Influence of respiration on systemic venous and pulmonary arterial flow pattern after Fontan operation: Direct intravascular Doppler analysis

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“Those who sow in tears will reap with songs of joy. He who goes out weeping, carrying seed to sow, will return with songs of joy, carrying sheaves with him.”

May the name of the LORD be praised!

<TABLE OF CONTENTS>

LIST OF FIGURES

LIST OF TABLES

ABSTRACT

Influence of respiration on systemic venous and pulmonary arterial flow pattern after Fontan operation: Direct intravascular Doppler analysis

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Background: The flow pattern and efficiency in the Fontan circuit vary according to the surgical modification of the Fontan operation. Sporadic studies have reported that cardiac and respiratory cycles have important influence on Fontan circulation, the details concerning the role of each component and/or interactions of respiration and heart beats according to surgical modification has been poorly appreciated. We assessed the flow patterns in the systemic veins and pulmonary artery during different respiratory and cardiac cycles by novel technique of direct intravascular Doppler assessment to evaluate the influence of heart beats, respiratory efforts and technical modifications on established Fontan circulation.

Method: We surveyed 40 patients who had undergone a Fontan operation; 8 with an atriopulmonary connection (APC group), 22 with a total cavopulmonary connection with lateral tunnel (LTF group), and 10 with a total cavopulmonary connection with extracardiac conduit (ECF group). We used direct intravenous Doppler echocardiography with the Flowmap System (Medtronics, Minneapolis, MN, USA) and obtained Doppler measurements at the superior vena cava (SVC), inferior vena cava (IVC), hepatic vein (HV), left pulmonary artery (LPA) and Right pulmonary artery (RPA). We compared the average peak velocity (APV), velocity-time integral (VTI), net antegrade flow integral (NAFI), mean flow rate (MFR = Q), pulsatility index (PI), respiratory variability index (RVI) and inspiration/expiration MFR (IEQ) at each vessels among the three Fontan groups. The RVI and IEQ were also compared among vessels in each group.

Results: On the comparison of VTI, APV and NAFI, the values in the ECF group showed tendency toward increase than those in the APC group, especially during inspiratory phase at the HV and both PAs ($P<0.05$) . However, in systolic phase during expiration, the VTI and APV at the HV were larger in APC group than other 2 groups ($P<0.05$). The PIs were significantly increased at all vessels in the APC group, regardless of the respiratory cycle ($P < 0.05$). The RVIs of APC group were significantly reduced at all vessels compared to those of other groups ($P < 0.05$). On comparison of RVIs among 5 vessels, the HV showed significantly increased RVIs in all 3 groups.

Conclusion: Our findings provide integrated information concerning the influence of respiration and heart beats on the established Fontan circulation and its difference according to surgical modifications. Blood flow profiles shows superior efficiency in patients undergone ECF operation than in those with APC Fontan operation, and the flow efficiency is augmented during inspiratory phase. APC is associated with higher pulsatile flow mainly attributed to heart beats which pertains potential benefit of less endothelial dysfunction in long-term. Higher respiratory dependency of flow in the HV in all groups suggests the need of surveillance on their long-term effect on hepatic function and splanchnic circulation in post-Fontan patient.

Key words: Congenital heart defect, Fontan operation, Hemodynamics, Doppler ultrasonography

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I. INTRODUCTION

Despite the outstanding contributions of Fontan operation[1] for complex cardiac defects with univentricular heart, long-term problems including significant morbidities and mortality[2] have driven clinician's interest to ongoing efforts for better understanding of Fontan physiology[3-6], and various surgical modifications have been introduced[7-9]. In 1988, the total cavopulmonary connection (TCPC) was presented as a substitutional surgery for classic Fontan operation with atrio-pulmonary connection (APC), along with experimental data showing hemodynamic superiority of TCPC over APC[8]. Further technical modification using extracardiac conduit interposition (ECC) between inferior vena cava and the pulmonary artery, instead of intracardiac lateral tunnel in TCPC, has been reported in the following few years[9]. Currently, ECC Fontan (ECF) operation might be the most preferred surgical modification due to the technical advantages and the hemodynamic benefits from less turbulent flow-characteristic. Additional advantage pertaining to ECC Fontan procedure includes potential for less late arrhythmia which is attributable to avoidance of complex suture lines and exclusion of entire atrial tissue from the high-pressure Fontan circuit. Nevertheless, the TCPC-type Fontan procedures including ECF have persistent forward flow without pulsatility, which potentially inhibits growth of the pulmonary vascular bed, eventually resulting in an increase in pulmonary vascular resistance[10]. However, the hemodynamic characteristic and difference of flow patterns in individual settings of each surgical technique are not fully understood. On the other hand, it is known that both the intrathoracic pressure change during respiration[11, 12] as well as pulsatile energy by atrial contraction contribute to the driving force of pulmonary circulation in the absence of functioning right ventricle. While it could be postulated that the role of each component might be different according to the surgical modification, the integrated influence and/or interactions of respiration and heart beats have been poorly appreciated.

