Electrophysiologic Characteristics of Wide QRS Complexes during Pharmacologic Termination of Sustained Supraventricular Tachycardias with Verapamil and Adenosine: Observations from Electrophysiologic Study

Cengizhan Türkoğlu, M.D., Muzaffer Öztürk, M.D., Farid Aliyev, M.D., Inci Firatli, M.D., and Nilgün Incesoy, M.D.

From the Istanbul University, Institute of Cardiology, Division of Pacing and Electrophysiology, Haseki-Fatih, Istanbul, Turkey

Background: In this study we evaluate wide QRS complexes observed during pharmacologic termination of supraventricular tachycardias.

Methods: Patients with supraventricular tachycardia, undergoing electrophysiologic study were enrolled. 12 mg of adenosine or 10 mg of verapamil were administered during tachycardia, under continuous monitoring of intracardiac and surface electrocardiograms. Electrocardiographic features of ventricular ectopy were noted.

Results: Seventy-four patients were enrolled. 48 patients were randomized to adenosine and 26 to verapamil. Five different appearance patterns of ventricular ectopy were observed during termination of tachycardias. All wide QRS complexes were of ventricular origin and all of them were observed during the termination of tachycardia. Adenosine more frequently resulted in appearance of ventricular beats (15.4% vs 41.7%, $P = 0.003$), and this was more frequently observed in patients with atrioventricular nodal reentrant tachycardia. Patients with ventricular beats were younger than those without, in both, verapamil (47.5 ± 15.6 vs 65.0 ± 8.8 years, $P = 0.04$) and adenosine (40.9 ± 13.8 vs 49.7 ± 16.8 , $P = 0.03$) groups. Left bundle branch block (LBBB)/superior axis morphology was most frequent morphology in adenosine group (55%). Two of 4 patients in verapamil group displayed LBBB/inferior axis QRS morphology and another 2 patients displayed LBBB/superior axis morphology.

Conclusions: Noncatheter induced, five different appearance patterns and four distinct morphologies of ventricular origin were observed. Most of them do not directly terminate tachycardia, but are associated with its termination and are not observed in ongoing tachycardia.

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electrophysiologic study; supraventricular tachycardia (SVT); termination; ventricular beats; wide QRS

Wide and bizarre QRS complexes are frequently observed during termination of supraventricular tachycardia (SVT). These phenomena have been observed during pharmacologic termination with adenosine and verapamil, nonpharmacologic termination such as, carotis sinus massage and Val-

salva maneuver or during spontaneous termination of tachycardia. Although these complexes are suggested to be of ventricular origin, there are no objective data supporting this point of view and also there is lack of information about exact mechanism and clinical significance of these complexes.

Address for reprints: Farid Aliyev, M.D., Istanbul University, Institute of Cardiology, Division of Pacing and Electrophysiology, 34034, Haseki-Fatih, Istanbul, Turkey. Fax: + 90 212 570 40 98; E-mail: drfaridaliyev@yahoo.com.tr

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In addition, no other study presented information, regarding electrophysiological characteristics obtained from intracardiac recordings during termination of SVT.

This study was performed to evaluate frequency, origin, and probable mechanism of wide QRS complexes, observed during pharmacologic termination of SVT with verapamil and adenosine under continuous recording of intracardiac electrocardiograms.

METHODS

Patients

Seventy-four consecutive patients undergoing electrophysiologic study (EPS) for evaluation of SVT were enrolled into the study. Informed consent was obtained from all patients. Patients with atrial tachycardia were not enrolled, because of the fact that this type of arrhythmia rarely terminates with adenosine. First 48 consecutive patients were assigned to adenosine and remaining 26 patients to verapamil.

