JACC Vol. 18, No. 7
December 1991:1722–6

Pre-excited RR Intervals During Atrial Fibrillation in the Wolff-Parkinson-White Syndrome: Influence of the Atrioventricular Node Refractory Period

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The ventricular rate and percent of pre-excited QRS complexes during atrial fibrillation were compared in two groups of patients with the Wolff-Parkinson-White syndrome. Group A consisted of 22 patients whose anterograde effective refractory period of the accessory pathway was longer than that of the atrioventricular (AV) node. Group B consisted of 23 patients in whom this relation was reversed. No patient had organic heart disease.

Both groups had a similar effective refractory period of the accessory pathway (288 ± 37 vs. 280 ± 26 ms), whereas that of the AV node was shorter in group A than group B (242 ± 25 vs. 285 ± 27 ms, p = 0.0001). Patients in group A had a lower percent of pre-excited QRS complexes during atrial fibrillation (39 ± 43% vs. 93 ± 20%, p = 0.0001). In the 21 patients whose refractory period was measured, the difference was plotted against the percent of pre-excited QRS complexes; there was a significant correlation between the two (r = −0.83, p < 0.001).

In patients in whom pre-excited RR intervals were present, the pre-excited RR intervals were compared between the two groups. Both groups had similar effective refractory periods of the accessory pathway (265 ± 22 vs. 280 ± 27 ms) and ventricle (200 ± 17 vs. 211 ± 26 ms). The effective refractory period of the AV node was shorter in group A (248 ± 22 vs. 285 ± 28 ms, p = 0.0005). The shortest pre-excited RR interval did not show any difference (244 ± 37 vs. 265 ± 41 ms). However, both the average (328 ± 39 vs. 397 ± 56 ms, p = 0.001) and longest (495 ± 109 vs. 666 ± 205 ms, p = 0.02) pre-excited RR intervals were shorter in group A.

These data suggest that interaction between the refractory periods of the AV node and accessory pathway contributes to the percent of pre-excited QRS complexes. The effective refractory period of the AV node also indirectly contributes to the duration of pre-excited RR intervals. This contribution is greatest when RR intervals are long.

(J Am Coll Cardiol 1991;18:1722–6)

In patients with ventricular pre-excitation, atrioventricular (AV) conduction during atrial fibrillation takes place through the AV node or the accessory AV pathway, or both. Although the effects of the refractory period of the AV node and accessory pathway on the ventricular rate during atrial fibrillation have been investigated independently in patients with and without manifest pre-excitation (1,2), a systematic evaluation of the impact of AV node refractoriness on pre-excited RR intervals during atrial fibrillation has not been performed.

We speculated that disparities between AV node and accessory pathway refractory periods would directly and indirectly influence AV conduction through the accessory pathway. To test this hypothesis, we compared the ventricular rate and percent of pre-excited QRS complexes during atrial fibrillation in patients whose refractory period of the AV node was shorter than that of the accessory pathway in patients in whom this relation was reversed.

Methods

Study patients. The study group consisted of 52 consecutive patients with manifest ventricular pre-excitation who underwent electrophysiologic study. All patients had symptomatic tachycardia (reciprocating tachycardia or atrial fibrillation, or both). No patient had organic heart disease as assessed clinically and echocardiographically.

Electrophysiologic studies. Electrophysiologic studies were performed with the patient in a mildly sedated postabsorptive state after obtaining verbal and written consent. All antiarrhythmic medications were discontinued for at least five half-lives before the study. Three quadripolar electrode catheters were introduced through the femoral vein and placed in the high right atrium and right ventricular apex and across the tricuspid valve to record the His bundle electrogram. Another quadripolar electrode catheter was introduced through the left subclavian vein and placed in the coronary sinus. Bipolar recording with a frequency response

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Manuscript received March 20, 1991; revised manuscript received May 20, 1991, accepted June 6, 1991.

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0735-1097/91/$3.50

of 50 to 500 Hz was used to record atrial, ventricular and His bundle electrograms. Unipolar recording with filter settings of 0.5 to 500 Hz was used to record atrial sites in the coronary sinus. Intracardiac electrograms were displayed simultaneously with standard surface electrocardiographic (ECG) leads I, II, III, V_1 and V_6 on a multichannel strip chart recorder at paper speeds of 100 to 250 mm/s. Both the atrium and the right ventricle were stimulated using a custom-designed programmed digital stimulator (Bloom Associates) that delivered stimuli of approximately twice diastolic threshold at a stimulus duration of 2 ms.

