, salvos, or longer runs of ventricular tachycardia) are not commonly seen in most individuals (Table 2).¹⁻⁴ In contrast, both frequent and complex ventricular ectopy are often seen when underlying heart disease is present.^{3,5}

Definition of the term "frequent" is subject to variable interpretation. In a population of middle-aged individuals with underlying heart disease, frequent ventricular ectopy has been most commonly defined as averaging more than 10 to 30 PVCs per hour over 24 hours of monitoring (i.e., at least 240 PVCs/day).^{2,6-8} In contrast, among otherwise healthy, asymptomatic young adults, a much lower definition of "frequent" probably should be employed. As noted above, although up to half of these individuals have some PVCs on 24 hours of monitoring, it is unusual for them to have as many as 100 PVCs in a day.

A notable exception to the above generalities is in the small subset of patients with primary electrical disease. These individuals have extremely frequent and complex ventricular ectopy despite an apparent absence of underlying heart disease. Seventy-three such patients (with a mean age of 46 years) were studied prospectively by Kennedy, et al. and followed for a period of up to 10 years.⁹ Holter monitoring initially demonstrated a mean frequency of 566 PVCs/hour (range 78-1,994 PVCs/hour) for the group. Multiform PVCs were present in 63 percent, ventricular couplets in

Table 1. Pitfalls in Evaluation and Management of Ventricular Arrhythmias.

1. Failure to appreciate the prevalence and significance of PVCs in the general population
2. Forgetting the indications for treatment
3. Failure to consider extracardiac or exacerbating factors before initiating antiarrhythmic therapy
4. Not being aware of monitoring methods and their drawbacks
5. Not being aware of the proarrhythmic effect
6. Not balancing potential benefits of treatment with potential risks of antiarrhythmic agents
7. Forgetting the reasons why a patient may not respond to antiarrhythmic therapy
8. Inappropriate use of serum drug concentration levels
9. Not being aware of additional means of treating lethal arrhythmias
10. Not reevaluating the success of the treatment plan chosen

60 percent, and ventricular tachycardia in 26 percent. Extensive noninvasive cardiologic examination failed to reveal underlying heart disease in these asymptomatic individuals, although subsequent cardiac catheterization disclosed coronary artery disease in a small percentage of them. Survival data for the group as a whole showed a significantly lower mortality rate than would be expected for age-matched controls. Thus, even individuals with extremely frequent and complex ventricular ectopy will often have a relatively benign course when overt evidence of underlying heart disease is absent.

Clinical Significance of PVCs

The significance of ventricular ectopy depends on the clinical setting in which it occurs. Patients with PVCs who do not have underlying heart disease tend to have a benign prognosis. Even among individuals with primary electrical disease who may manifest alarmingly frequent and complex PVCs, treatment is probably not indicated in the absence of symptoms when there is no underlying heart disease. In contrast, in the setting of acute ischemia (i.e., in patients who have chest pain), any ventricular ectopy at all *must* be viewed as significant and as a potential triggering event of ventricular fibrillation. It is precisely for this reason that many physicians advocate prophylactic

treatment with lidocaine for patients suspected of acute myocardial infarction even when PVCs are infrequent or absent.¹⁰⁻¹²

Although left ventricular function is the most important predictive factor of mortality during the year following acute myocardial infarction, PVCs have also been shown to be a separate independent risk factor in these patients.^{8,13} Mortality in this year is related to the frequency of ventricular ectopy detected by Holter monitoring before discharge from the hospital. Patients with fewer than one PVC per hour have a low (i.e., less than 10 percent) mortality. The figure rises sharply as a function of PVC frequency in patients who demonstrate more than one PVC per hour. About half of this PVC-associated mortality increase is achieved at frequencies of three PVCs per hour, with a mortality plateau (20–30 percent for the ensuing year) being reached above PVC frequencies of 10 per hour.³ Thus, a Holter monitor recording obtained on a myocardial infarction patient before discharge from the hospital needs to be interpreted in a different light from one obtained on a patient with chronic ventricular ectopy. Following myocardial infarction, the definition of "frequent" ventricular ectopy probably should be adjusted downward, and treatment instituted for patients demonstrating more than 10 PVCs per hour. Whether consideration for treatment also should be given to those with a lesser frequency of ventricular ectopy is controversial.

The frequency of ventricular arrhythmias in the postinfarction period depends on the time that monitoring is performed. PVCs are at a minimum 3 to 5 days following infarction. They tend to increase over the next 6 to 12 weeks before finally leveling off.³ Despite this tendency of PVCs to increase after discharge from the hospital, it is far more practical to obtain a baseline Holter monitor *before* the patient is sent home.