EPS

All antiarrhythmic drugs were discontinued 5 days prior to EPS. No sedative agents were given before or during the procedure. EPS was performed in fasting state. Intracardiac recordings were obtained from high right atrium, His bundle electrocardiogram, right ventricular apex (RVA), and coronary sinus. Twelve-lead surface electrocardiograms and intracardiac recording were obtained simultaneously. All intracardiac stimulations were performed at twice diastolic threshold with pulse width of 1 ms. Programmed electrical stimulations were performed at basic drive cycle lengths of 600, 500, and 400 ms, consecutively. Tachycardia was induced with single atrial extrastimulus in all patients and none of them required ventricular stimulation or pharmacological provocation. Because of the fact that termination of tachycardias frequently associated with mechanical shifts in myocardial contraction that can lead to catheter-induced ventricular ectopy, all attempts were made, to avoid catheter-induced ventricular beats, and in case of occurrence of even single catheter-induced ventricular beat, we again attempted to change catheter position: we have performed continuous atrial pacing for at least 5 minutes at tachycardia cycle length and the suddenly interrupted pacing to visualize possible catheter-

induced ventricular beats. Following induction of tachycardia overdrive pacing from right ventricular apex was performed to evaluate possibility of catheter-induced ventricular ectopy. Once the sustained tachycardia lasting for more than 5 minutes was induced, either adenosine (12 mg) or verapamil (10 mg) was administered intravenously. Intracardiac recordings were obtained until the termination of tachycardia.

Assessment of Wide QRS Complexes

Ventricular beats during tachycardia were further evaluated with regard to their morphology and appearance pattern. Morphological assessment of wide QRS complexes was based on the bundle branch block pattern and its axis, thus suggesting a probable site of origin and mechanism of induction. Appearance pattern was first evaluated as it was suggested by Endoh et al.¹ and ventricular beats were classified into the three categories and were defined as type A, B, and C. Type A beats were defined as beats with coupling interval shorter than the tachycardia cycle length, type B were beats that appeared as a first beat following termination of SVT with coupling interval shorter than the cycle length of the following sinus rhythm, and type C beats appeared after a sinus beat that occurred after SVT termination. During the study, we observed two additional appearance patterns and these were classified consequently as type D and type E. So type D represented beats that appeared within tachycardia run, prior to termination and type E, appeared as escape beat/run of beats, if coupling interval after tachycardia termination was longer than the cycle length of the following sinus rhythm. All five types are presented in Figure 1.

Statistics

Descriptive data were expressed as mean $\pm$ standard deviation. Groups were compared with Student's *t*-test. Comparisons of frequencies were performed with chi-square test. For 2-tailed P values, level of 0.05 was considered to be statistically significant.

RESULTS

Seventy-four patients were enrolled in to the study. Study group consisted of 27 males (36.5%) and 47 female patients (63.5%) with mean age of 49.7 ± 15.6 years. Twenty-six patients had

atrioventricular reentrant tachycardia (AVRT) and 48 patients had atrioventricular nodal reentrant tachycardia (AVNRT). None of the patients had atrial tachycardia.

Intracardiac recordings, confirmed that all the wide QRS complexes, observed during SVT termination were of ventricular origin (earliest activa-

tion at RVA). According to the data obtained from surface 12-lead electrocardiograms, we have observed four different QRS morphologies of ventricular beats: left bundle branch block (LBBB)/superior axis, LBBB/inferior axis, right bundle branch block (RBBB)/superior axis and finally RBBB/inferior axis morphology.

Verapamil Group

Twenty-six patients with SVT were enrolled into this group. Nineteen (73.1%) of them had AVNRT and 7 (26.9%) had AVRT. Tachycardia was terminated after administration of verapamil in 19 patients (73.1%). One of these 19 patients had AVRT and other 18 had AVNRT. In overall, verapamil successfully terminated tachycardia in 94.7% of patients with AVNRT and in only 14% of patients with AVRT ($P = 0.001$).

Ventricular complexes were observed in 4 of 26 patients (15.4%). All of these patients had AVNRT and none of them had AVRT ($P < 0.05$). Patients who developed these complexes, were younger than those who did not (47.5 ± 15.6 vs 65.0 ± 8.8 years, $P = 0.04$). In all of these patients tachycardia was terminated following administration of verapamil, and none of drug nonresponders developed these ventricular complexes. Two of these patients developed single ventricular beat (50%), 1 had couplet (25%) and 1 had run of nonsustained ventricular tachycardia (VT) consisting of 4 beats (25%). Three of verapamil-associated ventricular beats had type A and one had type D appearance pattern. QRS pattern displayed LBBB/inferior axis morphology in 2 patients and LBBB/superior axis morphology in remaining two patients.

