First Postpacing Interval Variability During Right Ventricular Stimulation

A Single Algorithm for the Differential Diagnosis of Regular Tachycardias

Angel Arenal, MD; Jesus Almendral, MD; Julian Villacastin, MD; Raimundo Morris, MD; Eduardo Castellanos, MD; Juan Luis Delcan, MD

Background—Failure to differentiate supraventricular from ventricular arrhythmias is the most frequent cause of inappropriate implantable cardioverter-defibrillator therapies. Although a sudden-onset criterion is available to differentiate sustained monomorphic ventricular tachycardias (SMVTs) and sinus tachycardias (STs), SMVTs arising during ST and SMVTs gradually accelerating above the cutoff rate can remain undetected. Regular paroxysmal atrial tachycardias (ATs) also can be undetected by onset and stability algorithms. We hypothesized that the first postpacing interval (FPPI) variability after overdrive right ventricular pacing may differentiate SMVTs from STs and ATs.

Methods and Results—FPPI variability was measured in 23 SMVTs (cycle length [CL] 366±50 ms [VT group]), 27 supraventricular tachycardias, 15 episodes of induced or simulated ATs (CL 376±29 ms [AT group]), and 12 exercise-related STs (CL 381±24 [ST group]). Sequences of trains of 5, 10, and 15 beats were delivered with a CL 40 ms shorter than the tachycardia CL. An FPPI absolute mean difference between consecutive trains of 5 and 10 beats (ΔFPPI) ≥25 ms identified all VTs (mean difference 5±7 ms). In the AT group, the ΔFPPI was <25 ms in all sequences (mean difference 129±60 ms, P<0.01). In the ST group, the ΔFPPI was >50 ms in all STs (mean difference 118±47 ms, P<0.01).

Conclusions—FPPI variability may differentiate SMVT from AT and ST. This criterion is potentially useful in implantable devices that use a single ventricular lead. (Circulation. 1998;98:671-677.)

Key Words: diagnosis ■ tachycardia ■ pacing

The implantable cardioverter-defibrillator is becoming one of the most powerful therapeutic tools in the treatment of sustained ventricular arrhythmias and for the prevention of sudden death.1-4 The possibility of implanting transvenous systems5-7 and the availability of antitachycardia pacing therapies have undoubtedly increased the use of these devices for the treatment of patients with frequent episodes of SMVT, even if these tachycardias do not produce loss of consciousness.8-10 Currently, slower tachycardias are being treated by the new devices. The recognition of these tachycardias implies a lower cutoff rate and consequently an increasing risk for misdiagnosing atrial and STs because of the overlapping in CLs.11,12 This problem can be accentuated by the use of antiarrhythmic drugs.13 Inappropriate therapy delivery for supraventricular tachyarrhythmias has been documented in up to 16% of patients, whereas only a minority of them had the arrhythmia before the implant.14 Because aggressive antitachycardia pacing and low-voltage cardioversion capabilities delivered during supraventricular rhythms may induce VTs requiring additional therapeutic intervention,14 the recognition of supraventricular arrhythmias that reach the cutoff cycle is essential for the adequate functioning of this device.

Detection enhancements have been incorporated in the new devices to improve diagnostic accuracy. While the rate stability criterion is useful in differentiating atrial fibrillation,15 the sudden-onset algorithm may help to discriminate ST.16 Nevertheless, the onset criterion may provoke some discrimination errors: (1) VTs induced by ST, (2) gradual acceleration of VTs above the cutoff rate, and (3) ST and premature ventricular beats, simulating a sudden rate change. The first 2 limitations are particularly worrisome because they may leave VTs untreated. Finally, regular AT may have a sudden onset and thus may be diagnosed as VT by use of this criterion.

