Effects of Verapamil and Procainamide on Acute Atrial Electrical Remodeling Induced by Short-term Rapid Atrial Pacing in Humans

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Atrial electrical remodeling (ER) after spontaneous or pacing-induced atrial fibrillation has been previously described in humans. We investigated atrial ER induced by a 5-minute period of rapid atrial pacing and the pharmacologic effects of verapamil and procainamide on this atrial ER phenomenon. The atrial effective refractory periods (ERPs) at drive cycle lengths of 400 (ERP_{400}) and 600 (ERP_{600}) ms, at five representative atrial sites (high right atrium [HRA]; proximal, middle and distal coronary sinus; interatrial septum), were determined in 20 patients at baseline and immediately after cessation of a 5-minute period of rapid pacing from the HRA at a rate of 150 bpm. The degrees of atrial ERP_{400} and ERP_{600} shortening after pacing were calculated as acute atrial ER. The same protocol was repeated in another 15 patients after intravenous administration of verapamil (0.15 mg/kg) and in another 15 patients after intravenous administration of procainamide (15 mg/kg). The results demonstrated that, in the control state acute atrial ER can be significantly demonstrated at each atrial representative site ($p < 0.001$). The mean ERP_{400} and ERP_{600} shortenings were $9 \pm 4\%$ and $8 \pm 4\%$, respectively. After procainamide infusion, but not after verapamil, baseline ERP_{400} and ERP_{600} values were significantly prolonged at the five representative atrial sites ($p < 0.01$). Acute atrial ER could still be demonstrated at each atrial site after procainamide or verapamil infusion ($p < 0.001$). In conclusion, acute atrial ER can be demonstrated after only a 5-minute period of rapid atrial pacing in humans. Intravenous verapamil or procainamide does not abolish this ER process.

Key Words: antiarrhythmic agents, effective refractory period, electrical remodeling, rapid atrial pacing

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The pathophysiologic mechanisms of atrial fibrillation (AF), characterized by disorganized and high rates of atrial electrical activity, have been extensively explored during the past decade. The ectopic and focal firing activities within atrial tissues or thoracic veins may initiate AF, which requires favorable substrates for its maintenance and self-perpetuation in the fashion of multiple re-entry circuits with spatial and temporal variability [1]. The adaptation of atrial tissues to the rapid fibrillatory rhythm has been referred to as atrial remodeling, which includes the processes of both structural and electrical remodeling (ER) [2,3].

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The concept that "AF begets AF", first demonstrated in a goat experimental study by Wijffels et al, highlighted the important roles of ER in both short- and long-term rapid atrial rates [4]. Subsequent studies in animal models, using artificially rapid atrial pacing within days or weeks, have shown that ion remodeling is substantially involved in the process of ER [3,5]. In human studies, ER was previously demonstrated by measuring the changes in atrial electrophysiologic properties immediately after the termination of AF [6–9].

Both electrical cardioversion of paroxysmal/persistent AF and spontaneous conversion of short-term pacing-induced AF have been utilized to detect atrial ER induced by rapid atrial rates [7–10]. However, the potential limitation of the former method lies in the possibility that the alteration of atrial electrophysiologic characteristics observed immediately after electrical cardioversion may represent not only the effect of AF, but also that of electrical cardioversion itself. In human studies by Daoud et al using the latter method, several minutes of pacing-induced AF followed by spontaneous conversion sufficiently shortened the atrial ERP within minutes, and such changes in atrial electrophysiologic properties were markedly attenuated by pretreatment with verapamil, but not with procainamide [6,7].

Although the roughly 10-fold increase in atrial rate caused by AF has previously been shown to be the primary stimulus leading to ER, similar changes can also be produced by other forms of clinically rapid atrial tachyarrhythmia [11–14]. In this study, we further explore the manifestation of ER using rapid atrial pacing with a rate and period easily tolerated by humans. Accordingly, the aims of this study were: (1) to determine whether rapid atrial pacing at a relatively slow rate (150 bpm) and over a short period (5 minutes) could induce atrial ER in humans; and (2) to determine the pharmacologic effects of verapamil and procainamide (representative calcium and sodium channel blockers, respectively) on the manifestations of atrial ER induced by 5 minutes of rapid atrial pacing.

METHODS

Study patients

A total of 50 patients (28 female, 22 male; mean age, 52 ± 11 years) without structural heart diseases were referred to the Kaohsiung Medical University Hospital for electrophysiologic study due to paroxysmal supraventricular tachycardia and/or radiofrequency catheter ablation. Common forms of slow-fast atrioventricular nodal re-entrant tachycardia and atrioventricular reciprocating tachycardia using a concealed accessory pathway were disclosed in 32 and 18 patients, respectively. No history of paroxysmal AF was documented in any patient.

Electrophysiologic study

Electrophysiologic studies were performed in patients in a non-sedative and fasting state. All antiarrhythmic agents had been discontinued for a minimum of five elimination half-lives. No patients were treated with amiodarone. Using a conventional method, three quadripolar electrode catheters were introduced into the high right atrium (HRA), right AV junction and right ventricular apex for both recording and stimulation. Another decapolar electrode catheter with 2 mm intraelectrode and 5 mm interelectrode distances was introduced into the coronary sinus with the proximal pair of electrodes located at the coronary sinus orifice. Standard techniques for recording and stimulation were performed. The study protocol was approved by the institutional review board and was performed with the patients' informed consent after completion of the clinically indicated portion of the electrophysiologic procedure (Figure 1).

