

Ventricular Premature Depolarizations. Who To Treat? Current Concepts.

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I. AHMED **

Frederick Price wrote in his textbook of Practice of Medicine in 1937 : "the question of prognosis of extra systole is of some consequence - Apart from rare exceptions - when extra systoles are considered by themselves - that is, without reference to the condition with which they may be associated - there is so far no evidence for supposing that they are indicative of an impaired heart, or that they add to the gravity of any existing morbid condition - The prognosis therefore, should be based entirely upon the casual associated conditons".

Most of what Price wrote then holds true even half a century later. We know that VPB (ventricular premature beats) are ubiquitous in the population. In the last decade, our understanding of ventricular arrhythmias has increased tremendously. Considerable controversy, however, still exists regarding the indication for treatment, the choice and assessment of mortality and the course of treatment.

For centuries, the Galenic view that intermittent pulse was a manifestation of disease and was associated with a poor prognosis haunted the views of the medical profession and was reinforced by the widely publicized Tecumseh Study in 1969, which suggested that the presence of ventricular extra systoles on the resting ECG was associated with the significant increase risk of sudden death. But now we know that the risks posed by VPB's are determined not by the mere presence of VPB but by the complexity and the context in which they occur.

BACKGROUND KNOWLEDGE

Ventricular extra systoles occur in approximately 1% of clinically normal persons as deter-

mined by a standard ECG and in 40 - 75% of normal persons assessed by 24 - 48 hours ambulatory monitoring. The incidence and frequency of ventricular ectopy increases with age, and even frequent (greater than 60/hour) and complex forms have been described in apparently healthy subjects. Such persons constitute less than 1 - 4% of the general population. The following table shows the characteristics of ventricular arrhythmias in men.

TABLE I

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| <ol style="list-style-type: none"> 1. They are common 2. They increase with age 3. They increase with ventricular scarring <ol style="list-style-type: none"> a. infarction b. hypertrophy c. infection 4. They do not increase with coronary atherosclerosis per se 5. They can be precipitated/aggravated by exercise. <ol style="list-style-type: none"> a. ischemia b. increased sympathetic activity. c. increased heart rate. 6. Electrocardiographically similar arrhythmias may have different causes and significance. |
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The most pressing problem about PVC's concerns sudden death. Thousands of people die suddenly every year. A majority of these are believed to be arrhythmogenic; ventricular tachycardia or ventricular fibrillation. The major objective for us is to identify patients who are at high risk for sudden cardiac death. Thus, careful evaluation of the patients with ventricular arrhythmias usually permits the physician to classify the arrhythmias into one of the three

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TABLE II
CLINICAL CLASSIFICATION OF VENTRICULAR ARRHYTHMIAS

	BENIGN	POTENTIALLY MALIGNANT	MALIGNANT
Risk of sudden death	Very small	Moderate	High
Clinical presentation	Palpitations detected by routine exam	Palpitations detected by routine exam or screening	Palpitations, syncope, cardiac arrest
Heart disease	Usually absent	Present	Present
Cardiac scarring and/or hypertrophy	Absent	Present	Present
VPD frequency	Low to moderate	Moderate to high	Moderate to high
Repetitive VPD	Absent	Common; usually not sustained	Common; often sustained
Objectives of treatment	Relieve symptoms	Relieve symptoms, reduce arrhythmia, reduce mortality	Relieve symptoms, reduce arrhythmia, reduce mortality

following categories. 1) Benign ventricular arrhythmias; 2) Potential malignant arrhythmias; 3) Malignant arrhythmias.

This classification is useful in decision-making with respect to the intensity of additional diagnostic procedures and therapy. The main features of these three groups of ventricular arrhythmias can be summarized as shown in the table II

I. BENIGN VENTRICULAR ARRHYTHMIAS

These arrhythmias place the patient in a low risk group. These patients usually complain of palpitations or the PVC's are discovered on routine evaluation. Routine evaluation including history, physical examination, chest x-ray and 12-lead ECG reveals no evidence of heart disease. Echocardiogram and radionuclide studies are also normal. A 24 hour Holter almost always demonstrates lack of repetitive forms. Also,

another feature is that the PVC's often decrease in frequency during exercise.