This study aims to obtain a new algorithm to differentiate ST and AT from SMVT independent of the type of onset. The purpose of our study is to differentiate monomorphic VTs from regular ATs and STs, analyzing the variability of the FPPI or return cycle after synchronized trains of paced impulses with the same CL but with a different number of beats, delivered at the RVA during tachycardia. Our hypothesis is that the FPPI will remain constant in the setting of SMVTs, whereas this interval will change if the tachycardia originates in the atria. This hypothesis is based on the...
following: (1) There is stability of the FPPI during entrainment of reentrant VTs, provided the pacing CL is long enough to avoid the end of the shortest relative refractory period of the circuit, so the tissue has recovered full excitability. (2) The conduction time between a ventricular pacing site and the tachycardia origin is expected to be shorter in VTs than in ATs and STs (provided there are no accessory AV connections), entrainment of SMVTs will probably occur with ventricular trains of fewer beats. Thus, in VTs the FPPI is expected to remain stable when short and long trains are compared, whereas in ATs and STs if the short train does not reach the circuit and a longer train does, the FPPI will be different. (3) In cases of no 1:1 ventriculoatrial conduction at the tachycardia rate, trains with different number of beats might produce a different degree of retrograde AV nodal penetration, modifying the anterograde conduction time of the first postpacing beat.

**Methods**

**Study Groups**

**VT Group**
This group included 23 different SMVTs induced during the electrophysiological study in 22 patients (age 57 ± 8 years) with chronic myocardial infarction and at least 1 episode of spontaneous monomorphic VT. All the induced VTs were hemodynamically well tolerated, and the VT CL was 366 ± 50 ms (range from 470 to 280 ms). The morphology of the VT was similar to left bundle-branch block in 9 cases and similar to right bundle-branch block in 14. The maximal range of RR variability before ventricular pacing was 30 ms.

**AT Group**
This group included 15 ATs (11 of them were simulated by atrial pacing) evaluated during the electrophysiological study in 15 patients (age 49 ± 11 years). Four patients were included in the VT group; in the remaining patients the clinical indication of electrophysiological study was unexplained syncope. None of these patients had an accessory pathway or AV nodal reentrant tachycardia. The inclusion criterion for simulated tachycardias was a Wenckebach CL < 400 ms. The shortest regular ventricular CL was 376 ± 29 ms (range from 460 to 330 ms).

**ST Group**
This group included 12 STs (CL 381 ± 24 ms) observed during exercise testing in 12 patients (50 ± 10 years) in whom a third-generation implantable defibrillator with tiered therapies and electrogram storing capabilities was implanted.

**Electrophysiological Study**
After written informed consent was obtained, the electrophysiological study was performed in the postabsorptive state. At least 3 quadripolar catheters were placed at the right atrium, RVA, and right ventricular outflow tract or His bundle area. The distal pair of electrodes was used for pacing and the proximal pair for local electrogram recording. Intracardiac recordings were filtered at 30 to 500 Hz and displayed simultaneously with ≥ 3 ECG leads (I, aVF, V1) on a 12-channel photographic recorder (VR-12, Honeywell), at a paper speed of 100 mm/s. Digitized recordings from 6 patients were stored in a computer system (Bard Electrophysiology) for further analysis. Stimulation was performed with a programmable stimulator (UHS-20 Biotronik) set to deliver rectangular pulses of 1-ms duration at twice diastolic threshold. Programmed stimulation was performed to eliminate the possibility of an atroioventricular accessory pathway and to induce VT when indicated.

**Ventricular Stimulation Protocol During Tachycardia**
Sequences of synchronized trains at a CL 40 ms shorter than the tachycardia cycle, separated by 2-second intertrain pauses, were delivered at the RVA during VT or AT. Each sequence consisted of 3 trains: the first train was 5 beats, the second train 10 beats, and the third train 15 beats. The coupling interval of the first stimulated beat was the CL of the train. SMVTs usually present some CL variability, particularly soon after the initiation. To study if the FPPI duration was a function of the time after tachycardia initiation, each sequence was delivered 3 times: during the first 20 seconds, between 20 and 40 seconds, and between 40 and 60 seconds after tachycardia initiation.

**Specific Atrial Stimulation Protocol**
In 11 patients atrial stimulation was used to simulate AT. In these cases (1) The Wenckebach CL was determined during continuous atrial pacing. If the Wenckebach cycle was > 400 ms, the patient was not included in the following part of the study. (2) AT was simulated by continuous atrial pacing in AAI mode at a CL 20 ms longer than the Wenckebach CL to avoid ventricular CL changes caused by oscillations in the Wenckebach point. Only after the ventricular rate was stable for ≥ 10 seconds was the ventricular stimulation protocol started.

