Experimental Studies

The Relationship between Refractory Period and Conduction Time of the AV Node under Various Cycle Lengths in the Canine Heart

The Significance of Wavelength and Excitable Gap in Reentrant Tachycardia

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SUMMARY

To evaluate the significance of the refractory period and conduction time of the AV node for reentrant tachycardias incorporating the AV node, the effective refractory period of the AV node (ERP) and AH interval (AH) during atrial pacing at various cycle lengths were measured in 12 anesthetized dogs after verapamil administration. ERP-AH tended to be constant in each dog at different cycle lengths and increased as the AV node was suppressed. In reentrant tachycardia incorporating the AV node, assuming that the conduction time outside of the AV node is constant, the excitable gap decreases as ERP-AH increases and disappears if ERP-AH is prolonged up to the conduction time outside of the AV node. ERP-AH was calculated as an index of the excitable gap. On the other hand, ERP/AHs were significantly correlated with cycle lengths and tended to be similar at the same cycle length among the different dogs. ERP/AH is considered to be an index of the wavelength which is expressed as the product of refractory period and conduction velocity. However, because ERP was always longer than AH, ERP/AH was not applicable as an index of the wavelength in the AV node. The length through which the wavefront ran during the refractory period of the AV node was also dependent on ERP-AH. In conclusion, prolonging ERP-AH played an important role in suppressing reentrant tachycardias incorporating the AV node. (Jpn Heart J 1996; 37: 373–382)

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OST paroxysmal supraventricular tachycardias and sustained ventricular tachycardias have been shown to be due to ordered reentry circling around a fixed anatomical obstacle. It is essential for reentrant tachycardias that excitability of the tissue into which the impulse is reentering...
recovers from refractoriness. For tissue on the reentrant circuit to fully recover, the tachycardia cycle length has to be longer than the refractory period or the tachycardia circuit length has to be longer than the wavelength (expressed as the product of effective refractory period and conduction velocity). The mechanism by which tachycardia is terminated or prevented by antiarrhythmic drugs is thought to be the lack of excitable tissue as a result of prolongation of the refractory period and/or the wavelength of the tissue.

Because in the human heart the conduction velocity of excitation is relatively fast and it is impossible to have a sufficiently long circuit, a slow conduction area in the reentrant circuit is necessary. In clinical reentrant tachycardias, the reentrant circuits consist of electrophysiologically different multiple tissues incorporating slow conduction areas.

In slow conduction areas, a decremental conduction property is frequently shown. Under such circumstances, not only refractory period but also conduction time is modified by cycle length and/or some drugs. The modification of the conduction time should not be ignored because it affects the tachycardia cycle length.

Drug action on refractory periods and conduction times of slow conduction areas are considered to be important as determinants of the efficacy of antiarrhythmic drugs for reentrant tachycardias. In this study, the effect of cycle length on refractory periods and conduction times in the AV node was evaluated after verapamil and the significance of the mutual relationship in reentrant tachycardias incorporating the AV node discussed.

Wavelength theory is considered to be applied to the leading circle reentry proposed by Allessie. The leading circle concept is suggested as the mechanism of fibrillation. Rensma et al reported that neither refractory period nor conduction velocity was a good parameter, but the wavelength which was expressed as the product of both parameters was a more reliable index to predict the occurrence of atrial fibrillation. In this paper, whether the concept of the wavelength can be applied to the AV node is also discussed.

**Materials and Methods**

Twelve adult mongrel dogs weighing 7 to 11 kgs were anesthetized with sodium pentobarbital (30 mg/kg) and ventilated by a Harvard pump. The chest was opened by a midline sternotomy and the heart was suspended in a pericardial cradle. The femoral vein was used for isotonic saline solution and drug administration. A bipolar electrode was placed on the right atrium for atrial pacing. Another bipolar electrode catheter was inserted from the carotid artery to the aortic root and the His-bundle electrogram was recorded. The body surface
electrocardiogram (ECG) of lead II was also monitored. These ECGs were recorded with a paper speed of 100 mm per second (WS-681G, Nihon Kohden, Tokyo). The right atrium was paced by a programmable cardiac stimulator (BC-02, Fukuda Denshi, Tokyo). A premature atrial stimulation was delivered after every tenth basic atrial driving stimulus. The effective refractory period of the AV node (ERP) could not be determined because in most dogs the effective refractory period of the right atrium was longer than that of the AV node. Therefore, ERPs were measured after intravenous verapamil administration (loading dose of 0.5 mg/kg, maintenance dose of 0.6 mg/kg/hr). The initial basic cycle length of atrial pacing was set just below the sinus cycle length. The basic cycle length was decreased by 20 msec steps until Wenckebach AV block occurred. AH interval (AH) and ERP were measured under each atrial cycle length. ERP/AH and ERP-AH under each atrial cycle length were calculated.

Statistical comparisons between atrial cycle lengths and measured data were conducted using correlation analysis and correlation coefficients and regression lines were calculated. A \( p < 0.05 \) was set as statistical significance.