We assessed the flow patterns in the systemic veins and pulmonary artery during different respiratory and cardiac cycles by novel technique of direct intravascular Doppler assessment to evaluate the influence of heart beats, respiratory efforts and technical modifications on established Fontan circulation.

II. MATERIALS AND METHODS

1. Patients

During an 8-year period from November 1998 to October 2006, 239 consecutive patients underwent follow-up cardiac catheterization after Fontan-type operation for various indications. We investigated 40 selective patients (age 14.5±7.6 years, 9.9±6.3 years after Fontan operation, males:female=25:15, Table 1) who had normal sinus rhythm, normal systemic ventricular function and did not have any significant residual hemodymic sequelae such as Fontan circuit stenosis, valve regurgitation, intracardiac shunt and abnormally-high Fontan circuit pressure (mean pressure ≥ 20mmHg), as evidenced by electrocardiography, echocardiography and cardiac catheterization. Patients were divided into 3 groups according to the type of operation. Eight patients underwent atriopulmonary connection (APC group), 22 patients had lateral tunnel Fontan operation (LTF group) and remaining 10 patients underwent extra-cardiac conduit Fontan operation (ECF group). Patients' characteristics of each group are shown in Table. 1. We received informed consent from the patient or parents and the study was performed according to the protocol approved by the local ethics committee.

Table 1. Patient Characteristics

	APC (n=8)	**LTF (n=22)**	**ECF (n=10)**	**p**
Sex, male/female	5/3	14/8	6/4	
Age (years)	15.7±6.7	11.7±4.7	17.8±9.6	0.008*
Weight (kg)	48.9±18.0	37.0±15.4	52.8±14.9	0.015*
BSA (m^2)	1.47±0.33	1.18±0.37	1.54±0.32	0.014*
Time since surgery (years)	12.1±6.0	8.1±4.9	12.1±8.7	NS
Mean PA pressure (mmHg)	14.2±2.8	12.9±3.0	13.6±2.3	NS
PA index (Nakata index)#	230±67	225±96	217±71	NS
Indexed CSA_{SVC}#	85±19	98±61	88±19	NS
Indexed CSA_{IVC}#	170±82	173±88	158±53	NS
Diagnosis				
Tricuspid atresia	4	7	4	
Unbalanced AVSD	3	8	3	
Other complex UVH	1	7	3	

APC, atrio-pulmonary connection group; LTF, intra-atrial lateral tunnel Fontan group; ECF, extra-cardiac conduit Fontan group; NS, not significant; BSA, body surface area; PA, pulmonary artery; CSA, cross sectional area; SVC, superior vena cava; IVC, inferior vena cava; AVSD, atrioventricular septal defect; UVH, univentricular heart. #; cross sectional areas of vessels were indexed according to BSA.
Data are expressed as mean ± standard deviation. * Kruskal-Wallis test

2. Methods

1) Intravascular Doppler echocardiography

After routine cardiac catheterization including pressure recording and oxygen saturation measurements, a 0.018-inch intravascular Doppler wire with a 12 MHz piezoelectric ultrasound transducer integrated on its tip (FloWire™; Cardiometrics, Carolina, USA) was introduced through a 5 or 6 Fr end-hole catheter from femoral vein to position at SVC, IVC, HV, LPA and RPA. The intravascular Doppler signal was recorded from corresponding vessel using the FlowMap™ system (Cardiometrics, Carolina, USA) while the respiratory and cardiac cycles were simultaneously recorded in the same screen. Doppler signals were recorded at the midway between the innominate vein and PA for SVC, 2-3 cm inferior to the HV-IVC junction for IVC, 2-3 cm distal to the HV-IVC junction for HV, midway between SVC-PA junction and RPA bifurcation for RPA, and 1 cm proximal to LPA bifurcation for LPA. To avoid incorrect attains of values, the tip of the Doppler guide wire was not to be bent and was placed in the free lumen along the longitudinal axis of the vessels. Doppler interrogation was performed minimum of 5 times throughout the whole respiratory cycle for each vessel, and these results were analyzed by offline measurements for velocity-time integral (VTI), maximal peak velocity (MPV), minimal peak velocity (mPV) and time intervals, after video tape recording. Values from at least 3 different cardiac cycles for both inspiratory and expiratory phase were averaged, excluding the highest and the lowest values.

2) Interpretation and calculation of Doppler signals

The average peak velocity (APV), NAFI (net antegrade flow integral), PI (pulsatility index) and RVI (respiratory variability index) were calculated based on the measured values (VTI, MPV, mPV, time intervals) using the following equations.

$$1.\ \mathrm{APV}\ (\mathrm{m/s}) = \mathrm{VTI}\ (\mathrm{m}) / \Delta \mathrm{T}\ (\mathrm{s}) = \int_{t1}^{t2} v(t)dt / \Delta \mathrm{T}\ (\mathrm{s})$$

$$2.\ \mathrm{PI} = (\mathrm{MPV} - \mathrm{mPV}) / \mathrm{APV}$$

3. $RVI = {(VTI\ in\ inspiratory\ phase - VTI\ in\ expiratory\ phase)}/{Average\ VTI}$

4. $NAFI = VTI\ in\ systole + VTI\ in\ diastole - VTI\ in\ reversal$

We compared the flow parameters (VTI and APV according to the cardiac and respiratory cycles, NAFI according to the respiratory cycle), PI and RVI at SVC, IVC, HV, LPA and RPA among the 3 groups. We also compared the RVIs in the each group among 5 vessels (SVC, IVC, HV, LPA and RPA).

