Sinusoidal and Exponential Decays of Postextrasystolic Transient Alternans in Excised Blood-Perfused Canine Hearts

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Abstract We have recently reported that the postextrasystolic contractile potentiation decays in alternans after a compensatory pause in canine left ventricles even under normal coronary and contractile conditions. The transient alternans appears to consist primarily of a small-magnitude exponential decay and a large-magnitude sinusoidal decay. We, therefore, hypothesized that the contractility (y) of the postextrasystolic alternans beats (beat number x) could be expressed as $y = a \cdot \exp[-(x-1)/b] + c \cdot \exp[-(x-1)/d] \cdot \sin[\pi(x-0.5)] + y_0$, where a and c are the normalized magnitudes (relative to the preceding regular beat) of the two exponential terms in the first postextrasystolic beat, b and d are their time constants, and y_0 is the normalized magnitude of the post-alternans regular beat (≈ 1). The first exponential term represents the monotonic decay. The sine term multiplied by the second exponential term represents the alternating decay. Mathematical curve-fitting indicated: 1) the above equation very closely fitted the alternans data with a squared correlation coefficient of 0.9996 on average, 2) c was 7 times on average greater than a , indicating dominance of the sine component, 3) b and d were 2.5 and 1.0 beats on average, indicating a faster decay of the sine component, and 4) this b was comparable to the time constant of the exponential decay of the postextrasystolic potentiation after no compensatory pause. This study suggests that myocardium has a mechanism to switch the postextrasystolic potentiation between the exponential and alternans decays depending on the first postextrasystolic interval.

Key words: heart, postextrasystolic potentiation, extrasystole, compensatory pause, dog.

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Postextrasystolic potentiation does not always decay exponentially in normal hearts [1]. We have recently reported the predominance of postextrasystolic transient contractile alternans in the canine excised blood-perfused left ventricle under normal coronary perfusion and contractile conditions and constant-rate atrial pacing [2]. This type of transient alternans always followed a postextrasystolic compensatory pause [2]. On the other hand, the exponential decay of potentiation, which is generally recognized as the most representative, only followed a postextrasystolic interval without a compensatory pause during pacing failure under otherwise the same conditions in the same normal heart [2].

Arrhythmic changes in contractility generally accompany similar changes in the excitation-contraction (E-C) coupling, or more specifically the peak calcium (Ca) transient and the amount of released Ca [3–9]. The postextrasystolic exponential decay also accompanies exponentially attenuating Ca transients [9]. The Ca recirculation model of the E-C coupling reasonably accounts for the exponential decay [8, 10]. Although Adler *et al.* [3] have proposed a Ca handling model for a type of transient alternans different from ours, their model in its present form does not seem to account for our type of postextrasystolic transient alternans.

For a better understanding of the postextrasystolic transient alternans, its mathematical characterization will be helpful. The alternans decay we observed [2] appears to consist primarily of a small-magnitude exponential decay and a large-magnitude sinusoidal decay. We therefore hypothesized that the contractility (y) of the postextrasystolic individual beats (beat number x) could be expressed as the sum of an exponentially decaying function and a sinusoidally decaying function. To test this hypothesis, we performed mathematical curve-fitting to the contractility changes during postextrasystolic transient alternans observed in our canine heart preparations. We found that the alternans decay consisted of an exponential component and an exponentially decaying sine component with considerably different magnitudes and time constants. Our hypothesis supported by the results suggests that myocardial E-C coupling is capable of manifesting either alternans or exponential decay of postextrasystolic contractility potentiation whether or not the first postextrasystolic beat interval is a compensatory pause.

METHODS

Heart preparation. We obtained the present postextrasystolic transient alternans data in the left ventricles of the excised blood-perfused canine heart preparations cross-circulated with support dogs. We prepared these hearts for the main mechanoenergetic studies [11–13].