Baseline study

A baseline study for determining changes in the atrial effective refractory period (ERP) after rapid atrial pacing from the HRA was performed in 20 patients (11 female, mean age 56 ± 8 years). All patients received intravenous propranolol at a dose of 0.1 mg/kg over a period of 5 minutes, in order to decrease the interference from reflex sympathetic activity induced by rapid atrial pacing. The ERPs of the atrium were determined at the following sites: HRA, proximal coronary sinus (PCS), middle coronary sinus (MCS) and distal coronary sinus (DCS). The interatrial septum (IAS) was also included in part of this study protocol, before and after intravenous administration of verapamil or procainamide. The mean atrial capture threshold was 0.8 ± 0.2 mA. Stimuli were delivered as rectangular pulses of 2-ms duration, at twice the diastolic threshold.

Atrial ERPs were measured using the S_1S_2 method at the representative sites, at basic drive cycle lengths of 400 (ERP_{400}) and 600 (ERP_{600}) ms, for eight beats,

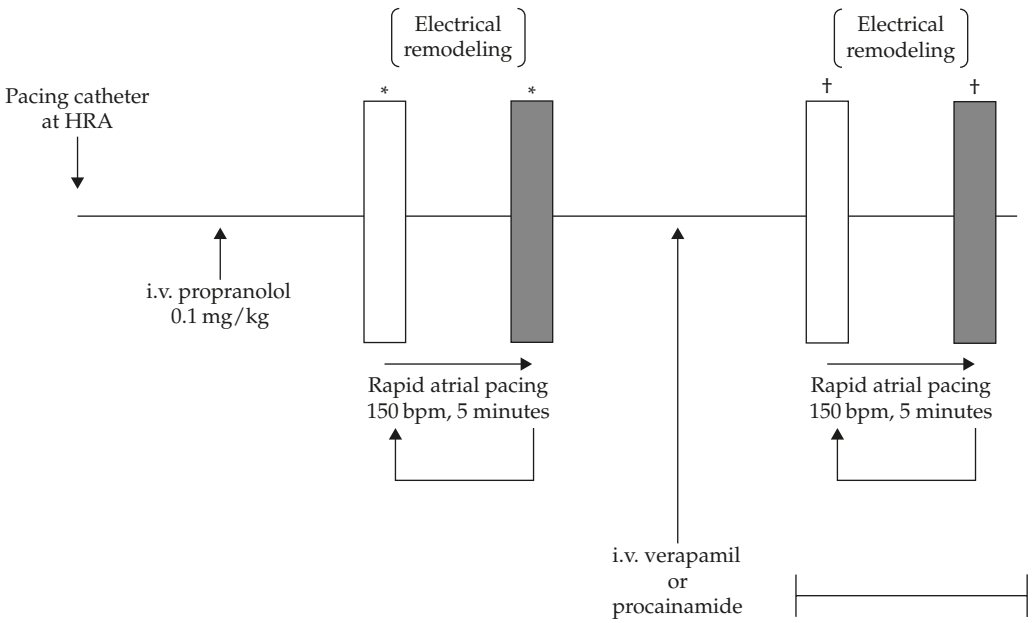

Figure 1. *Flow diagram of the study protocol. *Measurement of the atrial effective refractory period (ERP_{400} and ERP_{600}) from the high right atrium (HRA), proximal (PCS), middle (MCS) and distal (DCS) coronary sinuses and interatrial septum (IAS); †measurements of ERPs (ERP_{400} and ERP_{600}) from the HRA, PCS, MCS and DCS. Changes in atrial ERPs and atrial dispersions between baseline and immediately after cessation of a 5-minute period of rapid atrial pacing represent acute electrical remodeling.*

with a 2-second pause between pacing trains. The S_1S_2 coupling interval was decreased by 10-ms increments until loss of atrial capture; then, S_2 extra stimuli were applied with 1-ms increments until the S_2 stimulus recaptured the atrial tissue. The ERP was defined as the longest S_1S_2 coupling interval that failed to result in atrial capture. The mean durations from the end of rapid atrial pacing to the last capture in ERP_{400} and ERP_{600} were 58 ± 12 seconds and 76 ± 15 seconds, respectively. Atrial dispersion was calculated as the difference between the maximal and minimal ERPs (atrial dispersion = $ERP_{max} - ERP_{min}$) among all of the representative atrial sites described above [15].

Acute electrical remodeling after 5 minutes of rapid atrial pacing

After baseline atrial ERP_{400} and ERP_{600} were determined, acute ER was induced by rapid atrial pacing from the HRA, at 150 bpm, for 5 minutes. The ERP_{400} of the HRA was determined immediately after stopping the rapid atrial pacing and compared with baseline. Then, rapid atrial pacing from the HRA was performed repeatedly, at 150 bpm, for another 5 minutes. The ERP_{600} of the HRA was determined once again, immediately after cessation of rapid atrial pacing. The corresponding ERP_{400} and ERP_{600} of PCS, MCS and DCS were subsequently determined each time, immediately after stopping rapid atrial pacing. Changes in atrial ERP and their dispersions between baseline and immediately after cessation of a 5-minute period of rapid atrial pacing were referred to as acute atrial ER.

