The Relationship of Ventricular Asynergy in Coronary Artery Disease to Ventricular Premature Beats*

Sukh Dev Sharma, M.D.,** Frederick Ballantyne, M.D.,** and Sidney Goldstein, M.D., F.C.C.P.

The study reported here of the relationship between the frequency of ventricular premature contractions during longterm electrocardiographic recording and the presence of ventricular dysfunction due to coronary artery disease indicates that a direct relationship between these two factors exists. The presence of ventricular asynergy observed during ventricular angiography was the only parameter, among a number of other hemodynamic factors studied which demonstrated such a relationship. The degree of ventricular premature beats, aberrancy or coupling interval duration, did not appear to have any descriptive significance.

Sudden death still remains the major cause of death due to coronary artery disease. A number of investigations have indicated that there are certain electrocardiographic predictors in patients dying suddenly of coronary artery disease (CAD). Ventricular premature beats have been well documented to be statistically associated with sudden death both in general population surveys1,2 and in patients after infarction.3,4 Intraventricular conduction defects,5 ischemic ST segments5 and relative bradycardia4 have been associated with sudden death as well. In addition, Kuller et al7 have observed that patients with pre-existing and symptomatic coronary artery disease represent the major portion of those dying suddenly. Gordon and Kannel,8 however, reported that in 50 percent of patients dying suddenly of coronary artery disease, there was no history of cardiac symptoms. Freisinger9 in observing patients with symptomatic coronary artery disease studied by coronary angiography noted that the mortality increased with the extent of the coronary arterial lesions. More recently, Bruschke et al10,11 reported that both the extent of coronary arterial lesions and ventriculographic abnormalities are directly related to increasing mortality of coronary artery disease. In order to provide a link between the coronary and ventricular angiographic findings, and the occurrence and frequency of ventricular premature beats, these arrhythmias were studied in a group of patients referred to this laboratory for the study of angina.

METHODS

Sixty-four patients admitted to the cardiology unit of the

*From the Cardiology Unit, Rochester General Hospital and Department of Medicine, University of Rochester, School of Medicine and Dentistry, Rochester, N.Y.

**Supported by a Fellowship grant from the Genesee Valley Heart Association.

Manuscript received December 6; revision accepted April 11.

For editorial comment, see page 346

Rochester General Hospital for the investigation of chest pain resembling angina pectoris were studied. There were 52 men and 12 women, ranging in age from 36 to 64 years, with a mean of 50.3 years. Right and left heart catheterization, selective coronary and left ventricular angiography were accomplished in all the patients. The left ventricular angiograms were taken on 16-mm cine film at 60 frames/second, in two oblique projections. Localized abnormalities of ventricular contractions were carefully noted using the criteria of Herman et al.12 Selective coronary angiograms were obtained by the Sones technique and reviewed independently by at least two observers, and a composite score and assessment developed. The severity of the coronary artery disease was graded according to the criteria of Freisinger et al,9 in which lesions in each of the three major coronary arteries were scored from 0-5, depending on the anatomic narrowing seen. During cardiac catheterization, 34 patients with coronary artery disease were stressed with an isoproterenol infusion (1-3 μg/min) to assess their myocardial lactate extraction. The percentage of lactate extraction or production was calculated by the method of Krasnow et al.13 A negative percentage extraction was considered abnormal.

Longterm portable electrocardiographic tape recordings using the Holter recording device were obtained in all the patients at least 24 hours before or 48 hours after the cardiac catheterization when patients were free of arm pain from the procedure. A group of these patients was monitored before and after catheterization, and there was no change in ventricular premature beat (VPB) frequency observed as a result of either anticipation of the procedure or as a result of the procedure. The mean duration of the tape was 8.2 hours, with a range of 6-11 hours. These recordings were usually obtained during the day between 8 AM and 8 PM, while the subject was ambulatory in the hospital or as outpatient. The patients were encouraged to engage in activity which was as normal as possible for them and record any symptoms they might experience during the recording period. Administration of all cardiac drugs and sedative medications was discontinued three days or more prior to the recording period. Digitalis therapy was discontinued at least a week prior to the recording. All the patients were maintained on a normal diet. A modified V5 monitoring lead was used, with the electrodes placed over the fifth rib on the nipple line bilaterally.

Each tape recording was manually analyzed by the Avionics' electrocardioscanner using 60:1 speedup factor, which correlated the electrocardiographic findings with real time. In order to ensure that no premature beats were missed and to record accurately the rate trends during the recording, the arrhythmographic output of the electroscanner was fed...
into an Electronics for Medicine photographic recorder and the output (arrhythmograph) printed at 10 mm/sec. The eight-hour electrocardiographic record was analyzed for basic rhythm, average heart rate, the fastest and slowest rate and the frequency of ventricular premature beats. All the ventricular premature beats were identified and analyzed according to their frequency (the number of VPBs per 1,000 normal beats) coupling index and aberrancy index. The coupling index was calculated for the dominant VPB and expressed as the R-R' interval of the coupled VPB divided by QT interval of the normal QRS complex (R-R' of VPB/QT normal). The proximity of VPB to the preceding T wave, a factor that is felt to be related to repetitive beating, was expressed by the coupling index. The aberrancy index was obtained by measuring the QRS duration of the VPB divided by the QRS duration of the normal beat (QRS-VPB/QRS-normal). VPBs of multifocal origin, periods of bigeminal rhythm and the occurrence of a sequence of two or more VPBs were carefully noted.