Since we have often described the methods of heart preparation elsewhere [11–13], they are not provided in detail here. Briefly, two mongrel dogs were anesthetized with ketamine hydrochloride (50 mg, i.m.) and sodium pentobarbital (25 mg/kg, i.v.). Two cross-circulation tubes were cannulated into the common carotid arteries and the external jugular vein of the support dog. The chest of the

heart donor dog was opened and the cross-circulation tubes were cannulated into the left subclavian artery and the right ventricle via the right atrium. The brachiocephalic artery, descending aorta, superior and inferior venae cavae, azygos vein, and pulmonary hili were ligated to isolate the heart from the systemic and pulmonary circulation. The metabolically supported heart by the cross circulation was excised from the chest. These hearts did not experience any stop of coronary flow.

The left ventricle (LV) was fitted with a thin latex balloon (unstretched volume of 50 ml) through the opened left atrium and the mitral annulus. The balloon was filled with water and connected to the volume servo pump [11, 12]. The servo pump allowed us to control LV isovolumic volume at our discretion and to measure it accurately. LV pressure was measured with a miniature pressure gauge (Konigsberg, P-7) in the apical end of the balloon and recorded. The temperature of the heart was kept at 35–37°C with heaters.

The left atrium was paced constant at 149 ± 22 (SD) (range: 85–188) beats/min with bipolar electrodes placed on the left atrium and square pulses (2–5 ms) of a strength slightly above the threshold. LV anterior epicardial electrocardiogram (ECG) was detected with a pair of screw-in electrodes and analyzed.

Background. We had observed nearly 3,600 cases of spontaneous atrial and ventricular extrasystoles followed by postextrasystolic potentiation in a total of 68 hearts [2]. Our previous analyses have shown that the alternans decay was predominant (84%) in all the hearts and that the exponential decay was scanty (6%), the rest (10%) being other types. Of all these cases, we observed 76 cases in 37 hearts (ranging within 1–5 beats per heart) during fast recording periods and could analyze their beat-to-beat intervals with reasonable time resolution [2]. Since all the other cases were observed during slow recording periods, we could not analyze their beat-to-beat intervals. The selected 76 cases have shown that the alternans decay occurred when the first postextrasystolic beat had a compensatory pause, but it never occurred when there was no compensatory pause [2]. We subjected these 76 cases to the present study.

Decay analyses. Our previous results [2] were interesting in that we could decompose the postextrasystolic transient alternans into an exponential decay and a sinusoidal decay. Therefore, we intuitively proposed that the alternans decay could be fitted by a linear combination of an exponential function and an exponentially decaying sinusoidal function: $y = a \cdot \exp[-(x-1)/b] + c \cdot \exp[-(x-1)/d] \cdot \sin[\pi(x-0.5)] + y_0$. y is the contractility (or peak isovolumic pressure at a fixed LV volume) of every postextrasystolic beat, normalized to that of the preceding regular beat contractility. y_0 is the contractility level to which the alternans decayed, also normalized to the preceding regular beat contractility. x is the number of the postextrasystolic beat ($x=1-6$). a , b , c and d are the fitting parameters. a is the dimensionless magnitude of the monoexponential term. c is the dimensionless magnitude of the exponential term multiplying the sine term with unity amplitude. b and d are the time constants of the two exponential functions in

terms of beat number. The curve-fitting was performed using DeltaGraph® (Delta Point, Inc., Monterey, CA) on a Macintosh computer (Apple Japan, Inc., Tokyo).

We measured the regular, extrasystolic and postextrasystolic beat intervals in all 76 cases and normalized them with respect to the regular beat interval. We also measured the peak isovolumic pressures of the regular, extrasystolic, and postextrasystolic beats and divided them by that of the regular beat to obtain normalized contractility.

In addition to the alternans decay, we collected 35 cases of the exponential decay of postextrasystolic potentiation in the same canine hearts. We also measured peak isovolumic pressures during each exponential decay at a fixed volume for normalized contractilities. They were fitted by a monoexponential function: $y = a \cdot \exp[-(x-1)/b] + y_0$.