**Results**

ERPs under various pacing cycle lengths at which 1:1 AV conduction was maintained are shown in Figure 1A. Each line represents the data from one dog. ERP gradually increased as the cycle length was shortened. The shortest cycle lengths at which 1:1 AV conduction was maintained were positively correlated with ERPs of the shortest cycle lengths \( (y = 0.925x - 8.167, \ r = 0.985, \ p < 0.0001) \) (Figure 2A).

AHs under various cycle lengths at which 1:1 AV conduction was maintained are shown in Figure 1B. Each line represents the data from one dog. As the cycle length was shortened, AH was slightly prolonged. The shortest cycle lengths at which 1:1 AV conduction was maintained were not correlated with AHs of the shortest cycle lengths \( (y = 0.0620x + 132.567, \ r = 0.167, \ N.S.) \) (Figure 2B).

ERP-AHs under various cycle lengths are shown in Figure 1C. ERP-AHs were almost constant in the same dog under the different cycle lengths. This suggests that in spite of the change in cycle length the increase in AH is equal to that in ERP. On the other hand, in comparisons between different dogs, the shortest cycle lengths at which 1:1 AV conduction was maintained were positively correlated with ERP-AH of the cycle length \( (y = 0.863x - 140.733, \ r = 0.926, \ p < 0.0001) \) (Figure 2C).

ERP/AHs under various cycle lengths are shown in Figure 1D. Cycle lengths were positively correlated with ERP/AHs \( (y = 0.003618x + 0.834, \ r = 0.988, \ p < 0.0001) \).
Figure 1. ERP (A), AH (B), ERP-AH (C), ERP/AH (D) under various cycle lengths. Each line and symbol represents the data from one dog.
Figure 2. The relationship between the shortest cycle length at which 1:1 AV conduction was maintained and ERP (A), AH (B), ERP-AH (C), ERP/AH (D). Each symbol represents the data from one dog.
The shortest cycle lengths at which 1:1 AV conduction was maintained were also positively correlated with ERP/AHs of the cycle lengths ($y = 0.005039x + 0.301$, $r = 0.746$, $p < 0.01$) (Figure 2D).

ERP-AHs had a constant value unless the degree of suppression of the AV node was changed. ERP/AHs determined by the cycle lengths had no relation to the degree of suppression of the AV node.

**DISCUSSION**

In 1913, Mines$^5$ proposed the concept of ordered reentry around a fixed anatomical obstacle. Mines described a schema of the circulating rhythm which was precisely comparable to the state of affairs produced in rings cut from the bells of Medusae in the experiments of Mayer$^6$ in 1906. This was a simple model in which refractory period and conduction velocity of the tissue in the circuit were homogeneous. On the other hand, most clinical reentrant tachycardias consist of multiple myocardial tissues which have different electrophysiological properties and include slow conduction areas in part of the circuit.$^7$ The property of the slow conduction areas is often critical for the reentrant tachycardias. In AV reentrant tachycardias associated with WPW syndrome and AV nodal reentrant tachycardias, conduction delays usually occur in the AV node. If the ERP is longer than the tachycardia cycle length, an AV reentrant tachycardia is terminated with AV nodal block. It is often observed that administration of verapamil

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![Figure 3](image.png)

**Figure 3.** Schematic representation of the relationship between tachycardia cycle length and excitable gap (A) and between tachycardia circuit length and corrected wavelength (B) ($V_1$: conduction velocity of AV node $V_2$: conduction velocity outside of AV node).
in patients with AV reentrant tachycardias or AV nodal reentrant tachycardias prolongs the tachycardia cycle length before the tachycardia is terminated. Occasionally the tachycardia cycle length is markedly prolonged by verapamil and the heart rate slows down but tachycardia is not terminated. The AV node has a decremental conduction property,\textsuperscript{8-10} and prolongation of the conduction time as well as prolongation of the refractory period occur as a result of suppression by some drugs or shortening cycle length of excitation. Prolongation of tachycardia cycle length is caused by prolongation of the AH interval, and tachycardia is terminated by block at the site where the refractory period is sufficiently prolonged. Since the modification of the conduction time affects the tachycardia cycle length, the interval of the excitable gap, expressed as the difference between the tachycardia cycle length and the refractory period, is determined by both the refractory period and the conduction time.

Assuming that the conduction time outside the AV node is constant, the relationship among tachycardia cycle length, excitable gap, ERP, and AH is expressed as follows (Figure 3A).

\[
\text{Tachycardia cycle length} = \text{ERP} + \text{Excitable gap} = \text{AH} + \text{Conduction time outside of AV node}
\]

Therefore,

\[
\text{Excitable gap} = \text{Conduction time outside the AV node} - (\text{ERP - AH}).
\]

By increasing the ERP-AH up to the conduction time outside the AV node, the excitable gap of the AV node disappears and tachycardia is prevented. Because the excitable gap of the AV node is equal to the difference between conduction time outside the AV node and ERP-AH, if ERP-AH is constant and if the conduction time outside the AV node is long, the excitable gap is also long (Figure 3A). For example, in AV reentrant tachycardias associated with right accessory pathway and right bundle branch block or associated with accessory pathway with slow conduction, as a result of the long conduction time outside the AV node, the long excitable gap in the AV node may make it difficult to terminate tachycardia by block in the AV node.