For extrastimulus testing, single atrial or ventricular extrastimuli were delivered at progressively shorter coupling intervals after every eighth constant paced cycle (generally 400 and 600 ms) until the effective refractory period of the atrium or the ventricle was reached. For incremental pacing, the atrium or ventricule was paced at a constant cycle length for approximately 10 s, followed by a sudden change to a shorter cycle length. This sequence was repeated until atrioventricular (AV) block occurred anterogradely or retrogradely or until a pacing cycle length of 250 ms was reached. Atrial fibrillation was induced by rapid atrial pacing if it did not occur spontaneously during the course of the study. Intervals were measured over a 1-min episode of atrial fibrillation (3). The shortest, longest and average RR intervals between consecutive pre-excited or normal beats were measured. To minimize the effect of increased catecholamine levels on ventricular response during atrial fibrillation, all intervals were measured immediately after induction.

Definitions. *The effective refractory period of the AV node* was defined as the longest interval between the atrial electrogram of the basic drive (A1) and that of the premature beat (A2) measured at the His electrogram that failed to provoke His bundle depolarization.

The anterograde effective refractory period of the accessory pathway was defined as the longest A_1-A_2 interval measured at the electrode closest to the accessory pathway that failed to propagate to the ventricle.

The effective refractory period of the ventricle was defined as the longest interval between the stimulus artifact of the basic drive (S_1) and that of the premature beat (S_2) that failed to provoke ventricular depolarization. A drive train cycle length of 400 ms was used to determine effective refractory periods in this study.

All QRS complexes during atrial fibrillation were defined as normal if there was no evidence of pre-excitation in any ECG lead when visual comparison was made with tracings obtained during narrow QRS (orthodromic) tachycardia in the absence of bundle branch block.

Data analysis. For the purpose of the present study, patients were divided into two groups. Group A consisted of 22 patients whose effective refractory period of the accessory pathway was longer than that of the AV node. Group B consisted of 23 patients in whom this relation was reversed. The remaining patients (n = 7) were excluded because of inability to determine the anterograde effective refractory period of the accessory pathway. The effective refractory period of the AV node could not always be determined; if it was equal to or longer than the effective refractory period of the accessory pathway, the shortest value was selected for statistical purposes. Likewise, if it was shorter than that of the accessory pathway but could not be determined, the longest value was used for the same purpose.

Table 1. Clinical and Electrophysiologic Data in 45 Patients

	Group A (n = 22)	Group B (n = 23)	p Value
Age (yr)	31 ± 14	30 ± 13	0.86
Gender (M/F)	9/13	16/7	0.10
AP location			0.95
Left lateral	14	14	
Posteroseptal	4	7	
Right anteroseptal	2	1	
Right free wall	2	1	
AVN ERP (ms)	242 ± 25	285 ± 27	0.0001
AP ERP (ms)	288 ± 37	280 ± 26	0.41
RV ERP (ms)	201 ± 16	208 ± 24	0.38
% QRS (AF)	39 ± 43	93 ± 20	0.0001

AP = accessory pathway; AVN = atrioventricular node; ERP = effective refractory period; F = female; M = male; % QRS (AF) = percent of pre-excited QRS complexes during atrial fibrillation; RV = right ventricle.

Statistical analysis. Values were expressed as mean ± 1 SD. A two-tailed unpaired *t* test, chi-square test and linear regression were used when appropriate. A p value <0.05 was considered statistically significant.

Results

Clinical and electrophysiologic characteristics of the two groups (Table 1). Patients in groups A and B were well matched for gender, age (mean 31 vs. 30 years), site of the accessory pathway, anterograde effective refarctory period of the accessory pathway (288 vs. 280 ms) and effective refractory period of the right ventricle (201 vs. 208 ms). The effective refractory period of the atrioventricular (AV) node was significantly shorter in group A than group B (242 vs. 285 ms, p = 0.0001).

Percent of pre-excited QRS complexes during atrial fibrillation. Patients in group A had a smaller percent of pre-excited QRS complexes during atrial fibrillation than those in group B (39% vs. 93%, p = 0.0001) (Fig. 1). In patients whose refractory period of both the AV node and accessory pathway were measured (n = 21), the difference between these values was plotted against the percent of pre-excited QRS complexes. There was a significant correlation between the two (r = −0.83, p = 0.001) (Fig. 2).