RESULTS

Figure 1 shows a representative case of the transient alternans of the postextrasystolic potentiation following a ventricular extrasystole. The regular beats (R) and postextrasystolic beats (PESs) had the same normal QRS waves. An extrasystole (ES) interrupted regular beats (R) with a coupling time (ESI) shorter than the regular beat interval (RI). The first postextrasystolic interval (PES1) between ES and PES1) was a compensatory pause. The first postextrasystolic beat

Fig. 1. A representative original tracing of left ventricular pressure (LVP) and electrocardiography (ECG). The ST segment was elevated as usual because the ECG was recorded soon after screwing electrodes into the LV anterior epicardium at the beginning of the experiment. Since this ST elevation disappeared gradually, as usual, it was not a sign of myocardial ischemia. R, regular beat; ES, extrasystole; PES1-6, 1st through 6th postextrasystolic beats. The ES was of the ventricular origin. The left atrium was paced at a constant rate, although the pacing artifact was not visible. Each tick mark coincides with the onset of the ventricular ECG.

(PES1) was markedly potentiated relative to R. However, the second postextrasystolic beat (PES2) was considerably depressed from R. This distinguished the postextrasystolic transient alternans from the monoexponential decay of postextrasystolic potentiation. The third postextrasystole (PES3) was again moderately potentiated and the fourth postextrasystolic beat (PES4) was moderately depressed relative to R. The alternans gradually waned over five or six postextrasystolic beats to the same level as the preceding R. All the other alternans decays showed essentially the same time course as this representative one [2].

On average ($n=76$), RI was 412 ± 72 ms. ESI was 327 ± 63 ms and 0.797 ± 0.078 (in terms of fraction) of RI, always shorter than RI. PESI1 was 496 ± 95 ms and 1.203 ± 0.078 of RI, always longer than RI. PESI2–6 were the same as RI. Thus, a postextrasystolic compensatory pause (PESI1 > RI) always preceded the postextrasystolic transient alternans. The peak isovolumic pressures of R and ES were 92 ± 31 and 55 ± 26 mmHg, respectively. ES was 0.59 ± 0.18 (always smaller than 1) of R. Peak isovolumic pressures of the PES1 and PES2 were 139 ± 41 and 81 ± 29 mmHg, respectively. They were 1.56 ± 0.32 and 0.87 ± 0.10 of the R, always greater and smaller than R, respectively. Peak isovolumic pressures of the subsequent postextrasystolic beats were: PES3 = 102 ± 34 mmHg (1.11 ± 0.11 , significantly greater than R), PES4 = 92 ± 31 mmHg (0.99 ± 0.04 , virtually equal to R), PES5 = 101 ± 30 mmHg (1.04 ± 0.07 , significantly greater than R) and PES6 = 96 ± 28 mmHg (1.00 ± 0.04 , virtually equal to R). Thus, the PESs decayed in alternans to R by PES6. These data characterize the transient alternans that we analyzed in the present study.

Figure 2 shows normalized contractilities (solid circles) of PES1–PES6 during a representative postextrasystolic alternans decay. The sinusoidally decaying (solid) curve is the best-fit curve consisting of a monoexponential decay component, an exponentially decaying sine component and a constant y_0 (see the inset equation). The goodness of fit was excellent with a squared correlation coefficient (r^2) of 0.999. The dotted curve shows the sine function in the best-fit equation. We modified the amplitude and level of the unity-amplitude sine curve so that it could fit within the range of the y coordinate (see the inset equation). The long-dashed curve shows the exponential term multiplying the unity-amplitude sine function. The short-dashed curve shows the first exponential component of the fitting equation. We also modified these curves so that their asymptotes became 1. The magnitude of the first exponential term in PES1 ($a=0.0722$) was considerably smaller than that of the second exponential term multiplying the sine function in PES1 ($c=0.398$). The results were similar in 54 of the 76 cases. Their squared correlation coefficients were 0.999 ± 0.002 . These results therefore support our present hypothesis.