3. Statistical analysis

Means with standard deviations for measured values of APV, PI, RVI, NAFI, MFR, and IEQ were calculated and compared among the 3 groups using the ANOVA test. The SPSS® statistics program (Version 12, IBM, Chicago, Illinois, USA) was used for all statistical analyses, and the statistical significance was adopted at P values < 0.05.

III. RESULTS

1. Characteristics of flow pattern in each group (Figures 1 to 6)

In the APC group, the SVC and IVC flows were composed of two positive (antegrade) waves, one prominent wave occurred during ventricular systole (S wave) which corresponding to the peak-of-R to end-of-T segment in the ECG and small early diastolic wave (D wave) which corresponding to the end-of-T to begin-of-P segement in the ECG. One reverse (retrograde) wave during late diastolic phase (atrial contraction; DR wave) corresponded to the P-R interval in the ECG (Figure 1A and 2A). In the HV, two positive waves (S and D waves) and two reverse waves (SR and DR wave) were observed among which S wave in the positive waves and DR wave in the reverse waves were predominant

(Figure 3A). The LPA and RPA flows in the APC were composed of two positive waves and one reverse wave as in the systemic veins. However, the reverse wave appeared during early systolic phase shortly after atrial contraction in 5 patients, during early diastolic phase in 2 patients and no reverse flow was seen in 1 patient (Figure 4A and 5A). The flow velocities were mainly dependant on the cardiac cycle and showed minor variation according to the respiratory cycle. In the LTF group, SVC, IVC, LPA and RPA flows showed continous flow pattern with two peaks corresponding to the S and D waves, and no reverse wave was seen in the vast majority of the patients (Figure 1B, 2B, 4B and 5B). Variation in the flow velocities was more affected by respiratory cycle than in APC group especially in HV, so that the S and D waves in HV frequently deflected below baseline during expiratory phase (Figure 3B). The ECF group showed similar patterns with those of the LTF group and the respiratory influence tended to be greater than in LTF group (Figure 1C, 2C, 3C, 4C and 5C).

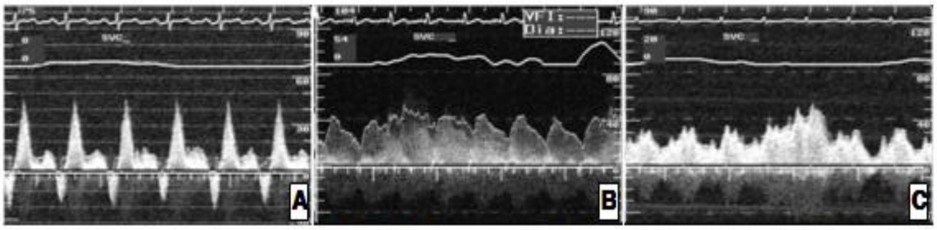

Figure 1. Intravascular Doppler spectrals at SVC in 3 groups (A;APC group, B;LTF group, C;ECF group)

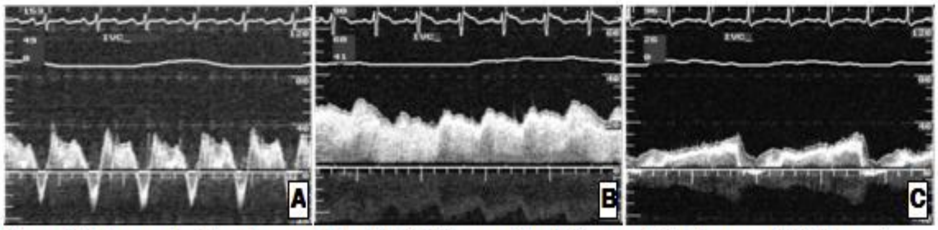

Figure 2. Intravascular Doppler spectrals at IVC in 3 groups (A;APC group, B;LTF group, C;ECF group)

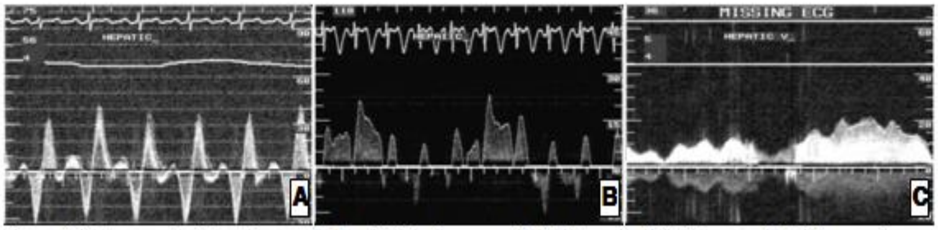

Figure 3. Intravascular Doppler spectrals at HV in 3 groups (A;APC group, B;LTF group, C;ECF group)