Repetitive forms of ventricular ectopy (i.e., ventricular couplets and especially salvos and longer runs of ventricular tachycardia) more than double the risk of mortality during the first year following infarction compared with the risk posed to patients who do not demonstrate repetitive forms.³ In contrast to what was previously thought, the prognostic significance of multi-form PVCs and R-on-T complexes is much less than that of repetitive forms.

Table 2. Occurrence of Ventricular Arrhythmias.

	Healthy Asymptomatic Young Adults	Asymptomatic Older Adults without Heart Disease	Asymptomatic Older Adults with Heart Disease	Survivors of Sudden Cardiac Death
Percent of subjects with some PVCs	Up to 50%	>50%	>50%	>90%
Presence of frequent PVCs	Uncommon to have >100/day*	More common	Common	Very common
Presence of complex PVCs	Uncommon*	Uncommon	Common	Very common

*Except for a small subset of patients with primary electrical disease who have both frequent and complex ventricular ectopy.

Classification of Ventricular Arrhythmias

When assessing the clinical significance of ventricular arrhythmias, it may be useful to divide them into those that are benign, potentially lethal, and lethal (Table 3). Approximately one-third of patients have benign arrhythmias, two-thirds have potentially lethal arrhythmias, and less than 5 percent have truly lethal arrhythmias. As implied in the name, benign ventricular arrhythmias place an individual at only minimal risk of dying suddenly from an arrhythmia. In contrast, patients with potentially lethal arrhythmias face a moderate to high risk of dying suddenly from their arrhythmias, while those with lethal arrhythmias face the highest risk. In this latter group, which includes survivors of sudden cardiac death, the rate of recurrence of ventricular tachycardia/fibrillation is as high as 30 percent within the year after the initial episode and 50 percent within 2 years.^{8,14}

Classification of patients into the categories shown in Table 3 may be helpful to the clinician in making decisions regarding therapy. Because of the almost negligible risk imposed by *benign* ventricular arrhythmias, there is little need to treat these patients unless the arrhythmia is causing symptoms that impact significantly on the individual's way of life. Most of these patients are relatively or entirely asymptomatic, and PVCs are usually only detected as an incidental finding when an irregular heartbeat is noted during the course of a physical examination performed for some other purpose.

In general, patients with benign ventricular arrhythmias do not have underlying heart disease. They most commonly manifest only *infrequent*

ventricular ectopy (i.e., an average of fewer than 10 PVCs per hour) with a lack of complex forms. Conservative measures including reassurance, elimination of exacerbating factors, and/or mild anxiolytics are often all that is needed in the form of treatment. When antiarrhythmic medication is indicated, β -blockers are often the drug of choice because they are usually better tolerated than other agents, and they are also less likely to cause a worsening of the arrhythmia (i.e., a proarrhythmic effect).

At the other end of the spectrum, patients with *lethal* ventricular arrhythmias by definition have already demonstrated the capacity for hemodynamic instability in the presence of their arrhythmia. This group includes patients who present with syncope from their ventricular arrhythmia and those who have experienced an episode of out-of-hospital cardiac arrest.

It is of interest that despite the almost universal presence of significant underlying coronary artery disease in survivors of sudden cardiac death, in only about one-third of this group is acute myocardial infarction thought to be the actual cause of the cardiac arrest.¹⁴ Subsequent mortality varies greatly, depending on whether acute myocardial infarction is the inciting mechanism. Ventricular electrical instability is commonplace during the early hours of acute infarction. This is the reason why more than half of the mortality from acute myocardial infarction still results from primary ventricular fibrillation that develops within the first few hours of the onset of symptoms, usually before the patient arrives at the hospital. Electrical instability associated with acute infarction is usually a transient phenomenon that resolves as the patient recovers. Thus, development of ventricular fibrillation during the early hours of acute

Table 3. Classification of Ventricular Arrhythmias.*

	Benign (30%)	Potentially Lethal (65%)	Lethal (<5%)
Risk of SCD	Minimal	Moderate to high	Very high
Clinical presentation	<i>Asymptomatic</i> Routine exam	+ Screening	+ Syncope or cardiac arrest
Underlying heart disease	<i>Symptomatic</i> Palpitations None —MVP— —Runner—	Yes Coronary artery disease Cardiomyopathy Valvular heart disease	Yes Coronary artery disease Acute myocardial infarction (in only about 1/3 of cases)
Types of arrhythmias	PVCs (usually not frequent or complex†) NSVT—rare	PVCs (may be frequent and complex) NSVT—occasionally	PVCs (almost always frequent and complex) NSVT—common VT/VF—common
Reason to consider Rx	To relieve symptoms	To reduce risk of SCD(?)	To reduce risk of SCD
Therapeutic measures	Treat extracardiac factors Reassurance Anxiolytics Antiarrhythmic agents (esp. β -blockers)	Conventional antiarrhythmic agents	Conventional antiarrhythmic agents Investigational agents PES studies AICD/surgery

