THE CLINICAL SIGNIFICANCE of the repetitive ventricular response (RVR) has become an issue of considerable interest and controversy.1-6 Despite the interest and efforts of several investigators, definite conclusions about its significance are not possible. In fact, the clinical and electrophysiologic aspects of the RVR have been a source of confusion, particularly for those not well acquainted with cardiac electrophysiologic studies.

Of primary importance is the fact that a uniform definition of RVR has not been established. In this communication, it refers to the occurrence of one or more (but less than five) nonstimulated ventricular beats after a paced ventricular premature beat (V2) either during basic atrial (sinus or atrial paced) or ventricular rhythms. A similar definition has been used in most of the published clinical studies, although the separation of multiple RVRs from nonsustained ventricular tachycardia (VT) has not been clarified.

Origin of Wide QRS Complexes After Premature Ventricular Complexes

Using the above definition, spontaneous QRS complexes after a paced V2 could have several causes. The mechanisms by which a paced V2 directly induces additional ventricular complexes include (1) macroreentry within the His-Purkinje system (Re-HPS), also referred to as bundle branch reentry (BBR), wherein the reentrant circuit incorporates the bundle of His and both the right and left bundle branches;7,8 (2) reentry localized to more peripheral areas of the Purkinje-muscle system, also referred to as intraventricular reentry (IVR), local reentry or non-BBR;9-12 (3) atrioventricular nodal reentry;13 and (4) reentry using retrograde conduction via the accessory and subsequent antegrade conduction over the normal pathway with aberrant intraventricular conduction. The reverse, i.e., retrograde conduction via the normal and antegrade ventricular depolarization over the accessory pathway, is also possible, even in the absence of overt preexcitation during sinus rhythm. In addition, wide QRS complexes may follow the paced V2 on occasions that are not initiated by the paced V2. These include aberrantly conducted supraventricular impulses due to retrograde concealed conduction of V2 in the HPS,6,29 spontaneously occurring ventricular extra beats and ventricular extra beats caused by mechanical irritation from the electrode catheters.13 A distinction between QRS complexes of different origins (which may follow V2) cannot be made without His or right bundle branch recordings.

The term RVR should include only responses that originate in the ventricles and are directly triggered by a paced V2, i.e., Re-HPS and IVR. Re-HPS is a physiologic phenomenon that occurs in approximately 50% of subjects with normal intraventricular conduction. Re-HPS occurs with similar frequency in patients with and without structural heart disease and in patients with or without spontaneous ventricular arrhythmias.6 Only patients with preexisting bundle branch block have a lower incidence of Re-HPS.6,29 RVR due to IVR, however, has been considered to represent an abnormal response. Its incidence and clinical significance have been studied by several investigators.1-6

Pacing Protocols

The overall incidence of RVR is significantly influenced by the pacing protocol. Electrophysiologic responses are notably different with ventricular premature stimulation during atrial vs ventricular drive and single (V2) vs two successive (V2 + V3) premature stimuli. The incidence of both Re-HPS and IVR is appreciably higher during ventricular vs atrial drive14 (Zipes DP; personal communication). The exact incidence of Re-HPS with one vs two premature stimuli is not known; however, IVR is more common with two extrastimuli (V2 + V3) than with one (V2), when the extrastimuli are introduced during ventricular drive.6,10 The incidence of either Re-HPS or IVR with a single stimulus vs two premature stimuli during atrial rhythms is not known.

Incidence and Clinical Significance of RVR in Different Patient Populations

Attention was first drawn to the clinical significance of RVR as a predictor of sudden death when the response occurred during atrial rhythms.1,2 Greene et al. reported that none of the 12 normal subjects (0%), 44 of 50 patients (88%) with recurrent VT, and 19 of 48 (39%) with recent acute myocardial infarction (MI) showed RVR.2 Within 1 year of follow-up, 15 of 19 patients with recent acute MI and RVR experienced VT or sudden death, whereas only four of 29 without
RVR developed VT or sudden death. This study suggested a relatively high sensitivity (0.79), specificity (0.85) and predictive value (0.79) of RVR as a predictor of VT or sudden death. Only RVR resulting from IVR can be entertained as having a possible predictive value, so it is significant that neither His nor right bundle branch recordings were obtained during this initial study by Greene et al., and the exact origin of RVR in that report therefore remains uncertain. However, in a subsequent study by the same authors in another group of patients, it was indicated that RVRs during atrial pacing are generally due to IVR. Therefore, the above studies implied that RVR due to IVR, when seen during atrial drives, have a predictive value for the development of VT or sudden death.

The report by Greene et al. is the only one that demonstrated a predictive value of RVR for subsequent VT or sudden death. A later study by Mason, using a comparable pacing protocol and patient population, could not substantiate these results. In the study by Mason, His bundle electrograms were used and RVR was noted in only nine of 59 (15%) patients with recurrent VT. In four patients (7%), RVR was due to Re-HPS, and in the remaining five (8%) it was probably due to IVR. In the series by Mason, eight of 59 patients died suddenly (all had previous MI) during an average of 13.6 months of follow-up. The incidence of sudden death was not different in patients with and without RVR due to IVR; however, none of the patients with Re-HPS died suddenly. In patients with ischemic heart disease the incidence of RVR was the same with or without previous MI. These results suggest that RVR is insensitive in predicting future VT or sudden death in patients with previous MI. It should be pointed out, however, that systematic studies specifically dealing with the predictive value of RVR in patients after recent MI (of comparable age) as originally reported by Greene et al. have not been carried out.