Effects of procainamide

After determining the atrial ERP_{400} and ERP_{600} at all representative sites, both in the control state and after rapid atrial pacing at 150 bpm for 5 minutes, intravenous procainamide at a dose of 15 mg/kg was given at a rate of 50 mg/min, followed by a maintenance dose of 4 mg/min, to 15 patients (8 female, mean age 51 ± 11 years). After intravenous administration of procainamide, the ERP_{400} and ERP_{600} of each representative atrial site were determined. The same protocol for determining atrial ERPs was repeated immediately after rapid atrial pacing at 150 bpm for 5 minutes. The changes in ERP at each representative atrial site were compared before and after intravenous administration of procainamide.

Effects of verapamil

Intravenous verapamil at a dose of 0.15 mg/kg was administered to 15 patients (9 female, mean age

54 ± 9 years) over a period of 3–5 minutes, followed by continuous infusion at a dose of 0.005 mg/kg/min. The same protocol for determining the atrial ERPs at representative atrial sites as described above was performed both in the control state and immediately after rapid atrial pacing at 150 bpm for 5 minutes. The changes in ERP at each representative atrial site were compared before and after intravenous administration of verapamil.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation. Comparisons between continuous variables were made using the paired *t* test. A value of $p < 0.05$ was considered to be significant. Statistical analysis was performed with SPSS version 11.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Acute electrical remodeling

The mean atrial ERP_{400} and ERP_{600} of the HRA, PCS, MCS and DCS in 20 patients are summarized in Table 1 and illustrated in Figure 2. The mean dispersion of atrial refractoriness at a pacing cycle length of 400 ms and 600 ms was 30 ± 17 ms and 34 ± 14 ms, respectively. After a 5-minute period of rapid atrial pacing at a rate of 150 bpm, the ERP_{400} values of the HRA were significantly shortened from 232 ± 29 ms to 211 ± 29 ms. In addition, the ERP_{400} and ERP_{600} values of the HRA, PCS, MCS and DCS were all significantly shortened (all $p < 0.001$; Table 1 and Figure 2). However, no significant changes in the spatial dispersion of atrial refractoriness could be demonstrated.

Effects of procainamide on acute electrical remodeling

Before procainamide infusion, acute atrial ER could be demonstrated at each representative atrial site following a 5-minute period of rapid atrial pacing at 150 bpm, in all 15 patients (all $p < 0.001$, Table 2 and Figure 3). After intravenous administration of procainamide, the baseline ERP_{400} values of the HRA, PCS, MCS, DCS and IAS were significantly prolonged from 215 ± 17 ms to 249 ± 21 ms, 227 ± 18 ms to 244 ± 22 ms, 225 ± 15 ms to 242 ± 21 ms, 223 ± 19 ms to 236 ± 17 ms and 226 ± 16 ms to 256 ± 21 ms, respectively (all $p < 0.01$). Significant prolongation of the baseline ERP_{600} in the atrium at the five representative atrial sites was also demonstrated (all $p < 0.01$). After rapid atrial pacing for 5 minutes following procainamide infusion, the ERP_{400} values of the HRA, PCS, MCS, DCS and IAS were significantly shortened from 249 ± 21 ms to 207 ± 19 ms, 244 ± 22 ms to 218 ± 22 ms, 242 ± 21 ms to 218 ± 20 ms, 236 ± 17 ms to 214 ± 15 ms and 256 ± 21 ms to 229 ± 20 ms, respectively (all $p < 0.001$). In addition, significant shortening of the ERP_{600} at the five representative atrial sites was also demonstrated (all $p < 0.001$; Table 2 and Figure 3). These results indicate that, although intravenous procainamide significantly prolongs baseline atrial ERPs, it cannot prevent the shortening of ERPs induced by short-term rapid atrial pacing. No significant changes in atrial dispersion were noted in the control state or

Table 1. Acute atrial electrical remodeling after 5-minute rapid atrial pacing ($n = 20$)

Sites	Baseline	Post-pacing	Shortening (%)	*p*
ERP_{400}				
HRA	232 ± 29	211 ± 29	9 ± 5	< 0.001
PCS	233 ± 19	214 ± 19	8 ± 2	< 0.001
MCS	221 ± 18	207 ± 17	6 ± 3	< 0.001
DCS	227 ± 16	210 ± 19	12 ± 5	< 0.001
Atrial dispersion	30 ± 17	30 ± 16		0.853
ERP_{600}				
HRA	234 ± 29	215 ± 32	9 ± 5	< 0.001
PCS	235 ± 22	218 ± 20	7 ± 5	< 0.001
MCS	240 ± 28	222 ± 25	7 ± 3	< 0.001
DCS	247 ± 20	228 ± 23	8 ± 3	< 0.001
Atrial dispersion	34 ± 14	37 ± 17		0.798

All patients were given intravenous propranolol at a dose of 0.1 mg/kg. ERP = effective refractory period; HRA = high right atrium; PCS = proximal coronary sinus; MCS = middle coronary sinus; DCS = distal coronary sinus.

after rapid atrial pacing, with or without the drug effects of procainamide.