*PVCs = premature ventricular contractions; NSVT = non-sustained ventricular tachycardia; VT = ventricular tachycardia; VF = ventricular fibrillation; SCD = sudden cardiac death; PES = programmed electrophysiologic studies; AICD = automatic implantable cardioverter-defibrillator.

†Except for the small subset of patients with primary electrical disease who have both frequent and complex ventricular ectopy despite an absence of underlying heart disease.

infarction does not seem to affect long-term survival, and patients who have an otherwise uncomplicated course demonstrate a prognosis that is as good as those with uncomplicated myocardial infarction who never had ventricular fibrillation.³ It is only when ventricular arrhythmias persist into the late infarction period (i.e., beyond the first 3 to 5 days) that long-term survival is adversely affected.^{3,13} These arrhythmias can be detected by routinely performing a Holter monitor before discharge from the hospital.

Spontaneous ventricular fibrillation that occurs in the absence of acute infarction is not easily explained. When Holter monitoring is performed in this group after an episode of out-of-hospital cardiac arrest, the overwhelming majority of patients demonstrate extremely frequent ventricular

ectopy with many complex forms.¹⁴ Runs of ventricular tachycardia are common and hard to eliminate by usual therapeutic interventions. Survivors of sudden cardiac death face an inordinately high risk of recurrence from their lethal arrhythmia, and aggressive therapy is indicated. Standard treatment with conventional antiarrhythmic agents is often not sufficient. Referral to a center that performs programmed electrophysiological stimulation (PES) studies, consideration of investigational antiarrhythmic agents, surgery, and/or implantation of an automatic implantable cardioverter-defibrillator (AICD) may be needed.

The final group of patients with ventricular arrhythmias is composed of persons with *potentially lethal* ventricular arrhythmias. This is by far the largest group. Like those with benign ventricular

arrhythmias, many individuals in this group are entirely unaware of their arrhythmias, which only come to the attention of a physician when an irregular heartbeat is noted during routine physical examination or when screening by Holter monitoring or exercise testing is performed. Others present with symptoms of palpitations, dizziness, chest discomfort, or dyspnea. Ventricular ectopy is often frequent with complex forms, and non-sustained ventricular tachycardia (NSVT) is not uncommon.

The presence of underlying heart disease is the principal feature that differentiates these arrhythmias from those that are benign. This may take the form of coronary artery disease (i.e., angina pectoris, prior myocardial infarction), cardiomyopathy (i.e., congestive or hypertrophic forms), valvular heart disease (i.e., mitral regurgitation, aortic stenosis, etc.), or congestive heart failure (from any of the above). Pure hypertensive heart disease in the absence of impaired left ventricular function does *not* qualify as "underlying heart disease." Therefore, patients with PVCs and mild to moderate hypertension but no underlying cardiac abnormality should be classified as having benign ventricular arrhythmias.

It is this group of patients with potentially lethal ventricular arrhythmias that the most uncertainty regarding the need for evaluation and treatment exists. Although it is known that the presence of ventricular arrhythmias in such patients increases the risk of sudden cardiac death, it has never been shown that this risk may be lessened by antiarrhythmic treatment. When one considers the cost, physical inconvenience, and high incidence of adverse effects that accompany antiarrhythmic therapy, it becomes apparent that the decision whether to treat a particular patient with drugs is often an exceedingly difficult one.

Mitral Valve Prolapse

Two groups of persons with PVCs merit special attention: joggers and individuals with mitral valve prolapse (MVP). Much has been written about the association between mitral valve prolapse and cardiac arrhythmias. However, despite frequent referrals to this association in the literature, the relationship may be greatly over-emphasized.