In the remaining 22 cases, this curve-fitting failed to converge to physiologically meaningful values, resulting in unusually large positive and/or negative a , c and y_0 values. We later subjected these strange cases to a different curve fitting (see Table 3).

Fig. 2. A representative example of the best-fit curve (solid) as a function of post-extrasystolic beat number: $y = a \cdot \exp[-(x-1)/b] + c \cdot \exp[-(x-1)/d] \cdot \sin[\pi \cdot (x-0.5)] + y_0$. The inset equations indicate best-fit parameters. r^2 = squared correlation coefficient, or coefficient of determination. The two exponential components (long-dashed: $a \cdot \exp[-(x-1)/b]$ and short-dashed: $c \cdot \exp[-(x-1)/d]$) and sine function (dotted: $\sin(\pi(x-0.5))$) are shown after modifications specified in the inset equations. Namely, the two exponential curves were raised by 1 so that their asymptotes became 1, and the sine functions were divided by 4 and raised by 1.25. These modifications were made so as to fit the full courses of these curves within the y range of the fitting curve.

Table 1 lists the statistical results of the 54 cases with successful curve-fitting to the alternans decay. a was positive in 39 cases and negative in the other 15 cases; a on average was significantly greater than zero. b , c , and d were always positive and significantly greater than zero. The mean values of b ($=2.5$ beats) and d ($=1$ beat) indicate that the exponential component decays to $1/e$ (≈ 0.37) in PES3 or PES4 and the sine component decays to $1/e$ in PES2 on average. On average, a/c was significantly smaller than 1 and it was always smaller than 1 except in one case. On average, b/d was significantly greater than 1 but it was smaller than 1 in 8 cases. These results indicate that the contribution of the sinusoidal decay was dominant in the initial few beats of most alternans cases. No significant difference of y_0 from 1 indicates that the alternans decayed to the same contractility level as that of the preceding regular beat.

Table 2 lists the correlation coefficients between the best-fit parameters and extrasystolic and postextrasystolic beat intervals and contractilities. The significant data indicate that 1) both a and c were positively correlated with PES1 and PES1, but negatively with ESI, 2) neither b nor d were correlate with ESI and PES1, 3) b positively correlated with ES whereas d was positively correlated with PES3 but negatively with PES2 and PES4, 4) a/c was positively correlated with PES1 and PES2, and 5) b/d was positively correlated with ES, PES2, and PES4. These

Table 1. Best-fit parameters of fitting the sum of a monoexponential function and an exponentially decaying sine function to the postextrasystolic transient alternans.

Coefficient or constant	Mean $\pm$ SD	Range	Unit
<i>a</i>	0.069 $\pm$ 0.138**	-0.375-0.381	dimensionless
<i>b</i>	2.50 $\pm$ 2.03**	0.46-4.53	beats
<i>c</i>	0.471 $\pm$ 0.216**	0.255-0.687	dimensionless
<i>d</i>	1.01 $\pm$ 0.42**	0.59-1.43	beats
<i>a/c</i>	0.140 $\pm$ 0.343##	-0.764-1.470	dimensionless
<i>b/d</i>	2.72 $\pm$ 2.06##	0.30-9.87	dimensionless
<i>y₀</i>	1.01 $\pm$ 0.04 ^{NS}	0.97-1.04	dimensionless

$y = a \cdot \exp[-(x-1)/b] + c \cdot \exp[-(x-1)/d] \cdot \sin[\pi(x-0.5)] + y_0$ was used for curve-fitting. Number of cases was limited to 54 that showed convergence in the curve-fitting. Squared correlation coefficients were 0.9996 ± 0.0021 , ranging from 0.9975 to 1.0000. Dimensionless values were normalized to the magnitude of the regular beat. ** indicates significant difference from 0 at $p < 0.01$. ## indicates significant difference from 1 at $p < 0.01$. NS for y_0 indicates no significant difference from 1.