Effects of verapamil on acute atrial electrical remodeling

Before verapamil infusion, acute atrial ER induced by 5-minute rapid atrial pacing was demonstrated in another 15 patients (9 female, mean age 49 ± 12 years) (Table 3 and Figure 4). After intravenous administration of verapamil, the baseline ERP_{400} and ERP_{600} values for the HRA, PCS, MCS, DCS and IAS showed no significant change. However, after a 5-minute period of rapid atrial pacing under verapamil infusion, the ERP_{400} and ERP_{600} values in all five representative atrial sites were significantly shortened (all $p < 0.001$; Table 3 and Figure 4). No significant changes in atrial dispersion

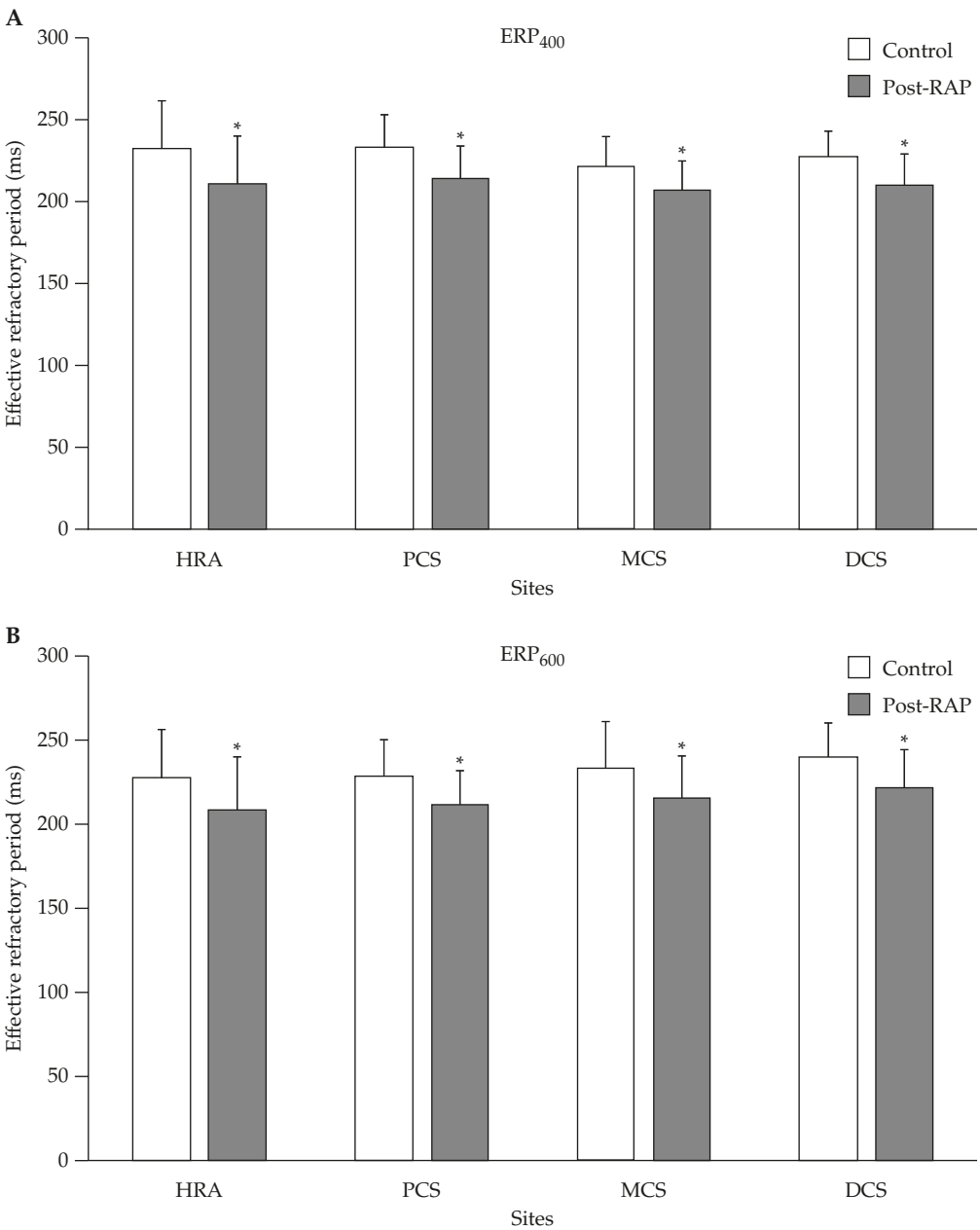

Figure 2. *In the control state, the atrial effective refractory periods at a driving cycle length of (A) 400 ms (ERP_{400}) and (B) 600 ms (ERP_{600}) at four atrial representative sites are significantly shortened right after a 5-minute period of rapid atrial pacing at a rate of 150 bpm. *$p < 0.001$. HRA = high right atrium; PCS = proximal coronary sinus; MCS = middle coronary sinus; DCS = distal coronary sinus; RAP = rapid atrial pacing.*

Table 2. Effect of procainamide on acute atrial electrical remodeling ($n = 15$)