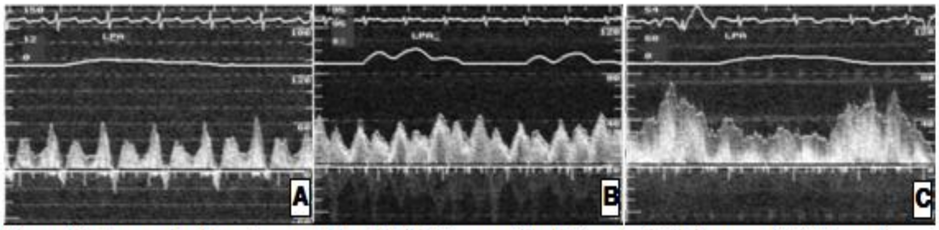

Figure 4. Intravascular Doppler spectrals at LPA in 3 groups (A;APC group, B;LTF group, C;ECF group)

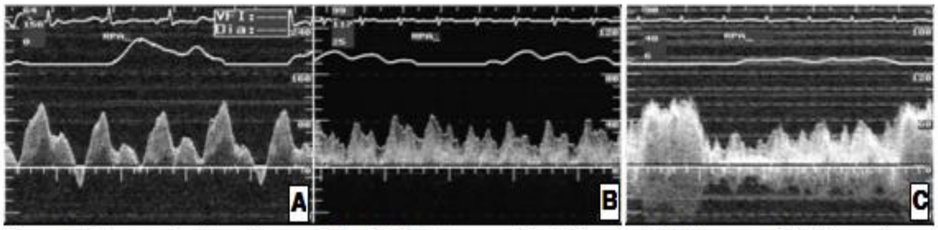

Figure 5. Intravascular Doppler spectrals at RPA in 3 groups (A;APC group, B;LTF group, C;ECF group)

2. Comparison of VTI, APV and NAFI (Tables 2, 3, and 4)

The VTIs, APVs and NAFIs in 3 groups according to the respiratory cycle and cardiac cycle are summarized in tables 2, 3 and 4.

In general, the values of the VTI, APV and NAFI in the ECF group showed tendency toward increase than those in the APC group, especially during inspiratory phase at the HV and both PAs except for increased values at the HV in APC group than other 2 groups in systolic phase during expiration.

Table 2. Comparison of VTI (cm) at each vessel among the APC, LTF and ECF groups according to the respiratory and cardiac cycles

VTI (cm)			APC	LTF	ECF	*Statistical significance*
SVC	**Insp.**	**S**	8.79 ± 3.31	9.72 ± 3.45	9.55 ± 4.08	
		D	5.03 ± 3.65	8.33 ± 2.99	9.23 ± 4.44	†
		R	-0.97 ± 0.62	-	-	
	Exp.	**S**	8.10 ± 3.13	7.24 ± 2.33	6.37 ± 2.69	
		D	4.42 ± 2.94	6.05 ± 2.20	6.07 ± 3.58	
		R	-1.03 ± 0.58	-	-	
IVC	**Insp.**	**S**	8.11 ± 3.21	8.89 ± 3.11	8.75 ± 2.13	
		D	6.15 ± 1.40	8.16 ± 3.13	8.04 ± 2.43	
		R	-1.65 ± 0.80	-	-	
	Exp.	**S**	5.80 ± 2.54	5.28 ± 2.14	6.63 ± 2.23	
		D	5.26 ± 2.31	5.39 ± 2.53	5.06 ± 1.71	
		R	-2.15 ± 0.63	-	-	
HV	**Insp.**	**S**	4.01 ± 1.55	4.89 ± 2.27	5.05 ± 2.77	
		D	0.71 ± 1.34	4.55 ± 1.56	6.04 ± 2.05	‡
		R	-3.21 ± 1.24	-	-	
	Exp.	**S**	3.54 ± 1.16	2.04 ± 1.33	1.86 ± 1.34	‡
		D	1.14 ± 1.36	1.42 ± 0.65	2.22 ± 1.49	
		R	-3.66 ± 1.39	-	-	
LPA	**Insp.**	**S**	8.28 ± 2.63	12.52 ± 6.06	15.50 ± 3.99	‡
		D	12.24 ± 5.19	13.29 ± 6.18	17.94 ± 7.42	
		R	-1.60 ± 0.50	-	-	
	Exp.	**S**	6.49 ± 2.24	8.74 ± 3.11	9.11 ± 3.43	
		D	9.91 ± 4.10	10.31 ± 2.75	11.48 ± 3.78	
		R	-0.98 ± 0.46	-	-	
RPA	**Insp.**	**S**	8.08 ± 4.27	13.35 ± 5.04	15.50 ± 3.99	†
		D	10.83 ± 10.01	14.01 ± 5.78	17.94 ± 7.42	
		R	-1.56 ± 1.50	-	-	
	Exp.	**S**	5.85 ± 2.94	8.32 ± 2.31	9.34 ± 3.12	†
		D	10.29 ± 8.14	8.79 ± 3.41	10.67 ± 3.68	
		R	-0.45 ± 0.07	-	-	

Insp.; inspiration period, Exp.; expiration period, †; Statistical significances were $p < 0.05$ between APC & ECF group. ‡; Statistical significances were $p < 0.05$ between APC & LTF group, APC & ECF group.