RESULTS

Nineteen patients had normal coronary and ventricular angiograms. Two patients had hiatus hernia, but in the other 17 patients exact etiology of chest pain could not be established. None of these patients

![Figure 1. Frequency distribution of VPBs in three groups.](image1)

had the systolic click-murmur syndrome. Fortyfive patients had significant coronary artery disease. The left ventricular contraction patterns were normal in 22 of these patients. Abnormal ventricular contraction was observed in 23 patients, manifested by localized hypokinetic, akinetic, or dyskinetic ventricular segments.

The distribution of VPBs according to their frequency in the normal patients and those with coronary artery disease with and without left ventricular asynergy is shown in Figure 1. There was a general trend for the normal patients to have fewer VPBs, although two patients in the normal group had greater than 5 VPBs/1,000. The patients with coronary artery disease and particularly asynergy had a greater frequency of VPBs but exhibited a wide distribution in the VPB frequency (Fig 2). The mean VPB frequency was 10.3±5.3/1,000 beats in the CAD-asynergy group as compared to 0.9±0.46 in the patients with coronary artery disease with normal left ventricles and 0.7±0.45 in the normal group (P = <.10). The median VPB frequency was significantly different between the groups (Fig 3). The median VPB frequency was 2 VPB's/1,000 in

![Figure 2. Frequency of VPBs/1,000 in three groups. Mean VPB frequency and one standard error of mean is shown. Each circle represents one patient.](image2)

![Figure 3. Median frequency of VPBs in three groups. There is significant difference in CAD-asynergy group from normal patients and those with CAD and normal left ventricle.](image3)

![Figure 4. Incidence of two VPBs/1,000 beats in three groups.](image4)
Table 1—Mean Coupling and Aberrancy Index in the Study Population*

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>CAD-Synergy</th>
<th>CAD-Asynergy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coupling index</td>
<td>(R-R'/QT)</td>
<td>1.7(1.2-3.0)</td>
<td>1.4(1.1-1.8)</td>
</tr>
<tr>
<td>Aberrancy index</td>
<td>(QRSvPQRSnormal)</td>
<td>1.3(1.2-1.7)</td>
<td>1.8(1.3-3.0)</td>
</tr>
</tbody>
</table>

*Numbers in parenthesis represent the observed range in each group. There was no significant difference in these groups.

The CAD-asynergy group, as compared to the CAD with normal ventricle and the normal group in which the median VPB frequency was less than 0.1/1,000 (P = <.05). Figure 4 illustrates the percentage of patients in each group who had more than 2 VPBs/1,000 beats.

The coupling index and aberrancy index of VPBs in the three groups are shown in Table 1. There was no significant difference in these indices between the groups, although the patients with coronary artery disease tended to have a shorter coupling and a higher aberrancy index.

Periods of ventricular bigeminy were noted in two patients with coronary artery disease, one of whom had asynergy of the left ventricle. Multifocal VPBs were seen in three patients with CAD and asynergy and one patient in each of the other two groups. Ventricular tachycardia (more than two consecutive VPBs) was noted in two patients with CAD; one with a normal ventricle and the other with ventricular asynergy. These two patients had VPB frequency of 9.9 and 19/1,000 beats, respectively.

In an attempt to eludicate other factors responsible for an increased frequency of VPBs in coronary artery disease patients, several other parameters were explored (Fig 5). There was no relationship between left ventricular end-diastolic pressure, coronary score or myocardial lactate extraction with isoproterenol stress, to increased frequency of VPBs.

Patients with asynergy tended to have more extensive coronary artery disease, although there was a considerable overlap of patients (Fig 6).

**Discussion**

Although coronary care units have resulted in a reduction of the in-hospital mortality of coronary artery disease, studies of the phase of acute myocardial infarction before admission to the hospital indicate that approximately two-thirds of the deaths from this disease occur suddenly and before admission. If we are to deal effectively with this problem short of prevention of coronary atherosclerosis, we must either deal more expeditiously with sudden collapse in the community, or be able to define that part of the population at risk of dying suddenly and develop medical or surgical therapy to prevent sudden death. The patients with pre-existing coronary heart disease are those who are clearly at a higher risk of subsequent myocardial infarction.
Clinical and epidemiologic surveys suggest that sudden death may be preceded by electrocardiographic abnormalities. Hinkle et al. reported that increased frequency of VPBs noted during long-term ambulatory monitoring in middle-aged men predicted a higher incidence of subsequent death and coronary artery disease. Studies by Chiang et al. in the Tecumseh population indicate that VPB, intraventricular conduction defects and A-V conduction defects noted on a routine ECG also were predictive of sudden death. In myocardial infarction survivors certain characteristics of VPBs such as their frequency and consecutiveness may bear on the higher long-term risk for sudden death, independent of other electrocardiographic abnormalities. The present study was undertaken to establish the relationship between the frequency and character of VPBs and cardiac function as defined hemodynamically, angiographically and biochemically.