Sites	Before procainamide			After procainamide		
	Baseline	Post-pacing	Shortening (%)	Baseline	Post-pacing	Shortening (%)
ERP_{400}						
HRA	215 ± 17	191 ± 19*	11 ± 4	249 ± 21†	207 ± 19*	17 ± 4
PCS	227 ± 18	197 ± 16*	9 ± 3	244 ± 22†	218 ± 22*	11 ± 2
MCS	225 ± 15	205 ± 13*	9 ± 2	242 ± 21†	218 ± 20*	10 ± 3
DCS	223 ± 19	194 ± 18*	12 ± 7	236 ± 17†	214 ± 15*	9 ± 3
IAS	226 ± 16	209 ± 19*	8 ± 3	256 ± 21†	229 ± 20*	11 ± 3
Atrial dispersion	37 ± 15	37 ± 15		38 ± 17	39 ± 17	
ERP_{600}						
HRA	227 ± 29	209 ± 26*	8 ± 3	260 ± 23†	211 ± 22*	18 ± 8
PCS	227 ± 25	207 ± 22*	9 ± 4	251 ± 24†	227 ± 21*	10 ± 2
MCS	225 ± 28	218 ± 16*	9 ± 3	255 ± 17†	224 ± 17*	12 ± 1
DCS	234 ± 9	213 ± 14*	9 ± 3	250 ± 16†	224 ± 12*	10 ± 2
IAS	230 ± 16	211 ± 15*	8 ± 2	262 ± 21†	232 ± 18*	12 ± 3
Atrial dispersion	36 ± 17	36 ± 18		34 ± 14	38 ± 17	

*$p < 0.001$ represents a significant difference between baseline and pacing; †$p < 0.01$ represents a significant difference in baseline ERP before and after procainamide administration. ERP = effective refractory period; HRA = high right atrium; PCS = proximal coronary sinus; MCS = middle coronary sinus; DCS = distal coronary sinus; IAS = interatrial septum.

were noted in control states or after rapid atrial pacing, with or without the drug effects of verapamil.

Discussion

Main findings

In this study, we demonstrated that atrial ERP could be significantly shortened after only a 5-minute period of rapid atrial pacing from the HRA, at a rate of 150 bpm. This finding indicates that acute atrial ER can occur even in the presence of short-term, modest heart rate changes. In addition, we demonstrated that, although intravenous procainamide can significantly prolong baseline atrial ERP, it cannot attenuate the degree of atrial ER induced by a 5-minute period of rapid atrial pacing. On the other hand, intravenous verapamil neither significantly changed baseline atrial ERPs nor abolished the acute atrial ER induced by a 5-minute period of rapid atrial pacing. Finally, we found that the spatial dispersion of atrial refractoriness was not affected by short-term atrial rapid pacing.

Tachycardia-induced atrial electrical remodeling

Previous clinical studies have demonstrated that any form of atrial tachyarrhythmia, including AF, atrial flutter and atrial tachycardia, can lead to a progressive shortening of atrial ERP and an increased susceptibility to AF development [11–14]. Atrial ER can be observed, even in the setting of spontaneous or artificially paced tachycardias of short or long durations [6,7,14]. Previous literature also demonstrated that atrial ERP could be shortened after rapid atrial pacing at pacing cycle lengths in the range of 250–400 ms for 10 minutes [13,16]. However, the shortening of the atrial ERP induced by such a short-term rapid atrial pacing may partially be explained by increases in sympathetic tone caused by the rapid atrial pacing rates. In this study, in the presence of intravenous propranolol, shortening of atrial ERP after 5 minutes of atrial pacing could still be demonstrated, indicating that the development of atrial ER induced by such a short-term rapid atrial pacing may not result from reflex sympathetic activity.

Effects of verapamil on atrial remodeling

Many reports have demonstrated that tachycardia-induced atrial remodeling is due to decreases in the action potential duration (APD) of atrial cells [17–19]. Shortening of the APD leads to a parallel decrease in the atrial ERP and a subsequent shortening of the wavelength for re-entry to occur [19,20]. Many types of ion channels, such as L-type calcium channels or I_{to}, I_{Kur}, I_{Kr}, I_{Ks} and I_{KAch} potassium channels, have