Pre-excited RR intervals during atrial fibrillation (Table 2). In patients in whom pre-excited RR intervals were present, the shortest, longest and average pre-excited RR intervals were compared between the two groups to evaluate the indirect contribution of the AV node. Patients with measurable pre-excited RR intervals in the two groups had a similar

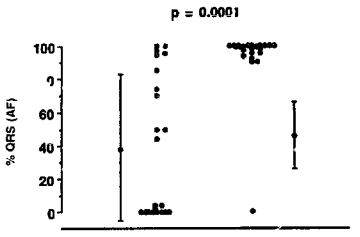


Figure 1. Percent of pre-excited QRS complexes during atrial fibrillation (% QRS [AF]). Both refractory periods were measured at a drive cycle length of 400 ms. The standard deviations are depicted by the error bars. AVN < AP (Group A) = patients whose effective refractory period of the accessory pathway was longer than that of the atrioventricular (AV) node; AVN ≥ AP (Group B) = patients whose effective refractory period of the accessory pathway was shorter than or equal to that of the AV node.

anterograde effective refractory period of the accessory pathway (265 vs. 280 ms) and effective refractory period of the ventricle (200 vs. 211 ms). The effective refractory period of the AV node was significantly shorter in group A than group B (248 vs. 285 ms, p = 0.0005); the shortest RR interval did not show any difference (244 vs. 265 ms) (Fig. 3). However, both the average (328 vs. 397 ms, p = 0.001) (Fig. 4) and longest RR interval (495 vs. 666 ms, p = 0.02) (Fig. 5) were shorter in group A than group B.

Figure 2. The difference between the effective refractory period of the accessory pathway and atrioventricular node (AP-AVN) plotted against the percent of pre-excited QRS complexes during atrial fibrillation (% QRS [AF]). Patients in whom both refractory periods (drive cycle length 400 ms) were measurable (n = 21) were used.

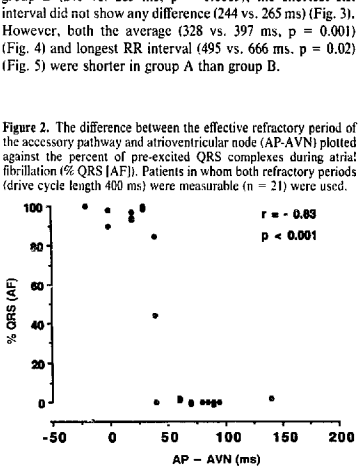


Table 2. Electrophysiologic Data in 33 Patients With Pre-excited RR Intervals During Atrial Fibrillation

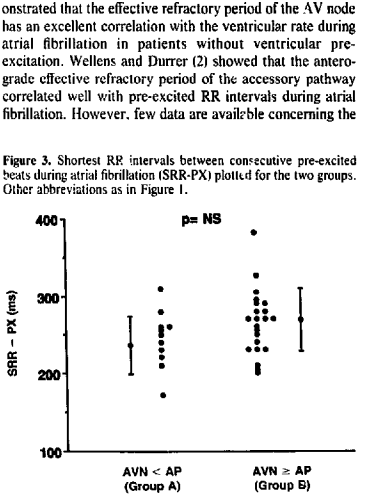
	Group A (n = 11)	Group B (n = 22)	p Value
AVN ERP	248 ± 22	285 ± 28	0.0005
AP ERP	265 ± 22	280 ± 27	0.10
RV ERP	200 ± 17	211 ± 26	0.23
SRR–PX	244 ± 37	265 ± 41	0.17
ARR–PX	328 ± 39	397 ± 56	0.001
LRR–PX	495 ± 109	666 ± 205	0.02

All intervals are reported in milliseconds. ARR = average RR interval during atrial fibrillation; LRR = longest RR interval during atrial fibrillation; PX = consecutive pre-excited beats; SRR = shortest RR interval during atrial fibrillation; other abbreviations as in Table 1.

Discussion

Direct **contribution of the effective refractory period of the atrioventricular (AV) node and its interaction with the accessory pathway.** Both the normal conduction system and the accessory AV pathway are responsible for AV conduction during atrial fibrillation in the Wolff-Parkinson-White syndrome. Factors that might affect the ventricular response to atrial fibrillation include the refractory period of the AV node (1,4), accessory pathway (2,4) and ventricle (4); atrial fibrillation rate (5); concealed conduction in the AV node (6) and accessory pathway (7); and autonomic neurohumoral activity (8). Among these factors, Toivonen et al. (1) demonstrated that the effective refractory period of the AV node has an excellent correlation with the ventricular rate during atrial fibrillation in patients without ventricular pre-excitation. Wellens and Durrer (2) showed that the anterograde effective refractory period of the accessory pathway correlated well with pre-excited RR intervals during atrial fibrillation. However, few data are available concerning the

Figure 3. Shortest RR intervals between consecutive pre-excited beats during atrial fibrillation (SRR-PX) plotted for the two groups. Other abbreviations as in Figure 1.