In this study, ERP-AH was constant at various atrial cycle lengths in each dog (Figure 1C). Therefore, when the cycle length is modified, the change in ERP is considered to be equal to that of AH. On the other hand, the shortest cycle lengths at which 1:1 AV conduction was maintained were positively correlated with ERP-AHs of the cycle length (Figure 2C). This result suggests that as the AV node is suppressed, prolongation of ERP is greater than that of AH and then ERP-AH increases, the excitable gap decreases, and the tachycardia will be unlikely to occur.
The ERP of the AV node is prolonged by accelerating the atrial rate.\textsuperscript{11-13} On the other hand, by incrementally increasing the atrial pacing rate, AH interval progressively increases and Wenckebach type second degree AV block appears.\textsuperscript{14-18} Fatigue phenomenon\textsuperscript{19} has been suggested as a mechanism of the Wenckebach phenomenon and this conduction property is defined as decremental conduction.\textsuperscript{8-10} When the AV node is suppressed by an antiarrhythmic drug used as therapy for the reentrant tachycardia incorporating the AV node, if the tachycardia cycle length is short, AH is prolonged and then conduction time outside of the AV node is relatively short. Therefore, a relatively small increase in ERP-AH may make the excitable gap disappear. On the other hand, if prolongation of ERP is relatively small compared with prolongation of AH by suppression of the AV node, the decrease in the excitable gap may be insufficient.

Based on the wavelength concept, it is necessary that in reentrant tachycardia the circuit length is longer than the wavelength. In ordered reentry, because the circuit length is unchanged, the length of excitable tissue is diminished by prolongation of the wavelength. If the wavelength is longer than the circuit length, reentrant tachycardia is no longer initiated. The wavelength concept is expressed as follows:

\[
\text{Wavelength} = \text{Refractory period} \times \text{Conduction velocity}
\]

\[
\text{Conduction velocity} = \frac{\text{Circuit length}}{\text{Conduction time}}
\]

Therefore,

\[
\text{Wavelength} = \text{Circuit length} \times \left(\frac{\text{Refractory period}}{\text{Conduction time}}\right)
\]

In ordered reentry, because circuit length is unchanged, the wavelength fluctuates in proportion to "refractory period/conduction time". Wavelength is equal to the length over which the wavefront runs during the refractory period on condition that conduction velocity in the reentrant circuit is constant, or that the refractory period is shorter than conduction time of the tissue in which conduction velocity is constant. However, in most clinical reentrant tachycardias, reentrant circuits consist of multiple tissues in which conduction velocities are different. Therefore, the first condition is not satisfied. In this study, ERP was always longer than AH under every cycle length (Figure 1C), so the second condition is not satisfied in the AV node either. In AV reentrant tachycardia, because the wavefront runs beyond the AV node and to the His-Purkinje system with rapid conduction velocity during the refractory period of the AV node, the product of the refractory period and conduction velocity of the AV node is not equal to the length over which the wavefront runs during the refractory period. Therefore, ERP/AH which was positively correlated with atrial cycle length (Figure 1D) is considered to be inadequate as an index of the wavelength of the
AV node. As shown in Figure 3B, “the corrected wavelength”, defined as the length over which the wavefront runs during the refractory period of the AV node, is expressed as follows:

\[
\text{Corrected wavelength} = AH \times V1 + (\text{ERP} - AH) \times V2
\]

\[V1: \text{conduction velocity of AV node}\]
\[V2: \text{conduction velocity of His-Purkinje system}\]

Because the product of the AH interval and conduction velocity of the AV node (V1) is equal to the length of the AV node, corrected wavelength is dependent on “ERP-AH”. Therefore, in reentrant tachycardias incorporating the AV node, the wavelength concept also suggests that the increase in ERP-AH decreases the length of the excitable tissue.

Antiarrhythmic drugs which increase the difference between ERP and AH will be effective in suppressing reentrant tachycardias incorporating the AV node. Prolonging the refractory period without any effect on conduction time is desirable to exhibit those effects by antiarrhythmic drugs. Verapamil, which is classified as a class IV antiarrhythmic drug, prolongs both the refractory period and the conduction time of the AV node, but increases the difference because prolongation of the refractory period is greater than that of the conduction time.

**Conclusion:** Suppression of the canine AV node by verapamil caused a greater prolongation of ERP than AH and increased ERP-AH. These results suggest that the excitable gap decreases and the wavelength increases in reentrant tachycardias incorporating the AV node by suppression of the AV node. In ordered reentry, increasing the difference between the refractory period and the conduction time in the slow conduction areas may be important for preventing those arrhythmias.

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