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P Wave Signal Averaged Electrocardiography in Patients Undergoing the Fontan Operation

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Abstract

Objectives. Supraventricular arrhythmias are one of the most common and fatal sequelae of the Fontan operation. P wave triggered signal averaged electrocardiography was performed in patients undergoing the Fontan operation to evaluate the presence of atrial degeneration, and to clarify which factors affected the development of atrial arrhythmias.

Methods. P wave triggered signal averaged electrocardiography was recorded in 14 patients after the Fontan-type operation (conventional atriopulmonary connection in 5 and total cavopulmonary connection in 9) and 15 healthy controls. The duration and area of the filtered P wave, and the signal magnitudes (M20, M30) at 20 Hz and 30 Hz obtained from the frequency domain analysis of the P wave (M20, M30) were evaluated and compared with the hemodynamic data.

Results. The duration and area of the filtered P wave, M20 and M30 in patients after atriopulmonary connection were significantly greater than in those after total cavopulmonary connection and the control subjects ($p < 0.05$). M20 was significantly greater in patients after total cavopulmonary connection than in the control subjects. Right atrial volume in patients after atriopulmonary connection was significantly ($p < 0.001$) larger than in patients after total cavopulmonary connection ($p < 0.05$). There were no significant differences in other indices including atrial pressure between the two groups.

Conclusions. Our results suggest that the substrate for atrial arrhythmias such as atrial myocardial degeneration and fibrosis is frequently present in patients after the Fontan operation, especially after atriopulmonary connection. Thus, the enlarged right atrium may be involved in the presence of a substrate for atrial arrhythmias. The developmental risk for late atrial arrhythmias seems to be present even in patients after total cavopulmonary connection.

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Key Words

■**Electrocardiography (signal averaged electrocardiogram)** ■**Congenital heart disease**
■**Arrhythmias (atrial, supraventricular)** ■**Cardiac surgery (Fontan operation)**

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INTRODUCTION

Supraventricular arrhythmias are one of the major complications after the Fontan-type operation[1,2], and still cause death[3,4]although some modifications to this operation have reduced the incidence of postoperative arrhythmia[5,6]. This complication may be related to extensive atrial surgery and elevated right atrial pressure with atrial enlargement[7,8]. Total cavopulmonary connection (TCPC)[9]has better flow characteristics and less energy dissipation compared with conventional atriopulmonary connection(APC). The right atrium was smaller after the TCPC procedure suggesting that fewer atrial arrhythmias will develop than after APC. In fact, some reports have found a lower incidence of arrhythmia in TCPC than in APC[10−12]. However, TCPC still involves extensive atrial surgery and may carry the risk of development of late arrhythmia after surgery.

Signal averaged electrocardiography has been recognized as a useful method to identify patients at risk for ventricular tachycardia[13]. We reported that time domain analysis of the P wave on signal averaged electrocardiography triggered by the P wave was also useful to detect patients with paroxysmal atrial fibrillation[14]. Frequency domain analysis of the P wave is also useful and necessary to identify these patients[15]. These results suggest that such P wave analysis might be useful to detect atrial myocardial degeneration[16]after the Fontan operation, which could be a substrate for arrhythmias.

This study assessed P wave triggered signal averaged electrocardiography in patients undergoing the Fontan operation to evaluate the presence of atrial degeneration, and to clarify which factors affected the development of atrial arrhythmias.

PATIENTS AND METHODS

Study subjects

Fourteen patients who underwent the Fontan-type operation were enrolled in this study and classified into two groups according to the operative procedure: atrial to pulmonary artery connection (APC: five patients)and total cavopulmonary connection with intra-atrial baffling(TCPC: nine patients; **Table 1**). The age at surgery in the APC and TCPC groups was 6.4±2.3 and 6.4±3.5 years, and the postoperative follow-up was 6.0±2.2 and 1.1±0.6 years, respectively. In all patients, standard 12-lead electrocardiogram and 24-hour Holter monitoring were used to assess electrical instability.

