The Normal Sequence of Right and Left Atrial Contraction

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Objective: To study the sequence of atrial activation and the interatrial electromechanical delay (IEmD) noninvasively in healthy subjects during sinus rhythm (SR).

Methods and Results: In 66 SR healthy subjects P-wave activation was analyzed by means of vectorcardiography. The timing of atrial contractions was measured as the intervals between the P-wave and the A-wave of the Doppler right and left ventricular inflows (P-A_r and P-A_m), and IEmD was calculated as the algebraic difference P-A_m - P-A_r. In the horizontal plane the vectorcardiographic P-loop was anteroposterior ("typical", 41 subjects), anterior (18), or posterior (7). IEmD (mean $\pm$ SE 17 ± 8 ms) was directly related to R-R and P-R intervals. IEmD was significantly shorter in anterior and posterior P loops than in the typical (6.5 ± 5.3 and 8.1 ± 10.1 , respectively, vs 24.2 ± 3.1 ms). In the posterior P-loop group, who exhibited longer P-A_r, mitral E-wave velocity and E/A ratio were reduced, and left atrial booster function was increased.

Conclusion: IEmD was widely variable in SR, reflecting the origin site of sinus impulse, which independently influenced ventricular filling dynamics. **A.N.E. 2001;6(3):222-228**

atrial activation; atrial function; diastole; Doppler echocardiography; vectorcardiography

Knowledge of the physiologic asynchrony between atria is useful in the search for more appropriate site and timing of atrial stimulation in dual-chamber pacing.^{1,2} The possibility to foresee the effects of different "physiologic" pacing on atrial hemodynamics in different pathological conditions may guide the selection of the most appropriate atrio-ventricular delay, that resulted to be effective, for example, in chronic heart failure.³⁻⁶ Right atrial contraction is thought to precede the left one, following the fact that in normal sinus rhythm, activation of the right atrium occurs before that of the left one, even if the interatrial electromechanical delay has been investigated only in few healthy subjects.⁷

No study has been performed in normal subjects evaluating the effects of P-R interval, heart rate and P-wave duration and morphology on the interatrial delay.

We have attempted to study the sequence of atrial contractions which we assessed by simple noninvasive techniques in a large group of healthy subjects with sinus rhythm. The timing of right and left atrial systole was inferred from the Doppler tracing of the corresponding ventricular inflow (A wave).

MATERIAL AND METHODS

Our study group consisted of 66 consecutive subjects (28 males, mean age $\pm$ SE 38 ± 2 years, age range 16-82 years), selected among in-patients submitted to standard ECG for minor noncardiac surgery. They were included if they had normal ECG, with P-wave duration < 120 ms, P-R interval < 200 ms in any lead, and normal echocardiogram. Subjects were excluded if they had any history or clinical evidence of cardiac or pulmonary

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diseases or arterial hypertension, if they had a technically poor two-dimensional and Doppler echocardiogram, or if they showed sinus arrhythmia or "wandering" pacemaker.

Vectorcardiogram (VCG) (according to the Frank method, placing the electrodes at the fifth intercostal space level) was recorded by means of a digital instrument (Mortara, Cardio 200) that allows the simultaneous recording of P-wave loops in the three orthogonal planes with a maximum calibration setting for the P wave of 1 mV equals 10 cm, and sampling frequency of 1 ms. P-wave duration and P-R interval were measured by means of a computer-aided system (Mortara, Cardio 200) on the 12-lead ECG.

Just after VCG recording, a complete echocardiographic examination was performed using a commercially available machine (Toshiba SSA-270 HG) with 2.5 MHz transducer. The reference ECG lead was adjusted to optimize recognition of the P wave and to obtain a P-R interval equal to that measured on the 12-lead ECG.

M-mode and two-dimensional parameters were obtained according to the American Society of Echocardiography,⁸ the Teichholz's formula⁹ was used to determine left ventricular volumes and cardiac output; the ellipsoidal model¹⁰ was used to work out atrial volumes from longitudinal and transverse axes of the right and left atria in the apical four-chamber view.