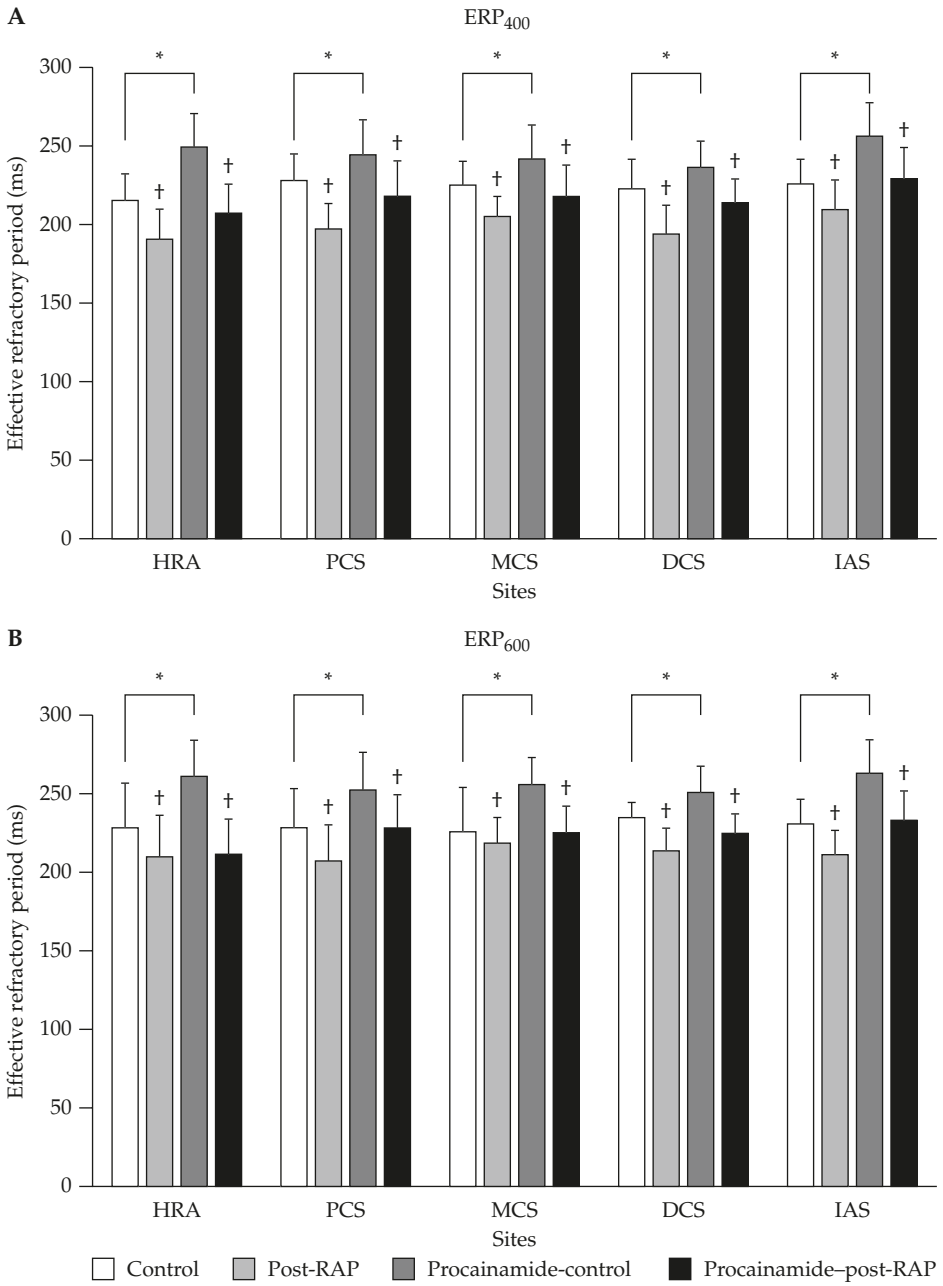

Figure 3. *After intravenous administration of procainamide, the (A) ERP_{400} and (B) ERP_{600} of all atrial representative sties are significantly prolonged (*$p < 0.01$). In the control state, electrical remodeling manifested by significant shortening of the ERP_{400} and ERP_{600} at all atrial representative sites was seen after rapid atrial pacing. Intravenous procainamide could not abolish the shortening of atrial refractoriness after rapid atrial pacing.* †$p < 0.001$. *HRA = high right atrium; PCS = proximal coronary sinus; MCS = middle coronary sinus; DCS = distal coronary sinus; IAS = interatrial septum; RAP = rapid atrial pacing.*

been reported to be involved in the shortening of atrial APD [19–23]. Tachycardia-induced intracellular calcium overload has been proposed to be one of the mechanisms involved in both electrical and structural remodeling [1,3,18,24]. Previous animal and human studies have demonstrated that pretreatment with calcium channel blockers can significantly attenuate or prevent the shortening of atrial ERP induced by rapid atrial pacing or paroxysmal AF [3,25]. However, the effects of verapamil on the atrial electrical properties in humans are still controversial because both attenuation of and no change in tachycardia-induced atrial ERP shortening have been previously reported [26–28]. These differences may result from the timing

Table 3. Effect of verapamil on acute atrial electrical remodeling ($n = 15$)

Sites	Control			Verapamil		
	Baseline	Pacing	Shortening (%)	Baseline	Pacing	Shortening (%)
ERP_{400}						
HRA	212 ± 15	192 ± 15*	9 ± 4	214 ± 20	199 ± 20*	7 ± 2
PCS	208 ± 16	191 ± 15*	8 ± 2	209 ± 14	193 ± 12*	8 ± 4
MCS	204 ± 14	191 ± 14*	6 ± 2	205 ± 12	191 ± 13*	7 ± 2
DCS	218 ± 12	200 ± 12*	8 ± 4	217 ± 12	201 ± 11*	7 ± 3
IAS	218 ± 15	200 ± 19*	8 ± 4	217 ± 16	203 ± 15*	6 ± 2
Atrial dispersion	33 ± 12	34 ± 16		35 ± 14	33 ± 13	
ERP_{600}						
HRA	231 ± 16	205 ± 17*	12 ± 3	234 ± 21	210 ± 17*	10 ± 2
PCS	221 ± 15	211 ± 17*	5 ± 4	226 ± 15	208 ± 15*	8 ± 2
MCS	219 ± 14	203 ± 13*	7 ± 1	230 ± 11	211 ± 12*	8 ± 2
DCS	236 ± 13	216 ± 15*	9 ± 3	233 ± 14	220 ± 14*	6 ± 2
IAS	233 ± 15	216 ± 14*	7± 2	231 ± 16	219 ± 16*	5 ± 3
Atrial dispersion	36 ± 14	39 ± 12		35 ± 13	37 ± 12	

*$p < 0.001$ represents a significant difference between baseline and pacing. ERP = effective refractory period; HRA = high right atrium; PCS = proximal coronary sinus; MCS = middle coronary sinus; DCS = distal coronary sinus; IAS = interatrial septum.

of verapamil administration and the duration of rapid atrial pacing or AF.