Table 1 Patient profiles

Group	Patient No.	Age(yr) /sex	Age at operation(yr)	Diagnosis of heart disease	Atrial arrhythmia	24-hour Holter monitoring
APC	1	18/f	9	SV, PS, CAVV	mPACs	PAC short run=0.4% TB, PVC<0.1% TB
	2	14/m	8	SV, PS, CAVV	Af	
	3	7/m	3	TA	None	PAC 1 beat
	4	12/m	5	TA	Af	PAC short run 4 times, PAC=0.4% of TB
	5	11/f	6	PA/IVS	cPAC	cPAC, PAC<0.1% of TB
TCPC	6	12/f	12	SV, PA, CAVV	None	
	7	6/m	3	SV, 2AVV	None	
	8	7/m	5	SV, 2AVV	None	
	9	6/f	5	SV, PA, CAVV	None	
	10	7/m	4	SV, 2AVV	None	PAC<0.1% of TB
	11	14/m	13	SV, 2AVV	None	
	12	6/m	5	TA, PS	None	PAC 10 beats
	13	5/m	4	TA, PS	None	
	14	4/f	4	DORV, PS	None	PAC<0.1% of TB

APC=atriopulmonary connection; TCPC=total cavopulmonary connection; f=female; m=male; SV=single ventricle; PS=pulmonary stenosis; CAVV=common atrioventricular valve; TA=tricuspid atresia; PA/IVS=pulmonary atresia with intact ventricular septum; 2AVV=two atrioventricular valves; DORV=double outlet right ventricle; PAC=premature atrial contractions; mPACs=multiple premature atrial contractions; Af=atrial flutter; cPAC=PAC with couplets; TB=total beat; PVC=premature ventricular contractions.

Fifteen healthy volunteers aged from 5 to 18 years (mean: 10.4 years), who had no signs of cardiovascular disease on physical examination and electrocardiography, underwent signal averaged electrocardiography as the control group. Informed consent was obtained from the parents of each patient and volunteer.

Hemodynamic study

Cardiac catheterization and angiography were performed at 0.2 to 9 years after the Fontan operation (mean: 2.9 years). After routine measurement of pressures and oxygen saturation, the cardiac output was measured by the dye-dilution method. The maximum right and left atrial volumes were calculated by the area-length method on the largest posteroanterior and lateral projections of the right atriogram and its levophase[17], and were corrected by body surface area (right and left atrial volume indices). Hemodynamic data from the APC and TCPC groups are summarized in **Table 2**.

Time domain analysis in signal averaged electrocardiography

The signal averaged electrocardiogram was recorded from a modified *X*, *Y* and *Z* lead system using the Multicardiner VCM-3000 (Fukuda Denshi Co.) in an electric shield room. The gain of the amplifier was 1,000 and the noise input was $<$ 0.6 μV. The signal from each lead was recorded from analog to digital data with 12-bit accuracy at a sampling rate of 1 kHz. All digital data were stored on a floppy disk. Ventricular ectopic beats and gross noise were eliminated by the conventional QRS template-triggering system as reported previously[14]. Briefly, a specially filtered P wave derived from the dominant P wave of the *Z* lead served as a reference signal for all processing. The signals were averaged on a trigger point within a specially filtered P wave after passing through a P wave template recognition program to eliminate ectopic atrial beats. The signals of 150 beats were usually averaged to reduce the noise level to $<$ 1 μV. Vector magnitude was calculated as $V=(X^2+Y^2+Z^2)^{1/2}$ by the method of Simson *et al*[18]. The onset and offset of the filtered P wave were detected by defining the filtered P wave as signals within the interval showing a persistent level of more than 1 μV and as noise signals when showing a persistent level of less than 1 μV. The duration and area of the filtered P wave were measured.

Table 2 Hemodynamic data

	APC group	TCPC group
CVP (mmHg)	14±2	13±2
PWP (mmHg)	6±2	6±3
CI (*l*/min/m^2)	2.8±1.3	3.3±1.2
Sa_{O_2} (%)	92±3	91±3
RAVI (ml/m^2)	96±30*	17±6
LAVI (ml/m^2)	34±16	22±6

Values are mean±SD. *$p<0.001$, vs TCPC.
CVP=central venous pressure; PWP=pulmonary arterial wedge pressure; CI=cardiac index; Sa_{O_2}=arterial oxygen saturation; R(L)AVI=right (left) atrial volume index. Other abbreviations as in Table 1.