MVP is an exceedingly common disorder. It is estimated that 5 to 10 percent of the entire population or 10–20 million people in the United

States have MVP.¹⁵ Yet, which of the individuals with MVP is the family physician most likely to see? The answer reflects an "iceberg effect." Although persons with MVP are occasionally identified when characteristic auscultatory findings are incidentally detected on a physical examination performed for some other purpose, the overwhelming majority of the estimated 10–20 million Americans with MVP are completely asymptomatic. Most such individuals probably never come to the attention of a physician. There are few studies in the literature that have examined the incidence of cardiac arrhythmias in this large group of asymptomatic individuals with MVP. Instead, most studies have selected their pool of MVP subjects from persons seeking medical attention (i.e., predominantly those with symptoms), determined the incidence of arrhythmias in this group, and compared this incidence to asymptomatic age-matched controls. Frequent use of different selection criteria for patients with MVP and control subjects, thus, could have introduced a selection bias into these studies, resulting in an exaggerated figure for the incidence of arrhythmias in persons with MVP. The question of how common arrhythmias really are in the majority of individuals who have MVP but who do not have symptoms remains unanswered. Also unanswered is the question of how common arrhythmias are in individuals with symptoms but no MVP.

Recently, Kramer, et al. looked at these very questions.¹⁶ Persons with MVP who had symptoms (palpitations, dizziness, shortness of breath, and chest discomfort) were evaluated and compared with a group of similar individuals who had comparable symptoms but in whom MVP was ruled out. No statistically significant difference in the frequency of either supraventricular or ventricular arrhythmias was found between the two groups. Individuals with symptoms but without MVP had a surprisingly high incidence of cardiac arrhythmias. Thus, although cardiac arrhythmias are common in symptomatic persons with MVP, they appear to be almost equally common in symptomatic individuals who do not have MVP. The true incidence of arrhythmias in persons with MVP who do not have symptoms is unknown and, perhaps, much lower than has been previously thought.

What about the clinical significance of these arrhythmias? Does MVP predispose to sudden cardiac death? Should ventricular arrhythmias that

occur with this entity be viewed as lethal or potentially lethal in nature? Or are they benign? Because of the frequency of this disorder, it is extremely important to view it in its proper perspective. Although the association between MVP and sudden cardiac death has received much attention, this complication is extremely rare, and the total number of cases reported in the literature is fewer than 100.^{15,17} Individuals who do appear to be at increased risk are those with a history of syncope, Q-T prolongation, ventricular tachycardia on Holter monitoring, or a family history of MVP and sudden death. In general, however, long-term prognosis of the overwhelming majority of persons with MVP is excellent, and the risk of sudden death almost negligible. Ventricular arrhythmias that occur with this entity are probably best classified as benign. Treatment is usually not indicated in the absence of symptoms. Instead, the major task faced by the clinician is to assure individuals diagnosed with MVP that they have an extremely common minor cardiac abnormality (and/or echocardiographic oddity) that usually does not lead to problems. To avoid creating undue anxiety or neurosis, many authorities in the field suggest that the physician not raise the specter of sudden death before individuals with MVP or their families.^{17,18}

Although the precise mechanism of arrhythmogenesis in MVP is not known, β -blockers have been generally accepted as the treatment of choice for symptomatic individuals. Experience with other agents is limited and often disappointing. It is also not known why some individuals with auscultatory and echocardiographic evidence of MVP manifest symptoms (i.e., palpitations, chest discomfort, dyspnea, and anxiety) and arrhythmias while others do not. One interesting theory suggests the existence of a hyperadrenergic state with resultant increased catecholamine secretion in persons with symptomatic MVP.^{15,17} This would help explain the beneficial clinical response that many symptomatic individuals exhibit to β -blockade. Other evidence is conflicting and suggests that a hyperadrenergic state is not an integral component of the MVP syndrome but, rather, a common phenomenon that is equally prevalent in symptomatic individuals without MVP.^{19,20} Were this the case, it would provide a rationale for selecting β -blockers to treat symptomatic individuals with benign ventricular arrhythmias regardless of whether MVP was present.

Joggers with PVCs

Joggers are the second group of persons with PVCs that merit special attention. This activity has become so popular a pastime in the United States today that more than 10 percent of the general population now run on a regular basis.²¹ Many of these individuals subscribe to the "exercise hypothesis," believing that running can protect against the development of ischemic heart disease.^{22,23} However, some question whether physical activity and running really protect against the development of ischemic heart disease or, instead, predispose to it.

The presence of ventricular ectopy in runners complicates matters further. Do PVCs predispose to sudden cardiac death? Should ventricular ectopy in joggers be treated? Or can people who exercise vigorously be given a clean bill of health and allowed to continue unsupervised and unrestricted activity?