Table 3. Comparison of APV (cm/sec) at each vessel among the APC, LTF and ECC during the respiratory and cardiac cycles

APV (cm/sec)			APC	LT	ECF	*Statistical significance*
SVC	**Insp.**	**S**	24.35 ± 8.13	30.26 ± 10.42	24.81 ± 11.03	
		D	16.69 ± 9.28	28.05 ± 9.50	24.39 ± 10.70	†
		R	-6.53 ± 2.21	-	-	
	Exp.	**S**	22.49 ± 8.41	22.64 ± 8.27	16.92 ± 7.52	
		D	15.88 ± 8.84	21.41 ± 8.59	16.31 ± 7.31	
		R	-6.62 ± 3.05	-	-	
IVC	**Insp.**	**S**	25.63 ± 6.21	27.14 ± 9.09	22.83 ± 5.63	
		D	19.23 ± 4.09	25.59 ± 10.06	22.75 ± 5.26	
		R	-9.27 ± 3.04	-	-	
	Exp.	**S**	19.33 ± 5.99	17.20 ± 7.00	15.50 ± 5.88	
		D	16.10 ± 5.60	17.27 ± 8.04	16.62 ± 6.35	
		R	-11.05 ± 2.03	-	-	
HV	**Insp.**	**S**	16.48 ± 6.70	15.21 ± 4.67	10.78 ± 4.57	
		D	9.22 ± 5.85	13.34 ± 4.02	12.40 ± 4.15	‡
		R	-13.46 ± 9.76	-	-	
	Exp.	**S**	13.28 ± 4.59	5.34 ± 6.11	3.80 ± 2.59	‡
		D	10.22 ± 6.81	4.51 ± 5.38	5.03 ± 2.81	
		R	-13.47 ± 4.27	-	-	
LPA	**Insp.**	**S**	30.51 ± 12.32	38.92 ± 10.90	45.89 ± 16.65	‡
		D	26.34 ± 6.94	36.50 ± 10.13	48.12 ± 13.64	
		R	-9.62 ± 2.97	-	-	
	Exp.	**S**	24.74 ± 9.09	26.15 ± 9.48	26.53 ± 11.16	
		D	24.03 ± 11.81	25.11 ± 7.74	30.39 ± 11.84	
		R	-14.42 ± 2.89	-	-	
RPA	**Insp.**	**S**	26.24 ± 20.74	41.36 ± 13.33	44.61 ± 15.37	‡
		D	28.46 ± 13.07	40.00 ± 14.73	47.29 ± 18.91	
		R	-3.35 ± 2.73	-	-	
	Exp.	**S**	24.49 ± 19.34	27.19 ± 7.47	29.08 ± 15.61	
		D	23.18 ± 6.97	28.64 ± 9.95	29.89 ± 14.14	
		R	-8.74 ± 5.93	-	-	

Insp.; inspiration period, Exp.; expiration period, †; Statistical significances were $p < 0.05$ between APC & LTF group. ‡; Statistical significances were $p < 0.05$ between APC & LTF group and APC and ECF group.

Table 4. Comparison of NAFI (cm) at each vessel among the APC, LTF and ECF group according to the respiratory cycle

NAFI (cm)		APC	LTF	ECF	*Statistical significance*
SVC	**Insp.**	13.29 ± 7.19	17.52 ± 5.65	18.75 ± 8.17	
	Exp.	12.12 ± 6.34	12.90 ± 4.23	12.43 ± 6.11	
IVC	**Insp.**	12.49 ± 4.20	16.80 ± 5.90	17.31 ± 3.81	
	Exp.	10.44 ± 2.79	10.49 ± 4.47	11.58 ± 3.44	
HV	**Insp.**	5.08 ± 2.55	8.86 ± 3.83	11.62 ± 6.46	†
	Exp.	2.76 ± 1.55	2.27 ± 1.47	3.90 ± 2.73	
LPA	**Insp.**	20.36 ± 7.56	26.62 ± 10.78	36.08 ± 10.65	†
	Exp.	16.04 ± 5.89	17.03 ± 6.52	20.58 ± 6.60	
RPA	**Insp.**	18.30 ± 12.91	26.46 ± 8.80	33.44 ± 9.70	†
	Exp.	15.78 ± 10.95	17.38 ± 5.08	20.01 ± 6.57	

*; Statistical significances were p < 0.05 between APC & ECF group.

3. Comparison of PIs (Table 5)

The PIs in the APC group were significantly increased in all vessels of the SVC, IVC, HV, LPA and RPA during both inspiratory and expiratory periods compared to those in the LT and ECC ($P < 0.05$).