Fast Fourier transform analysis in signal averaged electrocardiography

Frequency domain analysis was performed on a 100 msec segment from 75 msec before to 25 msec after the end of the P wave on the signal averaged *Z* lead[15]. This component was identified using a computer graphic cursor and standard electrocardiography criteria. These data were multiplied by the Blackmann-Harris four-term window function to reduce spectral leakage from edge discontinuities after the direct-current component was removed from the data. The data were padded with zeros to fill a 512-point array and fast Fourier transformation was applied to determine the frequency content. After the analysis, the magnitude versus frequency plot curve was obtained, and the signal magnitude at 20 Hz (M20) and 30 Hz (M30) was obtained from these curves.

Statistical analysis

All data were stored on a personal computer and values expressed as mean ± standard deviation. All analysis was performed using professional statistical software (StatView ver. 5.0, SAS Institute Inc.). When the mean values of two groups were compared, Student's *t*-test was used. The relationship between both indices was assessed by linear regression analysis. The mean values of the three groups were also compared by one-way ANOVA followed by post-hoc testing according to Fisher. Statistical significance was taken at $p<0.05$.

RESULTS

Patient characteristics

Symptomatic supraventricular arrhythmias,

Table 3 Signal averaged electrocardiography analysis

	APC group	TCPC group	Control group
DFP	142±18*	118±13	112±10
AFP	1,241±445*	858±265	336±296
M20	268±48*	126±34**	75±38
M30	110±39*	66±23	49±34

Values are mean±SD.*$p<0.05$, vs TCPC and control (ANOVA). **$p<0.05$, vs control (ANOVA).
DFP=duration of filtered P wave; AFP=area of filtered P wave; M20=signal magnitudes at 20 Hz; M30=signal magnitudes at 30 Hz. Other abbreviations as in Table 1.

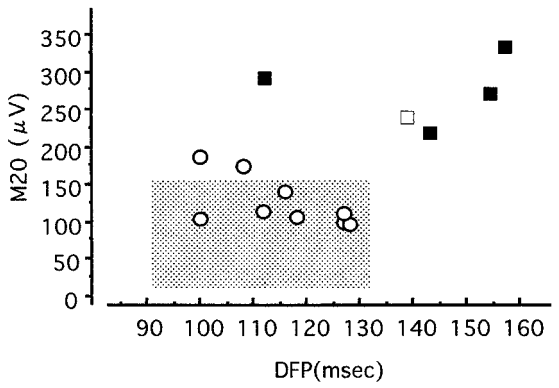

Fig. 1 Relationship between duration of the filtered P wave and M20 in individual patients
Closed and open squares show patients with and without symptomatic arrhythmias in the APC group, respectively, and open circles show patients in the TCPC group. Dashed area shows mean ± 2SD in the control group.
Abbreviations as in Tables 1, 3.

excluding isolated and monofocal premature atrial contraction (PAC) in less than 0.1% of total beats by 24-hour Holter monitoring, were detected in four patients of the APC group; multifocal PACs in one, atrial flutter in two and PAC with couplets in one. These symptomatic arrhythmias were detected only in the APC group, whereas no significant arrhythmia occurred in the TCPC group.

Comparison of hemodynamic data found right atrial volume index in the APC group was significantly larger than in the TCPC group ($p<0.001$). Other indices including atrial pressure and cardiac index showed no significant difference between the two groups (**Table 2**).

Comparison of signal averaged electrocardiography between APC and TCPC

The duration and area of the filtered P wave, M20 and M30 in the APC group were significantly greater than those in the TCPC or the control group, respectively (**Table 3**). M20 in the TCPC group was also greater than in the control group. Three of four patients with symptomatic arrhythmia had the highest values of both M20 and M30.