**Exercise Test**
The treadmill test, with modified Bruce protocol, was performed in a postabsorptive state ≥ 4 days after the implantation procedure if no contraindication was present. At least 2 therapy zones were programmed. To calculate the FPPI variability, we programmed in the VT zone 2 consecutive bursts of 5 and 10 beats at a CL of 91% of the tachycardia CL as the first therapy. The VT zone detection was activated at the peak of exercise if no angina, hypotension, or intense dyspnea was present. The detection interval was programmed 20 ms longer than the CL present at this particular moment.

**Measurements**
FPPI was considered as the interval, in milliseconds, between the last stimulus artifact of the pacing train and the first rapid deflection crossing the baseline of the first nonstimulated beat. Train-dependent FPPI variability was defined as the difference between the FPPI of consecutive trains. It was calculated between trains of 5 and 10 beats and between trains of 10 and 15 beats in VT and AT. In ST it was calculated only between trains of 5 and 10 beats.

The parameter of time-dependent FPPI variability was calculated only in tachycardia with sudden onset (AT and VT). It was the SD of the FPPI measured after the pacing train with the same number of beats but delivered at different intervals after VT and AT initiation. For example, the time-dependent FPPI variability after trains of 5 beats was the SD calculated with the FPPIs obtained during the first 20 seconds, between 20 and 40 seconds, and between 40 and 60 seconds after VT initiation.
Data Analysis

Values are expressed as mean±SD. FPPIs were compared by ANOVA. Post hoc comparisons between groups were made with the Tukey test. Two-tailed probability values <0.05 were considered significant.

Results

Time-Dependent FPPI Variability

VT Group

The time-dependent FPPI variability was minimal after pacing trains of 5, 10, and 15 beats (2±3, 3±4, and 3±3 ms, respectively). Thus, it could be considered that the FPPI was time independent in reference to VT onset when it was measured within the first minute after VT initiation (Figure 1, left).

AT Group

FPPI variability after pacing trains of 5, 10, and 15 beats was (24±28, 100±77, and 48±53 ms, respectively). Therefore, FPPI variability in the setting of AT was greater than the variability observed in VTs. The FPPI variability ranges from 5 to 98 ms, 0 to 230 ms, and 0 to 173 ms after 5-, 10-, and 15-beat trains (Figure 1, right).

Train-Dependent FPPI Variability

VT Group

All the pacing sequences were considered for this analysis. The FPPIs after 5, 10, and 15 beats were 477±90, 481±91, and 484±92 ms, respectively (Figure 2). When the FPPIs after 5 and 10 beats were compared, the ΔFPPI 5 to 10 was 5±7 ms (Figure 3). The ΔFPPI 5 to 10 was ≤10, 20, and 25 ms in 88%, 98%, and 100% of the sequences, respectively (Figure 4). Comparing the FPPIs after 10 and 15 beats, the ΔFPPI 10 to 15 was 4±6 ms. In 90% and in 100% of sequences, the ΔFPPI 10 to 15 was ≤10 and 20 ms, respectively (Figure 4).

AT Group

The FPPIs were significantly different after 5, 10, and 15 beats, 578±68, 639±152, and 618±83 ms (P<0.01, Welch ANOVA) (Figure 2). The ΔFPPI 5 to 10 was longer than in the VT group: 129±60 ms (Figure 5). In no sequence was the difference ≤25 ms, in 87% it was >50 ms, and in only 13% of sequences the difference was between 25 and 50 ms. Although the ΔFPPI 10 to 15 was similar to the ΔFPPI 5 to 10 (118±60 ms), in 7% and 17% of the sequences the...
difference was \( \leq 25 \) and 50 ms, respectively. In 83% of the sequences the difference was 50 ms (Figure 6).

**ST Group**

The FPPIs were significantly different after 5 and 10 beats (585±70 versus 663±132 ms, \( P < 0.01 \)) (Table). In no sequence was the difference \( \geq 50 \) ms (Figure 7) despite the sinus CL being identical before the first burst and after the last burst (380±25 and 381±25 ms).

**Discussion**

Our data suggest that a single comparison of the FPPI after 2 paced ventricular trains of 5 and 10 beats delivered during tachycardia, even during the first 20 seconds, can differentiate SMVTs from STs and ATs independent of the onset of the tachycardia. A \( \Delta \)FPPI 5 to 10 shorter than 25 ms identifies the regular rhythm as a VT, whereas if this difference is longer, the rhythm should be supraventricular.