Analysis of left and right ventricular inflows was performed in the apical four-chamber view by recording with pulsed-wave Doppler mitral and tricuspid flow velocities at the end of normal expiration at a sweep speed of 100 mm s⁻¹. The sample volume was positioned at the tip of the atrioventricular valve leaflets. The Doppler beam was always oriented as parallel as possible to the flow, so that no angle correction was used. Peak E-wave and A-wave modal¹¹ velocities were measured and used to calculate the E-wave-to-A-wave (E/A) ratio. Atrial booster function was determined according to Kuo et al.¹² as the percentage of the diastolic inflow time-integral. The left ventricular isovolumic relaxation time (IVRT) was obtained by positioning the sample volume in the left ventricular outflow tract, just beside the anterior mitral leaflet, in the apical five-chamber view.¹³

The following time intervals were measured: P-wave/tricuspid A-wave onset (right electromechanical interval); tricuspid A-wave (A_t) duration, tricuspid E-wave (E_t) duration, E_t deceleration time,

P-wave/mitral A-wave onset (left electromechanical interval); mitral A-wave (A_m) duration, E_m deceleration time. The interatrial electromechanical delay was measured as the algebraic difference between the left and right electromechanical intervals, therefore it had a positive value when A_t preceded A_m, and a negative value when A_m preceded A_t. Each parameter was calculated as the average of three nonconsecutive measurements. A-wave onset never encroached E-wave end, due to R-R interval ranging from 600 to 1302 ms; therefore no extrapolation to the zero line of the ascending limb of the flow-wave was ever necessary to measure the time to flow-onset.

To reduce the interobserver variability,¹⁴ all measurements were taken by a single sonographer, who was completely blinded to VCG findings.

On VCG recordings, the mean axis of P wave in the frontal plane was calculated by means of a software-aided system. The quadrants of inscription of the P loop in the horizontal plane were described as anteroposterior, anterior or posterior, while the direction of inscription as counterclockwise (CCW), clockwise (CW), "eight" shaped (CCW/CW or CW/CCW) or narrow (if P loop branches were almost superimposed). The steadiness of P-wave morphology was assessed by repeating ECG and VCG recordings after the echocardiographic measurements.

Statistical Analysis

Data are reported as mean $\pm$ standard error. The comparisons among subsets were performed by using ANOVA test followed by *t*-test with the Bonferroni correction. Univariate and multivariate correlations were obtained by using Pearson's method or multiple linear regression (backward method), respectively. Distribution was analyzed by means of χ^2 test with the Yates' correction when necessary. A *P* value < 0.05 was considered significant.

RESULTS

The interatrial electromechanical delay ranged from -40 to 60 ms (17.7 ± 2.8 ms); the right electromechanical interval from 20 to 100 ms (51.4 ± 2.2 ms), and the left electromechanical interval from 12 to 104 ms (68.5 ± 2.0 ms).

On the basis of the VCG P loop characteristics in the horizontal plane (Fig. 1), we subdivided the patients into "typical" P loop (anteroposterior P loop

Figure 1. Examples of P loop in the three planes (frontal, horizontal and left sagittal, from left to right) in the three subgroups: 1) typical normal sinus rhythm; 2) anterior P loop; and 3) posterior P loop.

inscription: 41 subjects, 19 males, age 37 ± 3 years, age range 16–82 years) and "variant" P loops: anterior P loop inscription: 18 subjects (6 males, age 39 ± 4 years, age range 19–67 years) and posterior P loop

inscription: 7 subjects (3 males, age 41 ± 6 years, age range 16–58 years).

Anterior and posterior P loop groups significantly differed with respect to the P-wave axis in

Table 1. Electrocardiographic and Vectorcardiographic Parameters in Sinus Rhythm Patients Grouped According to the Vectorcardiographic P Wave Pattern

Parameter	Anteroposterior Loop (n = 41)	Anterior Loop (n = 18)	Posterior Loop (n = 7)
R-R interval (ms)	893 ± 23	870 ± 37	807 ± 52
P-R interval (ms)	147 ± 3	146 ± 5	145 ± 12
P-wave duration (ms)	100 ± 2	101 ± 2	98 ± 7
P-wave axis (°)	58 ± 3	56 ± 4	41 ± 12*

* = $P < 0.05$ vs anteroposterior loop group.

the frontal plane, while no other difference was found in electrical parameters (Table 1).

The distribution of the rotation of inscription of the P loop in the horizontal plane was different among the three groups: all the CW loops pertained to the posterior loop group, while the CCW/CW loops were present only in the typical group (Pearson χ^2 4.288; $P = 0.019$).

Patients with anterior and posterior loops had a shorter interatrial electromechanical delay (6.5 ± 5.3 and 8.1 ± 5.1 ms, respectively, vs 24.2 ± 3.1 ms in the typical group, Fig. 2). This result appeared to be due to a significant lengthening of right electromechanical interval in subjects with posterior P loop (63.7 ± 3.5 vs 47.9 ± 2.9 in typical cases, Fig. 2) and to a significant shortening of the left electromechanical interval in anterior loop patients (61.7 ± 4.0 vs 71.0 ± 2.2 in typical cases, Fig. 2). E_m velocity and mitral E/A ratio were significantly reduced in the posterior loop group (Table 2).