Relationship between hemodynamic data, duration of the filtered P wave and M20

Comparison of signal averaged electrocardiography and the hemodynamic study found a positive correlation between right atrial volume index and duration of the filtered P wave ($r=0.80$, $p<0.001$), and M20 ($r=0.73$, $p<0.005$). The relationship between duration of the filtered P wave and M20 is shown in **Fig. 1**. M20 was significantly correlated with duration of the filtered P wave ($p<0.01$, $r=0.56$). Four of five patients in the APC group had higher duration of the filtered P wave and M20, and three had symptomatic arrhythmia. Another patient in the APC group had higher M20 in spite of normal duration of the filtered P wave. She had symptomatic arrhythmia and her postoperative time was the longest of all the patients (9 years). In the TCPC group, duration of the filtered P wave and M20 were almost normal except for two patients, whose M20 was abnormally high.

Effect of follow-up time on atrial degeneration

There was a positive correlation between follow-up time and M20 (**Fig. 2**). Four patients examined more than 5 years after surgery had symptomatic arrhythmia.

DISCUSSION

Previous clinical studies have reported that the incidence of atrial arrhythmias after the Fontan-type operation was greater in the conventional APC group than in the TCPC group[3,19], which was also confirmed in our study. The reason why TCPC was superior to APC may be that the postoperative wall stress of the right atrium becomes the substrate of atrial arrhythmia[20]. The wall stress of the right atrium in APC may be higher than that in TCPC because Laplace's law clearly indicates that larger diameter causes higher wall stress[1,7,9]. Investigation of the relationship between atrial arrhythmias and atrial wall stress in experiments

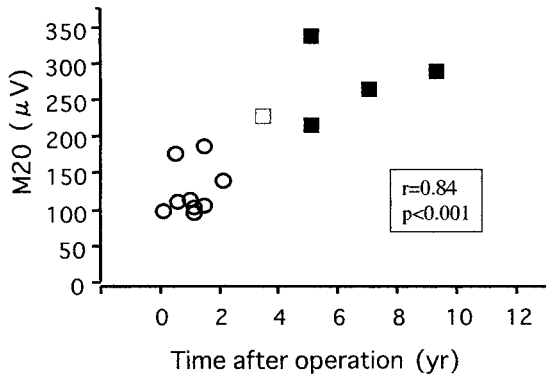

Fig. 2 Relationship between postoperative follow-up time and M20
M20 is closely correlated with postoperative follow-up time ($r = 0.84$, $p < 0.001$).
Explanation of the symbols as in Fig. 1. Abbreviation as in Table 3.

using an animal model with an enlarged atria showed it is easy to generate an atrial flutter[21]. Accordingly, this higher stress might introduce some fibrous change in the atrial muscle which could be the substrate of re-entrant tachyarrhythmia[22,23]. However, this substrate has not been demonstrated in patients undergoing the Fontan operation. In this study, we could demonstrate that both duration of the filtered P wave and M20 were significantly correlated with right atrial volume index ($p < 0.001$, $r = 0.80$; $p < 0.005$, $r = 0.73$, respectively), suggesting that the right atrium volume might affect the presence of a substrate for supraventricular tachyarrhythmias. All indices from the time domain analysis in signal averaged electrocardiography were significantly greater in the APC group than in the TCPC group, but only the right atrial volume was significantly greater in the APC group than in the TCPC group. These results suggest that the risk for supraventricular arrhythmias might be increased in the APC group compared with the TCPC group, and might be affected by the right atrial volume. However, our follow-up interval was significantly different between the APC and TCPC groups (6.0 ± 2.2 years in APC, 1.1 ± 0.6 in TCPC), and more follow-up data are needed.