It is obvious that the rate criterion is insufficient to discriminate between supraventricular and slow VTs. Although several algorithms have been proposed for automatic differentiation between ventricular and supraventricular arrhythmias, only those that compare the RR intervals are being widely used. The stability criterion that measures the variability of the tachycardia CL is useful for the differentiation of atrial fibrillation. For the diagnosis of ST, the sudden-onset algorithm has recently been incorporated into implantable devices. This algorithm measures the decrement in the CL at the onset of the tachycardia in relation to previous intervals. The decrement in CL during STs is

![Figure 3](http://circ.ahajournals.org/)

**Figure 3.** Response to overdrive pacing trains with different numbers of beats. Surface ECG leads I, aVF, aVR, V₁, and V₆ as well as intracardiac electrograms from the His bundle area; right ventricular outflow tract (RVOT), and RVA are displayed during a right-bundle, superior-axis VT (300-ms CL). A, Synchronized train of 5 beats at a CL of 260 ms (40 ms less than VT cycle) is delivered at the RVA. FPPI is 340 ms. B, During the same VT after a train of 10 beats, FPPI remains constant at 340 ms.

![Figure 4](http://circ.ahajournals.org/)

**Figure 4.** Percentage of sequences in which difference between the FPPI after trains of different number of beats (\( \Delta \)FPPI) is \( \leq 10, 20, \) and 25 ms in the VT group. \( \Delta \)FPPI 5 to 10 was \( \leq 25 \) ms in 100% of the sequences; \( \Delta \)FPPI 10 to 15 was \( \leq 20 \) ms in all sequences.

![Figure 5](http://circ.ahajournals.org/)

**Figure 5.** Differences in FPPI related to different duration of ventricular trains during an example of AT. Four surface ECG leads are recorded along with the intracavitary electrograms of the His bundle (HB), right ventricular outflow tract (RVOT), and RVA during ventricular pacing with trains of 5 (A) and 10 beats (B). FPPI is 125 ms shorter after a 10-beat train.
expected to be gradual in contrast to VTs, in which the shortening of the CL is usually abrupt. Swerdlow et al.\textsuperscript{20} prospectively evaluated the rate stability and sudden-onset criteria in 100 patients. Although a stability criterion of 40 ms allowed correct detection of all episodes of spontaneous or induced VT, the sudden onset was less effective; it failed to detect 0.5% episodes of spontaneous VTs. These VTs arose during periods of ST or gradually accelerated above the cutoff rate. Another limitation of the onset criterion is the impossibility to differentiate paroxysmal ATs with sudden onset.

**FPPI Variability in VT**

Our data have shown that the FPPI during overdrive pacing in SMVTs remains constant independent of the number of paced beats and the pacing delay from the VT initiation. Most monomorphic VTs observed in patients with chronic myocardial infarction are reentrant arrhythmias based in an anatomic circuit,\textsuperscript{21} in which it is possible to demonstrate a fully excitable gap between the head and the tail of the wave front.\textsuperscript{22} This fully excitable gap occurs when the wavelength of the reentrant impulse is shorter than the path length; in this situation a critical part of the circuit is fully excitable and can be invaded by impulses initiated from outside the circuit. Hence appropriately timed premature impulses can reset the tachycardia when they enter the circuit and propagate around it in the same way as the reentrant impulse.\textsuperscript{23,24} Entrainment involves continuous resetting of the tachycardia by overdrive stimulation.\textsuperscript{25,26} In the presence of a fully excitable gap, if the pacing CL is longer than the shortest functional refractory period of the circuit, the head of the activation will never impinge on the tail of refractoriness of the previous beat, therefore each stimulus will conduct in a fully recovered circuit. Consequently, the conduction velocity will be constant independent of the number of beats of the train. In cases in which the stimulation CL is shorter than the shortest functional refractory period, a stimulus will reach the reentrant circuit when it is relatively refractory, resulting in conduction delay. Because of this delay, subsequent stimuli will encounter tissue that has had even less time to recover, resulting in further conduction slowing and progressive increase in the return cycle. In this circumstance the return cycle can increase in relation to the number of beats.\textsuperscript{27} In our protocol we used a pacing CL of only 40 ms less than the VT CL, in an attempt to eliminate this possibility. Although resetting with single or double extrastimuli demonstrated some duration of a flat response curve compatible with a full excitable gap in only 70% of VTs,\textsuperscript{23} the FPPI stability observed in our study suggests that all included VTs presented a fully excitable gap; this discrepancy can be explained first by the fact that these VTs were relatively slow and second by the use of pacing train instead of extrastimuli. The pacing trains may avoid the shortest intervals needed by the extrastimuli technique; additionally the pacing trains may modify and shorten the refractoriness inside and outside the circuit.