Current evidence indicates that ectopy is more frequent in older age groups and more likely to be detected with longer recording periods. However, the frequency of repetitive ventricular premature depolarizations does not follow the same pattern as that of unifocal PVC's.

MANAGEMENT

This is a common problem in office medical practice. Most authorities agree on their approach to these arrhythmias, namely:

1. Identify and remove any potential any arrhythmogenic factors, example caffeine and nicotine.
2. Reassurance. When a patient is fully aware of benignity of his condition, he may

pay less attention to his palpitation, because he is less concerned about them.

3. If drug therapy is elected as a management option, most authorities believe that beta blockers should be the first drug of choice, the primary objective being to reduce the symptoms without causing harm. Although beta blockers reduce the frequency of VPB's in only minority, they reduce the symptoms in majority of patients.
4. Minimize the inconvenience of drug treatment for the patient. Therefore, long acting drugs are worth considering.
5. If beta blockers don't control the symptoms, there is no consensus on the next best alternative to take. Some use Class IB drugs, others use Class IC drugs.

II. MALIGNANT VENTRICULAR ARRHYTHMIAS

Approximately every minute in the United States 1 person dies of sudden cardiac death. Studies indicate that the mechanism of this condition in approximately 80% of patients is an acute ventricular tachyarrhythmia that leads to fatal ventricular fibrillation. In only 20% of the patients, sudden cardiac death due to an acute ischemic episode leading to bradyarrhythmia and asystole occurs. Despite reservations, Lown's grading system for ventricular ectopy is accepted as the standard for classification of ventricular arrhythmias and is reviewed in the table III.

There are three forms of malignant ventricular arrhythmias and these are :

1. Ventricular fibrillation
2. Recurrent sustained ventricular tachycardia
3. Torsade de pointes ventricular tachycardia in long QT syndrome.

Each of these conditions has high mortality rate.

Patients with malignant ventricular arrhythmias are at very high risk of sudden cardiac death. They present usually with a history of symptomatic sustained ventricular tachycardia, syncope or as survivors of out-of-hospital cardiac arrest.

TABLE III	
CLASSIFICATION OF VENTRICULAR ARRHYTHMIAS	
Grade	Characteristics
1A	Infrequent VPB's (< 30/hour); < 1/minute
1B	< 30 VPB's/hour and occasionally >1/minute
2	frequent VPB's, > 30/hour
3	Multiform VPB's
4A	Couplets (2 consecutive VPB's)
4B	Triplets (3 or greater than 3 consecutive VPB's) ventricular tachycardia
5	Early VPB's (R on T phenomena)

Routine evaluation usually reveals evidence of heart disease. The most common underlying disorder is coronary artery disease (80%). Other causes include cardiomyopathy and valvular heart disease. Patients may have evidence of heart failure or it may be detected by radionuclide study. A 24 hour Holter monitoring almost always shows repetitive ventricular arrhythmias. EPS can induce ventricular tachycardia/ventricular fibrillation in 80% of those who present with recurrent sustained VT, and in 70% of those who had out-of-hospital cardiac arrest.

MANAGEMENT

There is consensus again in this group of patients that it is mandatory to treat malignant ventricular arrhythmias vigorously because untreated patients have a recurrence of 25-30% within the year. There are two methods that have been used in predicting outcome in management of these patients.

1. Noninvasive methods using Holter and ETT. This approach has been mainly championed by Lown and his group in Massachusetts.
2. EPS using programmed ventricular stimulation.

Both methods require a high degree of expertise and are time-consuming. At present, carefully controlled perspective comparative study of patients randomly allocated to one or the other approach has not been completed. Until that's done, one cannot claim unquestioned superiority of one method over the method.

Generally speaking, cases in which ventricular tachycardia is incessant or sustained but does not cause severe hemodynamic effect, noninvasive approach is preferable. Otherwise EPS may be superior.