Daoud et al evaluated electrical remodeling after pacing-induced short-term AF by determining the changes in pre-AF and post-AF atrial refractoriness [6]. These authors also demonstrated that verapamil can markedly attenuate the ER process by altering atrial ERP, possibly by preventing calcium overload during AF [7]. Although similar degrees of shortening of atrial ERPs after rapid atrial pacing were found in our study and that of Daoud et al, verapamil did not prevent the shortening of atrial ERPs induced by 5-minute rapid atrial pacing in the present study. Possible explanations for this discrepancy might be related to: (1) the rate-dependency of tachycardia-induced changes in atrial ERPs [13,27]; (2) different regularities between these two different methods; or (3) differences in the mechanisms of cytoplasmic/mitochondrial calcium overload within atrial tissues in response to short-term AF versus short-term rapid atrial pacing [29]. Further studies to investigate the cellular effects of these two different methods on the mechanisms underlying atrial ERP changes might be warranted.

Effects of procainamide on atrial electrical remodeling

The electrophysiologic effects of procainamide are mediated both by procainamide itself and the active metabolite N-acetyl procainamide, which blocks sodium channels (I_{Na}), and also the rapidly activating component of the delayed rectifying current (I_{Kr}) [30,31]. These effects result in prolongation of the repolarization and ERP of both atrial and ventricular tissue. In this study, intravenous procainamide significantly prolonged the atrial ERP, consistent with the electrophysiologic effects of procainamide in humans reported previously [31]. After 5 minutes of rapid atrial pacing under procainamide, the atrial ERP could still be shortened significantly. This result indicates that, although procainamide can significantly prolong atrial ERP, it cannot attenuate or prevent the occurrence of atrial ER induced by short-term rapid atrial pacing. The degrees of shortening of atrial ERPs after rapid atrial pacing were similar in controls and patients administered intravenous procainamide, concordant with the study by Daoud et al using pacing-induced AF; this may indicate that neither I_{Na} nor I_{Kr} plays a significant role in the generation of atrial ER induced by short-term rapid atrial pacing [7].

Study limitations

Several limitations of this study need to be mentioned. First, most of the patients had no previous history of AF or significant organic heart diseases. Thus, the results of this study may not apply to patients with organic heart disease or patients with paroxysmal AF. Second, the electrophysiologic properties of right and left atrial tissue might be heterogeneous. Although we