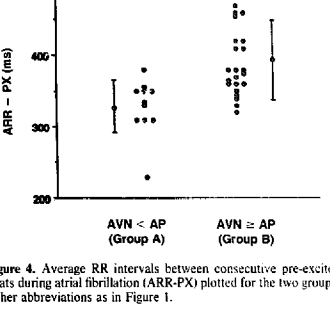
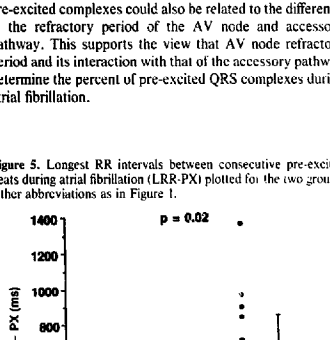


Figure 4. Average RR intervals between consecutive pre-excited beats during atrial fibrillation (ARR-PX) plotted for the two groups. Other abbreviations as in Figure 1.

influence of the interaction between the AV node and the accessory pathway on pre-excited RR intervals and the percent of pre-excited RR intervals in pre-excited QRS complexes during atrial fibrillation.

In the present study, not only was a longer AV node refractory period associated with a greater percent of pre-excited QRS complexes, but the percent of narrow or pre-excited complexes could also be related to the difference in the refractory period of the AV node and accessory pathway. This supports the view that AV node refractory period and its interaction with that of the accessory pathway determine the percent of pre-excited QRS complexes during atrial fibrillation.

Figure 5. Longest RR intervals between consecutive pre-excited beats during atrial fibrillation (LRR-PX) plotted for the two groups. Other abbreviations as in Figure 1.



Indirect contribution of the AV node refractory period. Our results indicate that when matched for their anterograde refractory period, the average and longest RR intervals were shorter in group A than group B. However, the shortest RR interval was similar in the two groups. Differences in pre-excited RR intervals during atrial fibrillation between the two groups cannot be explained by the direct contribution of AV node refractoriness itself. Retrograde concealed conduction into the accessory pathway can be demonstrated using extrastimulus techniques (7). This indicates that the ventricular refractory period or retrograde concealed conduction into the accessory pathway, or both, may play a role in this setting. Furthermore, the indirect effect contributed mainly to longer RR intervals through the accessory pathway. The shortest RR interval was not affected as long as pre-excited QRS complexes were present.

Clinical implications. It is known that intravenous verapamil can accelerate the ventricular response to pre-excited RR intervals during atrial fibrillation (9) and may result in ventricular fibrillation (10,11). Conversely, beta-adrenergic blocking agents have variable effects on the ventricular rate in this situation (12). Both agents have negative dromotropic effects on the AV node, but have no or minimal effects on accessory pathway refractoriness (13,14). This study implies that the average and longest RR intervals can be prolonged while the shortest RR interval remains unchanged if pure AV node blocking agents are administered. Thus, effects of verapamil on ventricular rate cannot be explained by these observations. One possible explanation is that acceleration of the ventricular rate is caused by catecholamine release. Verapamil given intravenously results in a decrease in blood pressure due to vasodilation. This in turn activates baroreceptors that release catecholamines. Isoproterenol is known to shorten the effective refractory period of the accessory pathway in a dose-related fashion (8). Beta-adrenergic blocking agents might offset the effect of catecholamines, thereby rendering the ventricular rate unchanged.

Limitations. Because the AV node refractory period could not be measured in all patients, the exact range of refractory periods tested was not clearly determined. Another limitation is that the atrial rate of atrial fibrillation was not measured, which might have influenced the ventricular rate (5). Because we carefully excluded atrial flutter from our study, there is no reason to suspect that the atrial rate during atrial fibrillation was different in the two groups.

Conclusions. Our data support the position that the refractory period of the AV node plays both direct and indirect roles in determining impulse propagation through the accessory pathway during atrial fibrillation in the Wolff-Parkinson-White syndrome. Interaction between the refractory periods of the AV node and accessory pathway contributes to the percent of QRS complexes that are pre-excited. The effective refractory period of the AV node also indirectly contributes to the duration of pre-excited RR intervals during atrial fibrillation. This contribution is greatest when pre-excited RR intervals are long.

We acknowledge the excellent technical assistance of Katie Martinez, RN and Lisa Cromwell, RN in the performance of these studies and Rachel Little and Cheryl Koch in the preparation of the manuscript.

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