Once again, the most important factor to consider appears to be whether the individual exercising has underlying heart disease. Among those who die suddenly while running, exercise-induced arrhythmias have been presumed to be the major precipitating cause. Virtually all such individuals have underlying structural heart disease, with the type of disorder depending on the age of the participant. Among athletes under 30 years of age who die suddenly during exercise, inherited structural cardiac abnormalities are responsible for the vast majority of cases. Idiopathic hypertrophic subaortic stenosis (IHSS) accounts for almost 50 percent of these deaths.²⁴

In adults over 40 years of age, the overwhelming majority of runners dying suddenly are found to have significant underlying coronary artery disease.²⁵⁻²⁷ Exercise alone cannot prevent progression of coronary atherosclerosis in those who are predisposed to this process. This has been demonstrated in studies of marathon runners who developed coronary artery disease despite years of long-distance training.^{22,25} However, it is possible that regular exercise may retard the process.^{23,26,29}

Practically speaking, athletes under 30 years of age with PVCs should be carefully screened for structural cardiac abnormalities. Echocardiography should be considered when there is a family history of IHSS or other congenital heart disease, the resting ECG is abnormal, or a potentially significant murmur is detected on physical examination. Stress testing may be helpful in demonstrating the effect of exercise on ventricular ectopy. In

general, a decrease in the frequency and complexity of PVCs with progressively increasing degrees of exercise is a good sign and suggests that an otherwise healthy, asymptomatic young adult faces an extremely low risk of sudden death during vigorous exercise.

In runners aged 40 and over with ventricular ectopy, detection of occult coronary artery disease is essential if one is to prevent the tragic occurrence of sudden cardiac death during exercise. A history of anginal-type chest discomfort and/or the presence of risk factors such as smoking, hypertension, hypercholesterolemia, positive family history, and low level of fitness identifies individuals at highest risk. Stress testing serves as an ideal screening tool in this population. Further evaluation by radionuclide studies or coronary angiography is indicated before allowing unrestricted activity if exercise on the treadmill produces chest pain, a marked increase in the frequency or complexity of PVCs, or an abnormal S-T segment response to exercise. In the absence of findings suggestive of underlying coronary artery disease, asymptomatic ventricular ectopy in adults more than 40 years of age should not be a deterrent to regular exercise.

Indications for Treatment

There are only two reasons for treating patients with ventricular arrhythmias: (1) to try to make them feel better, and (2) to make them live longer. Because patients with benign ventricular arrhythmias are at minimal risk of dying suddenly from their arrhythmia, the only real indication for treating such individuals would be to relieve symptoms if present. In contrast, patients with lethal ventricular arrhythmias are at significant risk of dying from their arrhythmias and in general treatment should be aggressive. The decision whether to treat patients with potentially lethal arrhythmias is much more difficult to make. Ventricular arrhythmias in this group do predispose these patients to an increased risk of sudden cardiac death. However, it has never been shown that treatment of such arrhythmias improves prognosis. Whether to institute therapy with antiarrhythmic agents that are costly, require long-term follow-up with careful monitoring, are often associated with intolerable side effects, and may sometimes exacerbate the very arrhythmias that one is trying to suppress is therefore debatable.

Clinically, it is often helpful to divide patients with potentially lethal arrhythmias into two groups—those who have symptoms and those who don't. In general, it is much easier to deal with the former group. Because they have symptoms, the clinician has an excellent parameter for judging the effect of treatment. If the patient tolerates antiarrhythmic medication and symptoms improve, treatment may be viewed as effective and probably should be continued. If, on the other hand, symptoms are unchanged or become worse on medication, and/or the patient develops intolerable side effects, the clinician may need to reassess the situation. Is treatment truly indicated? If so, an adjustment in dose or trial of another antiarrhythmic agent may be in order. Or has the treatment become worse than the disease? If this is the case, antiarrhythmic therapy probably should be stopped.

Deciding whether to treat potentially lethal ventricular arrhythmias in the absence of symptoms is a more difficult matter. Although the physician knows that arrhythmias in these individuals do increase the risk of sudden cardiac death, he/she is faced with the extremely difficult task of trying to make a group of asymptomatic patients feel better. Without symptoms, the major motivating factor for compliance is gone. Institution of antiarrhythmic drugs that are costly and commonly associated with untoward side effects is often not well received by these patients, and a majority simply do not take their medication as prescribed.³⁰ The approach to evaluation and management therefore poses a true challenge to the family physician.

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GLEANINGS FROM A COMMONPLACE BOOK—NJP

"The wise man's feeling toward all men is that of the physician's toward his patient."

Seneca

PHYSICIAN as defined by Ambrose Bierce in his *Devil's Dictionary* is:
 "One upon whom we set our hopes when ill, and our dogs when well."

To our friends in the academic world:

"Mediocre men often have the most acquired knowledge."

Claude Bernard

To our friends who thirst for office:

"Everybody wants to be somebody; nobody wants to grow."

Goethe