Table 2. Correlation and regression between best-fit parameters and postextrasystolic beat intervals and extrasystolic and postextrasystolic contractilities.

Correlation with	Interval (normalized)		Contractility (normalized)				
	ESI	PESI1	ES	PES1	PES2	PES3	PES4
<i>a</i>	-0.332*	0.332*	-0.237 ^{NS}	0.711**	0.347*	0.336*	0.144 ^{NS}
<i>b</i>	0.123 ^{NS}	-0.123 ^{NS}	0.349*	-0.218 ^{NS}	0.098 ^{NS}	0.119 ^{NS}	0.199 ^{NS}
<i>c</i>	-0.605**	0.605**	-0.641**	0.912**	-0.359**	0.372**	0.045 ^{NS}
<i>d</i>	0.123 ^{NS}	-0.123 ^{NS}	0.158 ^{NS}	-0.156 ^{NS}	-0.358**	0.533**	-0.426**
<i>a/c</i>	-0.059 ^{NS}	0.059 ^{NS}	-0.027 ^{NS}	0.348**	0.373**	0.176 ^{NS}	-0.081 ^{NS}
<i>b/d</i>	0.104 ^{NS}	-0.103 ^{NS}	0.356**	-0.247 ^{NS}	0.288*	-0.194 ^{NS}	0.395**

ESI, extrasystolic beat interval; PESI1, first postextrasystolic beat interval; ES, extrasystolic beat; PES1-PES6, first to sixth postextrasystolic beats. Number of cases was limited to 54 that showed convergence in the curve-fitting. *a*, *b*, *c*, and *d* are coefficients in $y = a \cdot \exp[-(x-1)/b] + c \cdot \exp[-(x-1)/d] \cdot \sin[\pi(x-0.5)] + y_0$. * indicates significant correlation at $p < 0.05$. ** indicates significant correlation at $p < 0.01$. NS indicates no significant correlation.

correlations characterize the postextrasystolic transient alternans that we observed and indicate the complex dependence and independence of the beat fit parameters and the time course and magnitude of the alternans decay. Although not shown in this table, *a* was positively correlated with *c* ($r = 0.396$, $p < 0.01$) and *b* was not correlated with *d*.

Table 3 lists the best-fit parameters in the above mentioned 22 strange cases after removing the monoexponential decay from the original fitting equation.

Table 3. Best-fit parameters of fitting a sinusoidal decay to the alternans cases which did not show convergent curve fitting to the sum of the exponential and sinusoidal decays.

Coefficient or constant	Mean $\pm$ SD	Range	Unit
c'	$0.562 \pm 0.353^{**}$	0.101–1.239	dimensionless
d'	$1.16 \pm 0.60^{**}$	0.37 –2.79	beats
y_0	1.01 ± 0.04^{NS}	0.97 –1.04	dimensionless

$y = c' \cdot \exp[-(x-1)/d'] \cdot \sin[\pi(x-0.5)] + y_0$ was used for curve-fitting. Number of cases was limited to the 22 that showed no convergence in the curve-fitting to $y = a \cdot \exp[-(x-1)/b] + c \cdot \exp[-(x-1)/d] \cdot \sin[\pi(x-0.5)] + y_0$. Squared correlation coefficients were 0.9898 ± 0.0130 , ranging from 0.9386 to 1.0000. Dimensionless values are normalized to the magnitude of the regular beat. ** indicates significant difference from 0 at $p < 0.01$. NS for y_0 indicates no significant difference from 1.

Table 4. Best-fit parameters of fitting an exponential curve to the monoexponential decay cases.