The mean frequency of VPBs was 5.6/1,000 beats in all patients with CAD in our study. This is lower than the frequency of 10/1,000 beats observed by Hinkle et al. in those patients dying suddenly. There was no observed morbidity in our study during the short followup period. Coupling interval and degree of aberrancy failed to correlate with the degree of coronary artery disease and left ventricular asynergy. A coupling index of less than one was reported in 9 percent and 4.5 percent of patients recovering from infarction studied by Moss, Lown and Wolf, respectively. This was not observed in any of our patients. The patients with repetitive ventricular beats had a greater frequency of VPBs but not a significantly shortened R-R' interval or greater degree of aberrancy. Blierer et al. observed that the occurrence of VPBs showing R on T phenomenon in ambulatory patients, per se, was not associated with a greater incidence of paroxysmal ventricular tachycardia. They did, however, note an increased incidence of ventricular tachycardia in patients having a high frequency, multifocality and pairing of VPBs.

Ventricular tachyarrhythmia as a complication of ventricular aneurysms has been noted for some time, and the surgical removal of akinetic and dyskinetic segments has been proposed as a means of treatment when these arrhythmias are refractory to usual medical treatment. In our study there appeared to be a relationship between the presence of ventricular dysfunction and the increased frequency of VPBs. Although ventricular asynergy tended to be associated with a greater extent of coronary artery disease, a high coronary artery score only was not related to the increased frequency of VPBs. Correlation of other hemodynamic and metabolic parameters also failed to help delineate those patients with greater frequency of VPBs.

Thus, from this study, the important characteristics of patients with coronary artery disease that related to increased frequency of VPBs was the presence of regional abnormalities of left ventricular contraction pattern. Although left ventricular end-diastolic volume and compliance may influence VPB frequency by stretching of the ventricular wall and Purkinje fiber, it is most likely that in and around the areas of asynergy there is a wide degree of heterogeneity of myocardial depolarization which leads to re-entrant ventricular impulses. Experiments with animals using ventricular mapping indicate that there are major areas of varying degrees of ischemia surrounding the infarcted area. Whether or not this heterogeneity of the ischemia-infarction process predisposes to concomitant inhomogeneity of depolarization and subsequent re-entry phenomenon is not clearly established, although electrophysiologic studies suggest that this is so. These studies do suggest that a relationship exists between ventricular asynergy and increased VPB frequency which may have etiologic significance in the mechanism of sudden death in patients with coronary artery disease.

ACKNOWLEDGMENT: We are grateful to Mrs. Marian Shellman for the technical assistance in this study.

REFERENCES

1 Hinkle LE, Carver ST, Stevens M: The frequency of asymptomatic disturbances of cardiac rhythm and conduction in middle-aged men. Am J Cardiol 24:828, 1969
4 The Coronary Drug Project Research Group: The prognostic importance of premature beats following myocardial infarction. JAMA 223:1116, 1973
6 Hinkle LE, Carver ST, Flakun A: Slow heart rates and increased risk of cardiac death in middle-aged men. Arch Intern Med 129:732, 1972
11 Bruschke AVG, Proudfoot WL, Sones FM: Progress study of 590 consecutive nonsurgical cases of coronary disease
followed 5-9 years. II. Ventriculographic and other correlations. Circulation 47:1154, 1973
14 Han J, Goel BG: Electrophysiologic precursors of ventricular tachyarrhythmias. Arch Intern Med 129:749, 1972

The Lasting Fame of a Musical Genius

Giovanni Pierluigi da Palestrina (1524-1594) was born in the little town, twenty miles or so outside of Rome, from which he took his name. While maestro di capella in his native town, he gained the good opinion of the Bishop of Palestrina. It was the young musician's good fortune that the Bishop should in 1550 become Pope Julius III and should appoint him director of the Julian Choir, a long established foundation that acted as a training ground for Italian recruits to the Sistine Choir, the Pope's own personal choral body. There was nowhere any doubt as to his eminence as a composer. In his music is found the quintessence of the Counter Reformation—otherworldliness, a sense of awe and spiritual elevation, an inexhaustable flow of melody and a dynamic expressiveness. His 29 motets comprising the Song of Songs settings glow with religious passion and contain some of his finest moments of vigor and expressive coloring. Palestrina's masses will always be held to be his supreme achievement. In the universally known Stabat Mater he employs two choirs separately and in combination.


362 SHARMA, BALLANTyne, GOLDSTEIN