**FPPI Variability in Exercise-Related ST**

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Mean±SD: 381±24 341±19 585±70 380±25 337±16 663±132 118±47 381±25

PCL indicates pacing cycle length; TCL, tachycardia cycle length; 1st burst, 5 beats; and 2nd burst, 10 beats.
Another important point is the supposed lack of effect in the FPPI stability of the VT CL variability. This variability is more marked in slower VTs and within the first 50 beats, the exact type of tachycardia and time in which this protocol was analyzed. However, we did not observe significant variability when the FPPI after trains with the same number of beats were compared 20 seconds apart within the first minute of the VT induction. The CL variability was not determined except for the period preceding the first ventricular train, nevertheless it is very improbable that we selected a group with such a low rate variability, which might explain our results. It seems more possible that the rapid pacing could stabilize the electrophysiological properties of the circuit and thus eliminate the spontaneous change in VT CL.

FPPI Variability in ST and AT
During pacing at the RVA, we observed important differences when the FPPIs after consecutive trains were compared. But even more important than these general differences was the fact that no sequence was found in which the difference was ≤25 ms for AT and 50 ms for ST, when FPPIs after 5 and 10 beats were compared, in contrast to the VT group, in which all the sequences the differences were ≤25 ms. There are some possible explanations for these differences: (1) The distance from the RVA to the atrial pacing site or sinus node is greater than it is to any VT circuit, so whereas a 5-beat train is long enough to reach the ventricular circuit, it is probably insufficient to reach the atrial focus; in this case the FPPI is usually shorter than the FPPI after a longer train in which the circuit is reset, such as a 10-beat train. (2) Trains with a different duration may produce different degrees of retrograde penetration in the AV node, modifying in a different degree the AV nodal conduction of the first post-pacing sinus beat. We did not observe, even with 15-beat trains, retrograde atrial capture during tachycardia, therefore the second explanation seems to be the most reasonable. These results seem to be independent of the AV nodal conduction state. In most simulated AT, a very long PR interval was observed, reflecting a stressed conduction status in the AV node, probably different from what is present during ST in which the AV nodal conduction is improved by catecholamines.

Limitations
Theoretically, in the following situations the FPPI algorithm may lead to misdiagnosis: (1) VT acceleration or induction of a different VT by the longest train can provoke substantial changes in the FPPI. (2) Use-dependent effect of antiarrhythmic drugs, a prolongation of the FPPI in response to longer pacing trains, might be observed in patients with VT under antiarrhythmic drug treatment. (3) Ventricular pacing trains, even during ST, may induce reentrant ventricular beats with a similar coupling interval simulating a VT. Nevertheless, we did not observe this response with our stimulation protocol. (4) Although we were able to entrain all tachycardias, even those with a morphology similar to right bundle-branch block, we cannot exclude the possibility of achieving entertainment with a short train in a VT located far from the RVA (laterobasal wall of the left ventricle). (5) Most of the cases of the AT group were “ATs” simulated by AAI pacing. This may be criticized as artificial. However, because AAI pacing is completely regular and does not present overdrive suppression, it will produce the most regular FPPI at the atrial level. Thus, this AT simulation would have been the most likely to behave against our hypothesis. (6) These data have been obtained from induced VT and simulated tachycardias; we do not have data about the applicability of this algorithm in spontaneous VT, nor therefore in clinical practice. Further studies with implanted devices should be conducted to validate the FPPI stability algorithms with the use of electrogram morphology during tachycardia.

Although we did not induce any VT by using ventricular trains, this is a possibility to keep in mind. Nevertheless, an electrophysiological study previous to hospital discharge could easily identify these cases in which the ventricular pacing could provoke some of the previously mentioned undesirable effects.

Potential Clinical Implications
The FPPI variability algorithm could be incorporated in the implantable cardioverter-defibrillator to enhance presently available detection criteria in devices with a single ventricular lead.

References


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