The three groups did not differ with respect to age, gender, weight, height, and blood pressure. All

subjects had normal echocardiographic findings and normal hemodynamic parameters (left ventricular volumes, mass and ejection fraction). Left and right atrial volumes, IVRT, deceleration time of mitral and tricuspid E waves and duration of mitral and tricuspid E and A waves were within normal limits, without significant differences among groups; left atrial booster function was significantly higher in subjects with posterior P loop (Table 3).

Interatrial electromechanical delay appeared to be statistically correlated with several variables. At univariate analysis, significant relations were found with the R-R interval and P-R interval (Fig. 3, top; $r = 0.434$, $P < 0.001$ and bottom, $r = 0.314$, $P < 0.01$, respectively). The strongest relations were found, as expected, with left ($r = 0.579$, $P < 0.001$) and right ($r = -0.707$, $P < 0.001$) electromechanical delays. Weaker relations were found with A_m duration ($r = -0.291$, $P < 0.05$), A_t duration ($r = 0.406$, $P < 0.001$), E_m duration ($r = 0.254$, $P < 0.05$), IVRT ($r = 0.257$, $P < 0.05$) and E_t deceleration

Figure 2. Intervals between the P wave and the onset of the Doppler mitral- (left electromechanical delay, left) and tricuspid- (right electromechanical delay, middle) A waves, and the interatrial electromechanical delay (right) in the three groups defined by the P wave vectorcardiographic pattern (see text). The * indicates significant statistical difference with respect to the typical pattern.

Table 2. Doppler Data

Parameter	Left Heart			Right Heart		
	Antero-posterior Loop (n = 41)	Anterior Loop (n = 18)	Posterior Loop (n = 7)	Antero-posterior Loop (n = 41)	Anterior Loop (n = 18)	Posterior Loop (n = 7)
A wave duration (ms)	180.8 ± 6.1	187.8 ± 7.8	180.3 ± 5.8	194.3 ± 6.0	202.4 ± 8.0	183.3 ± 12.0
E wave duration (ms)	287.4 ± 8.1	267.4 ± 12.4	280.0 ± 21.3	309.9 ± 9.1	306.8 ± 14.8	292.8 ± 22.9
E wave deceleration time (ms)	184.8 ± 6.3	167.9 ± 8.1	176.0 ± 8.8	211.9 ± 7.8	179.4 ± 12.1	188.0 ± 22.7
E wave velocity (m/s)	0.77 ± 0.02	0.74 ± 0.05	0.54 ± 0.02*†	0.54 ± 0.02	0.57 ± 0.03	0.46 ± 0.04
A wave velocity (m/s)	0.54 ± 0.03	0.47 ± 0.03	0.54 ± 0.04	0.33 ± 0.01	0.31 ± 0.02	0.32 ± 0.02
E/A ratio	1.56 ± 0.09	1.71 ± 0.14	1.03 ± 0.07*†	1.71 ± 0.08	2.01 ± 0.21	1.47 ± 0.08
Atrial booster function (%)	31 ± 2	30 ± 3	41 ± 3*	30 ± 1	29 ± 2	29 ± 1

* = $P < 0.005$ vs anteroposterior loop group.† = $P < 0.005$ vs anterior loop group.

time ($r = 0.352$, $P < 0.05$). Among the hemodynamic and volumetric parameters, weak correlations were found with right and left atrial systolic volumes ($r = 0.278$, $P < 0.05$ for both), left atrial booster function ($r = 0.288$, $P < 0.05$), interventricular septum thickness ($r = 0.253$, $P < 0.05$) and left ventricular mass ($r = 0.260$, $P < 0.05$). The most important determinants of left and right electromechanical intervals at multivariate analysis are listed in Table 3.

DISCUSSION

On studying the timing of right and left atrial systole and the interatrial electromechanical delay during sinus rhythm by simple noninvasive tech-

niques in a large group of healthy subjects, we demonstrated large variability in the left and right electromechanical intervals and interatrial electromechanical delay. Doppler measurements of IEMD obtained in this way were consistent with measurements of atrioventricular annulus motion obtained by means of tissue velocity imaging and reported very recently.¹³

Interatrial electromechanical delay was inversely related to heart rate and directly related to the P-R interval (Fig. 3), the latter correlation depending on the strict direct correlation between P-R and left electromechanical intervals. These relations suggest an influence of the sympatho-vagal balance on interatrial conduction similar to that on heart rate and atrioventricular conduction. In fact,