Coefficient or constant	Mean $\pm$ SD	Range	Unit
With an assumption of $y_0 = 1$			
a'	$0.845 \pm 0.172^{**}$	0.503–1.092	dimensionless
b'	$2.08 \pm 0.47^{**}$	0.59 –3.11	beats
Without an assumption of $y_0 = 1$			
a''	$0.908 \pm 0.180^{**}$	0.497–1.207	dimensionless
b''	$3.24 \pm 1.39^{**}$	1.14 –5.46	beats
y_0	$0.887 \pm 0.116^{##}$	0.645–1.09	dimensionless

$y = a' \cdot \exp[-(x-1)/b'] + y_0$ was used for curve-fitting with and without assuming $y_0 = 1$. Number of cases was 35. With assuming $y_0 = 1$, squared correlation coefficients were 0.951 ± 0.078 , ranging from 0.873 to 1.0000. Without assuming $y_0 = 1$, squared correlation coefficients were 0.981 ± 0.011 , ranging from 0.953 to 0.997. Dimensionless values are normalized to the magnitude of the regular beat. ** indicates significant difference from 0 at $p < 0.01$. ## indicates significant difference from 1.

Namely, the data were fitted by an exponentially decaying sine function: $y = c' \cdot \exp[-(x-1)/d'] \cdot \sin[\pi(x-0.5)] + y_0$. This fitting was successful in all 22 cases, indicating that the sinusoidal decay alone could reasonably fit the alternans decay. Note that these c' and d' values are comparable ($p > 0.05$) to the c and d values obtained in Table 1.

Table 4 list the best-fit parameters of the exponential curve $a \cdot \exp[-(x-1)/b] + y_0$ fitted to each of the 35 cases of the monoexponentially decaying postextrasystolic potentiation. These exponential decays accompanied no compensatory pause (i.e., PESI1 = RI) [2]. The fitting was made first by assuming $y_0 = 1$ (namely, $y = a' \cdot \exp[-(x-1)/b'] + 1$) and then assuming that y_0 is a best-fit variable ($y = a'' \cdot \exp[-(x-1)/b''] + y_0$) because ter Keurs *et al.* [8] have recognized reasonable fitting by both equations. The r^2 values for both equations were high in all these

cases. a' and a'' were considerably greater than a for the alternans decay and about two times greater than c listed in Table 1. However, b' and b'' were comparable ($p > 0.05$) to b listed in Table 1. Although not shown, a' and a'' positively and b' and b'' were negatively correlated with PES1 ($p < 0.05$) in a similar manner to a and b in Table 1. y_0 was significantly smaller than 1 as reported by ter Keurs *et al.* [8].

DISCUSSION

We have characterized the beat-to-beat contractility changes during the alternans decay of postextrasystolic potentiation in excised cross-circulated canine hearts under normal coronary blood perfusion and contractility conditions. The results have supported our hypothesis that the postextrasystolic transient alternans that we are interested in consists of primarily a sinusoidal decay and secondarily an exponential decay.

The hearts in which we observed the postextrasystolic transient alternans were not suffering from any obviously abnormal conditions such as myocardial failure, ischemia, overload, tachycardia, and hypothermia. These abnormal conditions predispose transient and sustained alternans [1, 7, 14–18]. However, in our study, the presence or absence of a compensatory pause alone seems to have determined whether postextrasystolic potentiation decayed monotonically or in alternans in the same heart [2]. Since we first recognized the predominance of the postextrasystolic transient alternans [2], we have always confirmed the same predominance in all excised cross-circulated, atrially paced canine hearts that we have used for recent mechanoenergetic studies. The same predominance obviously holds throughout every experiment despite the gradual deterioration of the heart over 4–6 h. Therefore, the postextrasystolic contractility alternans decay that we have observed and analyzed does not seem to derive from abnormal conditions of the dog heart.

Arrhythmic contractility changes, including the postextrasystolic exponential decay, sustained alternans and transient alternans, accompany proportional changes in Ca transient [6–9]. This suggests that the alternation of excitation-contraction (E-C) coupling may also underlie the transient contractility alternans that we observed. The monoexponential decay has been accounted for by the extra transsarcolemmal Ca influx during the extrasystole and its gradual efflux over several postextrasystolic beats under a constant recirculation fraction [4, 5, 8]. However, this constant recirculation fraction model cannot simulate the postextrasystolic transient alternans.