Another reason for the development of supraventricular arrhythmias is extensive atrial surgery. In the TCPC procedure, especially, atrial incisions and multiple suture lines for intra-atrial baffling could result in the interruption of the conduction pathways and scarring which might be a substrate for arrhythmia. In fact, the incidence of various supraventricular arrhythmias including sinus node dysfunction increases with postoperative time after the Mustard or Senning operations for transposition of the great arteries, in which the baffling operation is similar also to the TCPC procedure[24]. Therefore, the incidence of late atrial arrhythmias might be increased in TCPC. The duration and area of the P wave obtained from signal averaged electrocardiography analysis were not significantly different between patients with TCPC and with other congenital heart diseases or normal control subjects[25,26]. However, the frequency analysis of signal averaged electrocardiography was not examined. In our study, the time domain analysis did not show any difference between the TCPC and control groups, but M20 obtained from the frequency analysis was significantly greater in the TCPC group compared with the control. The terminal portion of the P wave contains significantly more components in the 20−50 Hz range, especially around 30 Hz, in patients with than in patients without paroxysmal atrial fibrillation and this component might reflect slow fragmented atrial activity[15]. Based on this evidence, our results suggest that the developmental risk of late atrial arrhythmias may be present even in the TCPC group. Indeed, one patient (Case 1) with abnormally higher M20 in spite of normal duration of the filtered P wave died suddenly of ventricular fibrillation 5 years after the signal averaged electrocardiography study, and another patient (Case 2) with extremely high M20 and duration of the filtered P wave died of atrial flutter 4 years later. These results suggest that the developmental risk of late atrial arrhythmias may be present even in the TCPC group, and that frequency analysis is a much better method to detect the substrate for atrial arrhythmias.

Postoperative time could be an important factor in the development of late atrial arrhythmias[27,28]. In our study, the four patients with symptomatic atrial arrhythmia were all in the APC group and their postoperative follow-up times were longer than 5 years. Consequently, patients more than 5 years after APC procedure might carry high risk of developing late atrial arrhythmias. In fact, Case 4 (postoperative time 7 years) developed atrial flutter later and needed to change APC to TCPC. On the other hand, the postoperative time of the TCPC group was too short for any significant analysis.

Study limitations

In this study, we demonstrated that the incidence of supraventricular arrhythmias in the APC group was much higher than that in the TCPC group, which might be associated with a larger atrial volume. However, there were some limitations. First, the patient number was small and the background of the APC and TCPC groups was different. Second, the postoperative time in the APC group was significantly longer than that in the TCPC group. These limitations may influence our results. This study of frequency analysis of the P wave in patients undergoing the Fontan operation demonstrated delayed atrial conduction and frequency disturbance that could indicate the presence of a substrate for supraventricular arrhythmias, especially in the APC group. To confirm whether the TCPC procedure is better to reduce the occurrence of late supraventricular arrhythmias, more clinical follow-up studies are necessary.

要　　約

Fontan術後例におけるP波同期体表面加算平均心電図

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目　的: Fontan型手術後の上室性不整脈は，同手術後の生命予後を左右する重要な合併症である．Fontan型手術後の心房に上室性不整脈の基質が存在するか否かを明らかにする．

方　法: Fontan型手術後の小児14例［atriopulmonary connection（APC）法5例とtotal cavopulmonary connection（TCPC）法9例］と健康小児15例を対象とした．P波同期体表面加算平均心電図を行い，空間マグニチュード法によるP波の持続時間，時間積分値とP波の周波数解析による20Hz，30Hzの信号強度（M20, M30）を計測した．これらP波同期体表面加算平均心電図の指標を術後の血行動態を表す指標と比較した．

結　果: P波同期体表面加算平均心電図の全指標でAPC法がTCPC法や健康小児より高値であり（$p < 0.05$），またTCPC法のM20は健康小児より高値であった（$p < 0.05$）．血行動態的指標の比較では，APC法の右房容積だけがTCPC法より大きかった（$p < 0.001$）．しかし，他の血行動態的指標は心房圧も含め2群間で有意差は認められなかった．

結　語: 上室性不整脈の基質は，Fontan型手術後（とくにAPC法）で高頻度に存在し，右房の拡大がこの基質の存在に影響していることが示唆された．またTCPC法にも術後不整脈発生のリスクが存在すると考えられた．

J Cardiol 2002 Feb; 39(2): 101−107

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