The definition of efficacy for noninvasive approach is lack of ventricular tachycardia during Holter andETT. On the other hand, the efficacy of EPS is less than 5 repetitive ventricular responses inducible by programmed ventricular stimulation.

Outcome of treatment programs for malignant ventricular arrhythmias is listed in the following tables IV and V.

III. POTENTIALLY LETHAL ARRHYTHMIAS

The much more common clinical presentation of PVC's which accounts for the vast majority of the cases of sudden death, is seen in those patients in whom their presence causes no important hemodynamic consequences. Studies performed over the last ten years have identified several "potentially malignant" ventricular arrhythmias. These include frequent and repetitive but non-sustained ventricular premature contractions. They are at intermediate risk of sudden cardiac death.

Again, the patient may occasionally complain of palpitations or dizziness but in fact the vast

TABLE IV

OUTCOME OF TREATMENT PROGRAMS FOR MALIGNANT VENTRICULAR ARRHYTHMIAS

	Responder		Nonresponder	
	3 - Year		3 - Year	
	N	Mortality Rate	N	Mortality Rate
Holter/Exercise	98	14%	25	84%
Electrophysiologic Studies	103	20%	102	68%

TABLE V

CONDITION PRESENT	MEANS OF MEASUREMENTS	DEFINITION
LV Dysfunction	2-D Echo/Radionuclide	EF 40%
PVC	24 Hour Holter Monitor	Frequency 10-30 per hr/24 hr. Repetitive form, couplets or VT 3/hr

Table V indicates those patients who are at highest risk for sudden cardiac death, i.e., patients with ventricular arrhythmias and left ventricular dysfunction.

majority are unaware of even frequently occurring PVC's. Some of these patients may have frequent episodes of nonsustained ventricular tachycardia. Routine evaluation reveals clear-cut evidence of heart disease, such as cardiac hypertrophy or myocardial fibrosis. Most often these patients have coronary artery disease.

APPROACH TO POTENTIALLY MALIGNANT VENTRICULAR ARRHYTHMIAS

Recent studies indicate that these are independent predictors of mortality. But there is still controversy as to whether therapy directed at this group of patients will significantly reduce mortality. There are studies underway namely CAPS, TEST studies which should help us with this question.

CONVENTIONAL THERAPY OF POTENTIALLY MALIGNANT VENTRICULAR ARRHYTHMIAS

As indicated, there is no mandate to treat these arrhythmias. In absence of such data, treatment remains empiric. One cannot be criticized for treating or not treating these patients. Most physicians nevertheless do tend to treat post infarction patients who have high frequency of ventricular premature depolarizations and nonsustained ventricular tachycardia.

However, such patients can clearly be treated in terms of diagnostic and therapeutic measures as ambulatory outpatients. Noninvasive methods are a logical approach for diagnostic and therapeutic decisions in this group of patients. Exercise testing is complimentary and especially indicated when VPB's are associated with exertion.

PHARMACOTHERAPEUTIC GUIDELINES

We have tried to describe the three types of ventricular arrhythmias' and the implications that they canote. However, it is beyond the scope of this essay to review pharmacology and pharmacokinetics of antiarrhythmic drugs and we refer the reader to recent reviews on this subject at the end of this essay. However, the following table will hopefully give broad guidelines as to the pharmacotherapeutic management of patients with ventricular premature contractions.

1. Minimize the number of medications.
2. Choose convenient times of administration if possible.
3. Avoid/minimize long-term toxicity from drugs.
4. Insist that the patient know the name of the medication as well as indication for its use and its potential toxicity.
5. Select least expensive preparation.
6. Document blood levels if possible.
7. Document response to medication.
8. Use conventional drugs prior to investigational agents.
9. EPS should be available ideally.
10. Establish a firm authorization patient relationship for successful management.
11. Choose investigational agents that electrophysiologically would be most likely to succeed, based on prior experience with conventional agents.
12. If this fails, choose the agent with the highest probability of success even though conventional drugs with similar electrophysiological characteristics were unsuccessful.

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