Table 5. Comparison of PIs at each vessel among the APC, LTF and ECF groups according to the respiratory cycle

PI		APC	LTF	ECF	*statistical significance*
SVC	**Insp.**	1.42 ± 0.60	0.56 ± 0.21	0.83 ± 0.18	†
	Exp.	1.35 ± 0.64	0.57 ± 0.29	0.81 ± 0.23	†
IVC	**Insp.**	1.63 ± 0.42	0.65 ± 0.40	0.37 ± 0.21	†
	Exp.	1.73 ± 0.49	0.68 ± 0.45	0.35 ± 0.16	†
HV	**Insp.**	3.82 ± 1.40	1.32 ± 1.25	1.10 ± 0.53	†
	Exp.	6.81 ± 3.68	2.41 ± 2.02	1.65 ± 1.09	†
LPA	**Insp.**	1.41 ± 0.40	0.64 ± 0.36	0.61 ± 0.21	†
	Exp.	1.40 ± 0.49	0.72 ± 0.44	0.58 ± 0.27	†
RPA	**Insp.**	1.67 ± 0.79	0.67 ± 0.32	0.60 ± 0.16	†
	Exp.	1.63 ± 0.68	0.68 ± 0.38	0.58 ± 0.15	†

†; Statistical significances were p < 0.05 between APC & LTF group and APC & ECF group.

4. Comparison of RVIs among APC, LTF and ECF groups (Table 6)

The RVIs of the SVC, IVC, HV, LPA, and RPA in the APC group were significantly decreased compared to those in the LTF group (*P* < 0.05) and ECF group (*P* < 0.05).

Table 6. Comparison of RVIs at each vessel among the APC, LTF and ECF groups

RVI	APC	LTF	ECF	*statistical significance*
SVC	0.09 ± 0.04	0.31 ± 0.16	0.41 ± 0.19	†
IVC	0.17 ± 0.09	0.43 ± 0.21	0.51 ± 0.23	†
HV	0.54 ± 0.53	1.06 ± 0.38	1.07 ± 0.37	†
LPA	0.23 ± 0.11	0.44 ± 0.16	0.56 ± 0.16	†
RPA	0.15 ± 0.06	0.39 ± 0.17	0.51 ± 0.18	†

*; Statistical significances were $p < 0.05$ between APC & LTF group and APC & ECF group.

5. Comparison of RVIs among SVC, IVC, HV, LPA and RPA (Table 7.)

The RVI of the HV was significantly increased than those of SVC and IVC in APC group. The RVIs of the HVs were significantly increased than those of SVCs, IVCs, LPAs and RPAs in LTF and ECF groups (*P* < 0.05, Table 7.)

Table 7. Comparisons of RVIs among vessels in the 3 groups

RVI	SVC (group 1)	IVC (group 2)	HV (group 3)	LPA (group 4)	RPA (group 5)	*Statistical significance*
APC	0.09 ± 0.04	0.17 ± 0.09	0.54 ± 0.43	0.21 ± 0.11	0.22 ± 0.12	†
LTF	0.31 ± 0.16	0.43 ± 0.21	1.06 ± 0.38	0.44 ± 0.16	0.39 ± 0.17	‡
ECF	0.41 ± 0.19	0.51 ± 0.23	1.07 ± 0.37	0.56 ± 0.16	0.51 ± 0.18	‡

†; Statistical significances were $p < 0.05$ between SVC & HV and IVC & HV.

‡; Statistical significances were $p < 0.05$ between SVC & HV, IVC & HV, HV & LPA and HV & RPA.

IV. DISCUSSION

The flow pattern in the APC is usually tri-phasic[14] except for quadric-phasic flow pattern is more frequent in HV. One reversal flow and two positive flows are shown; the reverse waves in the SVC, IVC and HV (systemic veins) are due to atrial systole (simultaneous with ventricular diastole) corresponding to the 'P' wave in the ECG and the 'a' wave in the RA pressure curve. The first positive waves in the systemic veins are due to atrial diastole with ventricular systole accorded to the 'QRS' wave in the ECG and the 'c' wave in the RA pressure curve. The second positive waves in the inflows are due to atrial filling with ventricular dilatation accorded to the 'T' wave in the ECG and the 'v' wave in the RA pressure curve (Figures 1A, 2A, 3A). Among these 2 positive waves, the former one (accorded to ventricular systole; S wave) was predominant. On the contrary, predominant positive waves in the LPA and RPA (pulmonary arteries; PAs) are due to atrial systole with ventricular diastole accorded to the 'P' wave in ECG and the 'a' wave in the RA pressure curve. The reverse waves after larger positive waves in PAs are due to atrial diastole with ventricular systole accorded to the 'QRS' wave in the ECG and the 'c' wave in the RA pressure curve. Smaller positive waves in the outflows are due to atrial filling with ventricular dilatation accorded to the 'T' wave in ECG and the 'v' wave in the RA pressure curve (Figures 4A, 5A).

Therefore, atrial contraction with ventricular dilatation causes backward flow to systemic veins and forward flow to PAs. On the other hand, atrial dilatation with ventricular contraction causes forward flow in systemic veins and backward flow in PAs.