Table 3. Multiple Regression Analysis

Right electromechanical interval	R = 0.665 Adjusted R square = 0.405	F = 11.909 P < 0.001
Tricuspid A-wave duration	t = -4.966	P < 0.001
Tricuspid A-wave end—QRS interval	t = -3.262	P < 0.002
Tricuspid E/A ratio	t = -2.630	P < 0.02
Left electromechanical interval	R = 0.607 Adjusted R square = 0.328	F = 9.147 P < 0.001
P-R interval	t = 3.293	P < 0.002
Mitral A-wave duration	t = -2.896	P < 0.01
Left ventricular mass index	t = 2.178	P < 0.05

Figure 3. The scatter plot of interatrial electromechanical delay versus R-R interval (top) and versus P-R interval (bottom). Lengthening of R-R and P-R intervals are associated with an increase in the delay between tricuspid and mitral A waves.

the earlier occurrence of left atrial systole might reflect a faster intra-atrial conduction in the presence of prevailing sympathetic drive.

Even if at univariate analysis interatrial electromechanical delay was statistically correlated to several hemodynamic variables, in multivariate analysis the most significant determinants of right and left electromechanical intervals were different, the former depending on the time between the end of A_t and the QRS onset, and the latter on the P-R interval.

The different temporal sequence of right and left atrial systole may be the consequence of a different site of origin of atrial activation in the framework of a complex and extensively distributed system of atrial pacemakers,¹⁶ as opposed to the first hypothesis of a unifocal atrial impulse origin.¹⁷⁻¹⁹

The typical anteroposterior inscription of the P loop in the horizontal plane is in keeping with an atrial activation originating from a sinus impulse at the superior cavoappendicular junction. The pattern of atrial depolarization characterized by the anterior inscription of the P loop in the horizontal plane may be due to a more posterior position of the pacemaker complex, likely at the posterolateral superior vena cava-right atrium junction.¹⁶ In keeping with this hypothesis, the mean P axis in the frontal plane was similar to that of the typical pattern. The posterior inscription of the P-wave may correspond to an anterior origin of the sinus impulse located in the anterior aspect of right atrium, near the origin of Bachmann's bundle.¹⁶ According to this anterior site of origin, the mean frontal axis of P-wave was significantly more horizontal, and the P loop often showed a CW rotation in the horizontal plane.

The two variant P loop patterns differed from the typical one in the atrial electromechanical delay. The anterior P loop pattern was characterized by a shorter left electromechanical delay, in keeping with the results of atrial epicardial mapping, in which the left atrium was activated earlier than in patients with a normal pattern of atrial activation.¹⁶ The posterior P loop inscription was characterized by a longer right electromechanical delay, again in keeping with the data by Boineau et al.¹⁶

Inexplicably, in the posterior P loop pattern there was an increase in left atrial contribution to ventricular filling despite the fact that left atrial electromechanical interval was unchanged. In this condition an increase in left atrial reservoir function or a shift along the left ventricular compliance curve are unlikely explanations. Whether the lengthening of right electromechanical interval represents a concealed conduction delay²⁰ over the electrical connections between the atria or the hemodynamic alteration depends on the interatrial septal compliance⁷ is not known today.

Limitations

The site of origin of sinus impulse was inferred from the atrial vectorcardiogram, taking into account the direction of the P vectors in the horizontal plane. The spread and timing of atrial activation in subjects classified as having a typical or a variant P loop (anterior or posterior) appeared to be similar to those shown by Boineau et al. in single patients by means of epicardial atrial mapping. Even if in

healthy subjects with normal ECG and VCG the morphology of P-wave loop should reflect the behavior of atrial depolarization, we are aware that this indirect method is open to criticism.

The timing of right and left atrial systole was inferred from the Doppler tracing of the corresponding ventricular inflow wave (A wave). Although several variables such as atrial pressure, atrial and ventricular compliance, ventricular relaxation, and systolic function²¹ influence diastolic Doppler inflow waves, the A wave likely represents the time when atrial pressure exceeds ventricular pressure in late diastole, after diastasis equalization of atrial and ventricular pressures, as an almost immediate consequence of atrial contraction.²² On the other hand, no advantage would have resulted from inferring the onset of atrial contraction from the atrioventricular valve annulus motion timing, either measured by means of M-mode or tissue Doppler echocardiography.²³ In fact annular motion reflects structural mechanics^{24,25} more than atrial contraction; furthermore, its timing has been demonstrated to be almost coincident with Doppler flow waves,²³ independently of any consideration on the reciprocal dynamic relationships between annulus motion and Doppler sample plane during atrial contraction. We believe, therefore, that it is conceivable to approximate atrial contraction to its hemodynamic effects on flow motion, and, if any error was introduced by this method, it should fall within 10 ms.²⁴

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