Adenosine Group

Forty-eight patients with SVT were enrolled into this group. Twenty nine (60.4%) of them had AVNRT, and 19 (39.6%) had AVRT. Tachycardia was terminated after administration of adenosine in 43 patients (89.9%). Five patients who did not show termination of tachycardia in response to adenosine had AVRT.

Ventricular complexes were observed in 20 of 48 patients (41.7%). And, like patients in verapamil group, ventricular complexes were observed only in patients who showed termination of tachycardia in response to adenosine. Thirteen (65%) of these 20 patients had AVNRT and 7 (35%) had AVRT ($P = 0.005$). Patients who developed these complexes were younger than those who did not (40.9 ± 13.8 vs 49.7 ± 16.8 years, $P = 0.03$). Twelve of these patients developed single ventricular beat (60%), 4 of them had couplets (20%) and 4 had runs of nonsustained VT consisting of more than 3 beats (20%).

Twenty of adenosine-associated ventricular beats displayed type A appearance pattern in 3 patients, type B in 5 patients (1 of them had combined type B and type D pattern), type C in 8 patients, type D in 2 patients (1 of them had combined type D and type E pattern) and finally type E appearance pattern was observed in remaining 2 patients. Adenosine-associated ventricular complexes had LBBB/superior axis morphology in 11 patients (55%), LBBB/inferior axis morphology in 3 patients (15%), RBBB/superior axis morphology in 4 patients (20%) and RBBB/inferior axis morphology in 2 patients (10%).

As it was separately presented above, when compared to verapamil, adenosine was more frequently associated with appearance of ventricular complexes during the termination of SVTs (15.4% vs 41.7%, $P = 0.003$), and AVNRT was more frequently associated with appearance of ventricular beats, when compared to AVRT.

DISCUSSION

As it was suggested by previous reports, wide QRS complexes are not unusual during termination of spontaneous SVT. They have been observed during administration of adenosine, verapamil, and with nonpharmacological interventions such as carotid sinus massage, Valsalva maneuver, etc.²⁻⁷ Cases of verapamil- and adenosine-induced VT and fibrillation also had been reported in the medical literature.^{5,7-9} Despite all this information, there is lack of data obtained from intracardiac recordings and little is known about the underlying mechanism.

One of the main findings of our study was the demonstration that all of the wide QRS complexes have ventricular origin. We also observed that wide QRS complexes do not terminate SVT itself, but by some way they are associated with termination of tachycardia. This point of view is supported by the fact that none of the patients who did not respond to drug administration developed wide QRS complexes (specificity of 100%). So, it may be speculated that observation of ventricular ectopy after administration of verapamil or adenosine predicts response to treatment and termination of tachycardia.

One of the questions which we addressed is "could these ventricular beats seen merely as a consequence of mechanical stimuli of electrophysiology catheters positioned in the right ventricular

apex?" Based on our methodology, we have minimized this possibility and it was demonstrated that they are not catheter induced. Especially those with RBBB and inferior or superior axis, and those with LBBB/inferior axis morphology are not expected to occur secondary to catheter positioned at the right ventricular apex. The fact that termination of tachycardia, is frequently associated with mechanical shifts in myocardial contraction, which can lead to catheter-induced ventricular ectopy, was considered and atrial pacing at tachycardia cycle length for at least 5 minutes with subsequent sudden cessation was performed to analyze above mentioned possibility. But we did not observe this kind of beats in any of our patients. Before administration of study drug, we also performed overdrive pacing during tachycardia from right ventricular apex and again no ventricular ectopy was observed during this maneuver.