The characteristics of the flow pattern in the TCPC groups (LTF and ECF) are quite different from those in the APC group. The flow patterns of systemic veins and PAs in the LTF is usually biphasic with two positive flow waves;

only small reversal flow waves were observed in the IVC and/or rarely in PAs in a small number of patients, whereas the reversal flow was not observed in the ECF. This difference is probably due to the influence of atrial contraction in the LTF group in which the atrium had partially been included in the Fontan circuit[15]. HV flow patterns in the LTF and ECF groups showed swing of the baseline of flow velocities which were mainly influenced by respiratory cycle which resulted in the wide range of flow-velocity change in the HV. This respiratory dependence has been suggested as a potential risk factor of chronic hepatic dysfunction in post-Fontan patients[16].

Basically, the origin of flow energy in the pulmonary arteries is dependent on the transpulmonic pressure gradient which is generated by ventricular contraction (cardiac output) and resistance of the pulmonary vascular bed[17]. Additional sources of flow energy include atrial contraction (in APC group) and thoracic negative pressure from respiration at resting state; during exercise, peripheral muscle pump may provide with an extra-source for flow energy[11, 17]. The difference in the Fontan circuit of APC, LTF and ECF is characterized by physical properties of connecting part between IVC and PA. APC has pulsatile, dilated and compliant atrial chamber just before the pulmonary circulation, and the dilated atrium may acts as a reservoir chamber which absorbing the inspiratory suction energy. This may explains the relative lack of respiratory influence in APC group. On the other hand, the pulsatile energy generated by atrial contraction may contribute to the antegrade flow in PAs, whereas interfering with flows in systemic veins at the same time. This combination proved to be unbeneficial in the setting of Fontan physiology[18].

However, the predominance of S waves in the systemic veins (Figure 1A, Figure 2A, Figure 3A) and the predominance of D waves in the PAs (Figure 4A, Figure 5A) may indicate the importance of atrial contraction in APC, as these may mean the dominant waves are the result of augmented repulsion after atrial contraction.

The hemodynamic advantages of laminar flow in TCPC groups are reflected as larger VTIs, APVs and NAFIs especially in PAs and HV of ECF group, despite the power of resolution appears not to be strong, probably because of limited study population as well as complex nature of post-Fontan patients carrying multiple hemodynamically-relevant factors other than defined in this study.

According to the superiority of these flow profiles, the TCPC groups especially ECF group appears to have more efficient circuit than the APC group.

The pulsatility index (PI) was obtained in each vessel in each respiratory (inspiratory and expiratory) cycle; therefore PI reflects the flow velocity change according to the cardiac component. Accordingly, the APC group is more influenced by cardiac cycles than the TCPC groups (Table 5).

However, the pulsatile flow pattern in the APC group has a beneficial effect in that it may lower the pulmonary vascular resistance by the passive recruitment of capillaries and shear stress–mediated release of NO causing endothelial relaxation[19]. On the contrary, a decrease in the pulsatility in the TCPC groups may reduce the growth of the pulmonary vascular bed and increase the pulmonary vascular resistance, thus possibly promote late complications[10, 20]. Indeed, a study reporting superior long-term functional outcome in APC patients over TCPC-type patients has been published in relatively early era of TCPC-type operation[21].

The respiratory variability index (RVI) is the parameter that measures changes in the VTI according to the respiratory cycle. The TCPC groups are more influenced by respiration as RVI(s) of the LTF and ECF groups were larger than those in the APC group. This finding is consistent with previous observations reported that pulmonary blood flow in patients who have undergone the TCPC is more dependent on variation in intra-thoracic pressure and respiration[22]. On this basis, patients who have undergone the TCPC-type Fontan procedure should be at a higher risk than in those who have undergone the APC operation in clinical settings requiring positive pressure ventilation such as immediate post-operative period or serious respiratory problem.

The RVI of the HV was significantly increased than those of remaining systemic veins and PAs, especially in TCPC groups. The significantly wider range of flow change in the HV seems to be attributable to the higher compliance or capacitance of hepatic venous system than other vessels. The rapid change in the flow also includes retrograde flow reversal which means hepatic circulation is exposed to intermittent and cyclic pressure load. This may have an effect on hepatic congestion and portal vein hypertension. Also, reverse flow in the HV may increase the pressure of splanchnic circulation and possibly linked to the pathogenesis of protein-losing enteropathy. On the contrary, it is known that pulsatile stretch and shear stress are needed for production of endothelium-derived relaxing factors for adequate vascular compliance[23], whereas nothing is known about the role of periodic change in the flow velocity rather than pulsatile change. Therefore, further studies are mandatory to investigate whether certain variations in HV flow pattern are related to any of the long-term complications in post-Fontan patients.

Limitations

The flow patterns in the systemic veins and PAs may influenced by multiple factors such as systemic ventricular function, pulmonary function, pulmonary resistance, morphologic characteristics of cardiac defects, loading conditions of blood volume and patients' physical status, etc. We could not control all of the individual factors because each patient has his or her own characteristics which could not be categorized into certain numbers of groups. The studied population was not sufficient for a clearly conclusive comparison because of the lack of patients' pool of each subgroups after Fontan-type operation.