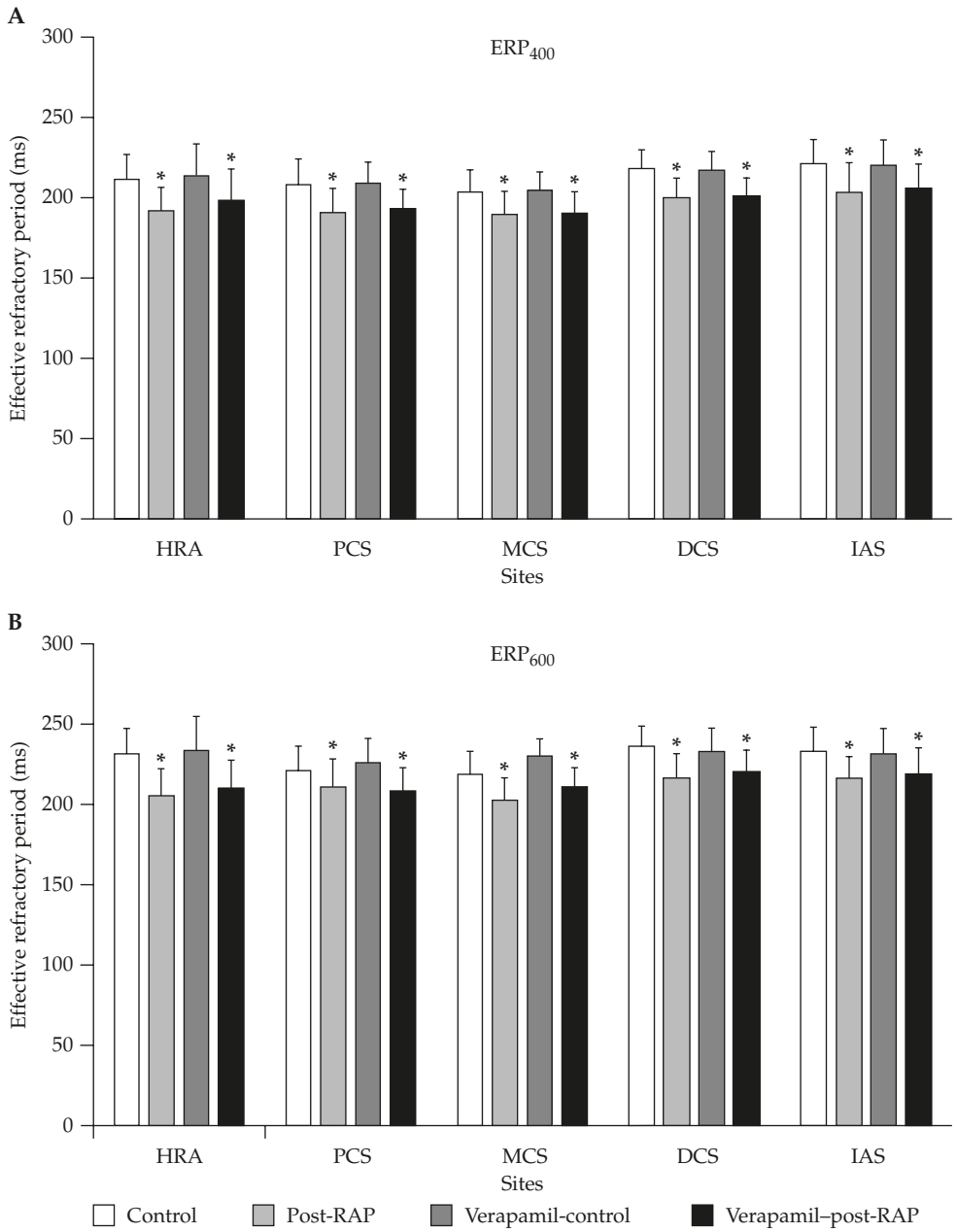

Figure 4. *After intravenous administration of verapamil, no significant differences in (A) ERP_{400} and (B) ERP_{600} could be demonstrated at any atrial representative site (p = NS). In the control state, electrical remodeling manifested by significant shortening of ERP_{400} and ERP_{600} at all atrial representative sites was seen after rapid atrial pacing. Intravenous verapamil could not prevent the shortening of atrial refractoriness after rapid atrial pacing. *p < 0.001. HRA = high right atrium; PCS = proximal coronary sinus; MCS = middle coronary sinus; DCS = distal coronary sinus; IAS = interatrial septum; RAP = rapid atrial pacing.*

measured the atrial ERPs from five representative sites, the results cannot represent the electrophysiologic properties of entire atrial tissues. Third, in this study, all patients were administered propranolol before atrial pacing to attenuate sympathetic effects on atrial ERP. Full autonomic blockade through the addition of atropine was not performed in the present study.

Clinical implications

In this study, we demonstrated that acute atrial ER could occur even after a 5-minute period of rapid atrial pacing, which may indicate that subclinical short-term atrial tachyarrhythmias can induce transient atrial ER. In addition, this acute atrial ER could not be suppressed by sodium or calcium channel

blockers. Since many patients may have episodes of silent short-term atrial tachyarrhythmias, the acute atrial ER induced by such short-term atrial tachyarrhythmias might accumulate and progressively contribute to the pathogenesis of clinically documented atrial arrhythmias.

In summary, atrial ER can be demonstrated after only a 5-minute period of modest rapid atrial pacing at a rate of 150 bpm in humans. This acute atrial ER induced by short-term rapid atrial pacing is not abolished by calcium or sodium channel blockers.

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Verapamil 及 Procainamide 對於人體心房組織短期快速電刺激所誘發的電氣重塑效應之影響

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過去文獻報導指出，不管是自發性或是電刺激所引發的心房顫動之後，都可以發現在人體有急性電氣重塑的效應。本研究欲探討是否單純只利用 5 分鐘快速電刺激的方式，也能誘發電氣重塑效應，以及抗心律不整藥物 verapamil 及 procainamide 對於此效應之影響。總共有 20 位控制組患者於電氣生理學檢查中，接受從右心房高側位、速度每分鐘 150 下的快速電刺激五分鐘前後，測定其心房組織五個不同解剖位置 (包括右心房高側位，近端、中端與遠端冠狀靜脈竇，以及心房中隔) 之有效不反應期 (分別以 400 毫秒與 600 毫秒之週期長度取得；有效不反應期 400 與有效不反應期 600)。電刺激後所引起的有效不反應期縮短程度定義為急性心房電氣重塑效應。利用相同的研究架構，另外分別有 15 位受試者於當中接受靜脈 verapamil (0.15 毫克/公斤) 及 15 位受試者於當中接受靜脈 procainamide (15 毫克/公斤) 來評估藥物影響。研究結果顯示沒有藥物的控制組，急性心房電氣重塑效應可以在各個不同心房組織位置顯著地表現出來 (所有 p 值 < 0.001)。平均有效不反應期 400 與有效不反應期 600 的縮短程度分別為 9 ± 4% 與 8 ± 4%。在接受靜脈注射藥物後，procainamide 可以顯著延長有效不反應期 400 與有效不反應期 600 (p 值 < 0.01) 的基礎值，但是 verapamil 則沒有顯著影響。而急性心房電氣重塑效應，即使在接受完 procainamide 或是 verapamil 仍然可以在各個不同心房組織位置顯著的表現出來 (所有 p 值 < 0.001)。本研究結論為，在人體急性心房重塑效應，即使只利用五分鐘快速電刺激的方式，就可以誘發出來。靜脈注射 procainamide 或是 verapamil 都無法阻斷這急性心房重塑效應的表現。

關鍵詞：抗心律不整藥物，有效不反應期，電氣重塑，快速心房刺激
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