Öztürk et al. observed that 56% of patients developed wide QRS complexes during termination of spontaneous SVT with verapamil, and they strongly suggested ventricular origin of these beats.² In another study, DiMarco et al. reported that ventricular beats following SVT termination occur in 27% of patients after administration of verapamil, in 33% of patients after adenosine and in 50% of patients given placebo, and it was suggested that these beats led to termination of tachycardia.³ But, in contrast to findings of DiMarco et al. we have found that not all of the ventricular beats directly terminate tachycardia themselves, rather most of them are only related to its termination. In our study, only 15.4% of patients administered verapamil developed ventricular premature beats during termination of SVT. Although this value is lower than it was reported before, we suggest that this finding may be a reflection of difference between spontaneously occurring SVTs and those induced by programmed electrical stimulation. In our opinion, effect of autonomous nervous system and its role in induction, maintenance, and termination of tachycardia may have an important impact on occurrence of ventricular premature beats. This concept is supported by findings obtained from Tan et al. study,⁹ where they found that 56% of adenosine-induced VT (both sustained and nonsustained) had RBBB/superior axis, the morphology indicating on origin within left posterior fascicle. The mechanism of tachycardia and premature beats originating from this location and those from right- and left-ventricular outflow tracts

are similar and appear to be due to either triggered activity or abnormal automaticity.^{10,11} The mechanism underlying adenosine-induced premature beats and VT is suggested to reflect enhanced automaticity due to adenosine-induced increase in adrenergic tone¹² or more likely delayed after depolarizations (DADs). The last mentioned theory, is supported by the fact that these premature beats are observed after fast heart rates (tachycardia-induced DAD). Also, we suggest the same mechanism, we observed RBBB/superior axis morphology in only 4 patients, and the most frequent morphology that we observed after adenosine administration was LBBB/superior axis morphology, and it is more interesting that we found an approximate frequency of 55% for a quite different QRS morphology. We do not exactly know, whether this finding can be attributed to the difference between spontaneously occurring and extrastimulus-induced SVT. Although the number of patients in our study was not enough to make an exact conclusion, we had observed predominance of LBBB/inferior axis QRS morphology following administration of verapamil, and in our opinion this finding supports the theory, that underlying appearance of these ventricular complexes can be explained by theory of DADs.

In our study, adenosine was more frequently associated with appearance of ventricular beats during the termination of SVT, when compared with verapamil. We suggest, that this finding, can be explained with two probable mechanisms. First of all, it has been reported before that in contrast to verapamil, adenosine increases sympathetic nerve traffic in humans by activating afferent nerves, including arterial chemoreceptors.¹² And this finding, further supports above mentioned role of autonomic nervous system. The second probable explanation is the fact that in contrast to verapamil, adenosine more frequently causes high-degree atrioventricular block, which leads to appearance of ventricular escape rhythm (type E appearance pattern), and this is supported by the fact that we did not observe type E pattern in patients administered verapamil.

We have also observed that ventricular beats more frequently occurred in patients with AVNRT, rather than AVRT, but we do not know an exact mechanism, underlying this observation.

What is the clinical significance of wide QRS complexes during SVT? We suggest that appearance of ventricular ectopy after administration of adenosine or verapamil, predicts success of therapy

and termination of tachycardia with specificity of 100%.

We have also demonstrated two additional subgroups of wide QRS complexes appearing during termination of SVT and together with those described by Endoh et al.,¹ we propose that in overall there are five categories (Fig. 1)

- (1) Type A: Beats with coupling interval shorter than SVT cycle length, which terminate tachycardia.
- (2) Type B: Beats appearing as a first beat following termination of SVT, with coupling interval shorter than the cycle length of the following sinus beat.
- (3) Type C: Beats that appear after sinus beat, which follows termination of tachycardia.
- (4) Type D: Wide QRS complexes appearing within tachycardia run, which is suggested to be associated with termination of tachycardia, but not leading to termination by itself.
- (5) Type E: Wide QRS complexes appearing as escape beats/run after termination of tachycardia.

CONCLUSION

Our findings suggest that wide QRS complexes observed during pharmacologic termination of SVTs, are all of ventricular origin and related to termination of tachycardia. They are not catheter induced. Although most of them do not directly terminate tachycardia themselves, they are associated with its termination and are not observed in patients with ongoing tachycardia. These beats

are suggested to be influenced and driven by the effect of autonomic nervous system, although this hypothesis has to be further investigated.

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