V. CONCLUSION

Our findings provide integrated information concerning the influence of respiration and heart beats on the established Fontan circulation and its difference according to surgical modifications. Blood flow profiles shows superior efficiency in patients undergone LTF or ECF operation than in those with APC Fontan operation, and the flow efficiency is augmented during inspiratory phase. APC is associated with higher pulsatile flow mainly attributed to heart beats which pertains potential benefit of less endothelial dysfunction in long-term. Higher respiratory dependency of flow in the HV in all groups suggests the need of surveillance on their long-term effect on hepatic function and splanchnic circulation in post-Fontan patient.

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ABSTRACT (IN KOREAN)

폰탄술 후의 혈류 양상과 호흡의 영향
: 혈관내 도플러 검사를 통한 분석

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서론: 폰탄술 후의 혈류의 양상과 효율성은 폰탄술의 술기적 변형에 따라 달라질 수 있다. 심장의 박동과 호흡 운동이 폰탄술 후 체정맥과 폐동맥 혈류의 주요 영향 요인임이 보고되어 왔으나 술기적 변형에 따라 심박동과 호흡 운동 각각의 역할이 어떠한지 또는 그 상호작용은 어떻게 나타나는 지에 대한 것은 잘 알려지지 않았다. 저자들은 폰탄술 후 안정된 상태로 추적 관찰 중인 환자들에서 혈관내 도플러 검사법을 이용한 새로운 기술을 사용하여 심박동과 호흡 운동에 따른 체정맥 및 폐동맥의 혈류 양상이 어떻게 나타나고 서로 영향을 미치며 또한 수술의 술기적 변화에 따라 어떻게 다른 지를 조사하여 분석하였다.
방법: 폰탄 수술을 받은 40명의 환자를 대상으로 조사하였다. 이 환자들은 폰탄술의 술기적 변형에 따라 심방-폐동맥 문합술을 시행받은 8명 (APC 군), 심장내 외측 통로 폰탄술을 시행받은 22명 (LTF 군), 심장외 도관을 이용한 폰탄술을 시행받은 10명 (ECF 군)의 3 군으로 분류하여 분석하였다. 각 환자들은 추적 관찰 일정에 따라 심초음파검사 및 심도자 검사를 시행 받았으며 체정맥과 폐동맥 혈류에 영향을 줄 수 있는 잔류 혈역학적 이상, 심실기능 이상이 있거나 폰탄통로 압력이 20mmHg이상인 경우는 제외하였다. 일반적인 심도자 검사 후 각 환자의 상대정맥, 하대정맥, 간정맥, 좌폐동맥, 우폐동맥에서 Flow map system (Medtronics, Minneapolis, MN, USA)을 이용하여 혈관내 도플러 검사를 시행하였으며 심전도와 호흡계의 파형과 함께 도플러 신호를 기록하였다. 각각의 혈관의 평균최대유속(average peak velocity; APV), 속도-시간 적분치

(velocity-time integral; VTI)를 호흡 주기 및 심주기에 따라 측정하였고 각각의 측정치로부터 정방향 혈류 속도-시간 적분치 (net antegrade flow integral; NAFI)를 호흡 주기별로 계산하여 세 군간에 비교하였다. 또한 박동 지수(pulsatility index; PI)를 호흡주기 별로 세 군간에 비교하였으며 각 혈관에서 호흡의존 지수 (respiratory variability index; RVI)를 세 군간에 비교하였다. 각 그룹에서 혈관 위치에 따른 RVI의 차이를 또한 비교하였다.

결과: VTI, APV 및 NAFI의 비교에서 LTF 및 ECF 군이 APC 군에 비해 더 높은 혈류량 및 속도를 가지는 경향을 보였다. 특히 간정맥과 양측 폐동맥에서 ECF 군이 APC 군보다 높은 값을 보였으며 이러한 차이는 주로 흡기시 또는 심실 이완기에 의미있는 차이를 보여 주었다. PI 는 APC 그룹에서 호흡주기에 관계 없이 모든 혈관에서 유의하게 높았다. RVI 는 APC 그룹에서 다른 그룹에 비하여 모든 혈관에서 유의하게 낮았다. 모든 그룹에서 5개의 혈관 간의 RVI를 비교했을 때 간정맥의 RVIs가 유의하게 높았다.

결론: 본 연구의 결과는 폰탄술의 술기적 변형에 따른 호흡과 심박동의 영향의 차이에 관하여 통합적인 정보를 보여준다. 혈류의 양상은 APC 폰탄술의 경우보다 ECF 폰탄술을 시행받은 환자에서 더 효율적으로 나타났고, 혈류의 효율성이 흡기 단계에서 더 증가된 것을 보여 준다. APC는 심박동에 주로 기여하는 높은 박동성 흐름과 연관되어 있는데 그러므로 폰탄술 후의 혈류 박동성 소실에 기인하는 내피 세포 기능 부전이 덜 일어날 수 있다는 이론적 이점이 있다. 모든 군에서 간정맥의 혈류가 다른 부위에 비해 가장 높은 호흡 의존성을 보이므로 폰탄술 후 환자에서 이러한 간 혈류 순환의 변화가 간 및 복부 장기 순환에 미치는 장기적 영향에 대한 감시가 필요하다.

핵심되는 말: 선천성 심장병, 폰탄술, 혈역학, 도플러 심초음파