Our present analyses have shown that both the exponential component of the alternans decay and the monoexponential decay had comparable time constants (b , b' , and b''). These b , b' , and b'' values are comparable to that obtained for the monoexponential decay (approximately 2.5 beats) in *in situ* canine hearts [8]. The recirculation fraction of about 70% of intracellular Ca accounts for this time constant [8]. Therefore, the exponential component of the alternans decay that we

have analyzed in the postextrasystolic alternans decay may also reflect such a Ca recirculation fraction.

These b , b' , and b'' (2–3 beats on average) were 2–3 times longer than the d (1 beat on average) of the sinusoidal decay component. Moreover, b correlated only with ES whereas d correlated with PES2–4 (Table 2). These results suggest that the sinusoidal decay component in the alternans decay has a different underlying mechanism from the monoexponential decay component.

The sinusoidal decay can be an attenuating oscillation due to a delay in feedback. Such a delay may correspond to the delay of the Ca releasability after Ca uptake in the sarcoplasmic reticulum (SR) [19]. This delay model beautifully accounts for weak contractility of the extrasystole and enhanced contractility of the first postextrasystolic potentiated beat [19]. However, they have not studied the contractilities of the second and subsequent postextrasystolic beats. They did not demonstrate any PES2 data, either. Therefore, it remains unknown whether this delayed Ca releasability model can account for the weak PES2 which is characteristic of postextrasystolic alternans decay.

Adler *et al.* [3] proposed a Ca-handling model to explain both the force-interval relation and mechanical alternans. In this model, the exponential decay over several beats is a manifestation of a long-term memory of the SR, and the beat-to-beat sinusoidal change is due to a short-term memory of the SR. This model simulated transient mechanical alternans induced by a variably delayed beat interposed after regular beats [3], a type of alternans different from ours. The simulated alternans was symmetric in amplitude around the regular beat level, unlike most of ours. The symmetric alternans, however, resembles the alternans decay whose exponential decay component was negligible (Table 3). We, therefore, consider that the long- and short-term memories in Adler *et al.*'s model may manifest b and d , respectively. Then, the sinusoidal decay component of our type of transient alternans may be attributable to a short-term memory of SR. This short-term memory seems to correspond to the delayed Ca releasability model [19].

The present study has suggested that neither the exponential nor the sinusoidal model of Ca-handling alone can account for most of the postextrasystolic alternans decays that we observed frequently in canine hearts under normal coronary and contractile conditions. An appropriate combination of the Ca recirculation model [8] and the delayed Ca releasability model [3, 19] seems to account for our type of alternans decay.

We only examined the equation proposed in METHODS. We chose the sine function as the simplest one to express the oscillatory contractility changes, but there may be other equations that will fit the observed data reasonably well. For example, a triangular oscillation curve will equally fit the discrete data. The best-fit sinusoidal function does not mean that LV contractility, the E-C coupling, and the Ca releasability are changing sinusoidally between contractions.

Major limitations of this study arise from the excised heart preparation and the retrospective analysis. The generality of the present results remains to be studied in

in situ hearts. More controlled experiments remain to be carried out to determine whether the compensatory pause is the sole determinant of the transient alternans decay regardless of the regular beat interval and the coupling interval.

To summarize, we characterized the beat-to-beat contractility changes of the postextrasystolic transient alternans in excised cross-circulated canine hearts under normal coronary blood circulation and contractility. This type of postextrasystolic alternans decay proved to consist of a sinusoidal decay with a greater magnitude and a shorter time constant and an exponential decay with a smaller magnitude and a longer time constant. This study suggests that the E-C coupling has a mechanism capable of switching the postextrasystolic potentiation between the alternans and exponential decays, depending on the first postextrasystolic beat interval in the canine left ventricle.

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