Ruskin et al. report the incidence and clinical significance of RVR in three patient populations: those with recurrent sustained VT, recurrent non-sustained VT and prehospital ventricular fibrillation (VF). In this study, the term RVR was applied only to responses that occurred during sinus or paced atrial rhythms and that were not due to Re-HPS. If IVR indeed could detect the risk of serious ventricular arrhythmias, one should be able to elicit such a response in patients who already have malignant ventricular arrhythmias. All three groups studied by Ruskin et al. had life-threatening ventricular arrhythmias, and therefore were ideally suited to test the sensitivity of RVR to detect the presence of such arrhythmias. The relatively uncommon occurrence of RVR (11 of 85, 13%) in this series suggests that RVR is an insensitive index for detecting vulnerability to life-threatening ventricular arrhythmias. Can such a marked discrepancy between the series by Ruskin et al. and Greene et al. be resolved? There are no apparent major differences in pacing protocols, stimulus characteristics or chamber of pacing, although Greene et al. did pace from an additional site in the right ventricle in 14% of cases. Although no two patient populations are exactly alike, Ruskin et al. indicated that the clinical characteristics of patients with VT in both studies were quite similar. All patients in this series by Ruskin et al. were tested in an unmedicated state, whereas antiarrhythmic medications were continued in several patients studied by Greene and associates. With the introduction of antiarrhythmic drugs, the incidence of RVR (from all causes) may be increased or decreased, as demonstrated with Re-HPS and i.v. procainamide. The suppression of Re-HPS with an antiarrhythmic agent could unmask IVR, or vice versa. The origin of RVR in the report by Greene et al. remains uncertain, so the inclusion of other types of wide QRS complexes after V2 could collectively account for a significant number of cases with RVR in their series. Differences in length of the basic drive cycle and spontaneous variation in sinus cycle are other reasons for the disparate results. A combination of all of the above considerations might explain the differences in the incidence of RVR in more recent studies compared with that reported by Greene et al.

Clinical Significance of RVR with Different PACing Protocols

The studies by Greene et al., Ruskin et al. and Mason deal with RVR after V2 during atrial rhythms. Another recent study analyzed the RVR with ventricular premature stimulation during paced ventricular drives. Two hundred thirty-eight of 400 patients (59.5%) manifested RVR. Forty percent had isolated Re-HPS, 6.3% had only IVR and 13.3% had both. However, RVRs due to IVR were more common in patients with organic heart disease compared with those without (23.9% vs 8.1%, respectively). That is, in patients with IVR, 85.5% had organic heart disease and 11.5% did not. In this study, 43 of 58 patients (74%) with documented VT and/or VF manifested IVR. The incidence of RVR during ventricular drive presented in the study by Farshidi et al. is not comparable to any of the series discussed earlier because of differences in pacing protocols. Whether IVR induced during ventricular drive has higher sensitivity in detecting vulnerability to serious ventricular arrhythmias or sudden death is not known. Similarly, it is not known whether RVR in response to one vs two premature beats during either atrial or ventricular pacing have different clinical import. A uniform definition, clearly outlined recording and pacing protocols, a detailed description of clinical characteristics and comparable management during follow-up will help to resolve some of the problems of comparing results of different series. The nature and mechanism of RVRs must be categorized in order to examine their predictive value.

Evidence indicates that electrical induction of sustained VT correlates well with the occurrence of spontaneous arrhythmia. Similarly, suppression of inducible sustained VT with antiarrhythmic agents provides a more dependable objective end point in
search for a predictable therapeutic goal. Ruskin et al. also suggest that initiation of reproducible, non-sustained VT (more than five beats) may also have a similar clinical significance. The suppression of IVR with antiarrhythmic agents and its use as a dependable therapeutic end point does not appear justified at the present time.22 Aside from its low sensitivity, even the reproducibility of IVR has not been adequately tested, although obviously important before considering its abolition as a reliable indicator of effective therapeutic control of spontaneous ventricular arrhythmias.

In conclusion:
(1) There are several mechanisms for wide QRS complexes after paced Vp. The various types cannot be distinguished without His and/or right bundle branch recordings.

(2) RVR due to Re-HPS is common during ventricular (less so during atrial) drive; represents a physiologic phenomenon and occurs with equal frequency in patients with and without structural heart disease and in patients with and without spontaneous ventricular arrhythmias.

(3) RVRs due to IVR are more common in patients with underlying structural heart disease, in particular coronary artery disease.

(4) RVR due to IVR is an insensitive predictor of concurrent or future life-threatening ventricular arrhythmias or sudden death.

(5) Although specificity of RVR for VT or sudden death has not been adequately evaluated, the absence of RVR during atrial drive in any patient population is expected to be of little value due to its extremely low sensitivity.

(6) Suppression of IVR with antiarrhythmic agents cannot be considered a dependable therapeutic end point because of its low sensitivity and unknown reproducibility.

References
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