Young Fontan patients with strong regurgitation of atrio-ventricular valve possess cardiac overloads and also hepatic disorders

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【 Background 】

Regurgitation of atrio-ventricular valve (AVVR) potentially depresses cardiac functions in young Fontan patients. We also predicted strong AVVR would impair hepatic functions. However, it has been not reported the relation between degrees of AVVR and hepatic functions.

【 Objective 】

The purpose of this study was to investigate cardiac and hepatic functions in young Fontan patients with AVVR.

【 Methods 】

Subjects and examinations. The medical records of 174 Fontan patients were reviewed aged from 2 to 18 years. They underwent cardiac catheterization between 2010 and 2015.
Comparative methods. We divided the whole into two groups, such as patients with AVVR mild-to-moderate or over (Strong AVVR: n=27) and all remaining patients (n=147). First, we compared cardiac and hepatic performances between groups with and without Strong AVVR. Second, we excluded patients with Strong AVVR from 174 patients, using rest of whom we compared these indexes between patients with AVVR (Mild AVVR: n=65) and without AVVR (No AVVR: n=82). We analyzed continuous data by unpaired t tests and categorical data by χ-square tests.

Table1. Characteristics of Fontan patients with Strong AVVR

	Strong AVVR (n=27)	Non (n=147)	P value
Cath. age(yrs)	14.0±11.3	11.3± 10.5	0.22
Fon age (yrs)	6.0± 7.0	5.6±7.6	0.79
Right isomerism	8/27 (29)	18/147 (12)	0.041
Ventricular type	R (11) L (1) B (15)	R (37) L (35) B (75)	0.080
Single left vent. (%)	1/27 (3)	35/147 (23)	0.034
CAVV	4/27 (14)	30/147 (20)	0.68
1st strategy (n)	Shunt (11) PAB/NPS (7/3) Norwood (6)	Shunt (74) PAB/NPS (49/9) Norwood (15)	0.46
Coil emboliz. (%)	19/27 (70)	92/147 (62)	0.57
PTPA (%)	7/27(25)	50/147 (34)	0.94
TAPVC repair (%)	4/27(14)	6/147 (4)	0.079
AVV repair (%)	10/27(37)	25/147 (17)	0.017
AR (%)	7/27(25)	34/147 (23)	0.94
Fenest. Fon (%)	8/27 (29)	31/147 (21)	0.46
Internal medicine			
Furosemide (%)	15/27(55)	54/147 (36)	0.066
Spirono./ Eplere. (%)	19/27(70)	71/147 (48)	0.057
ACEI/ARB (%)	23/27(85)	111/147 (75)	0.39
enarapril (mg/kg)	0.21±0.09	0.19±0.06	0.24
B-blocker (%)	21/27(77)	74/147 (50)	0.015
carvedilol (mg/kg)	0.43±0.24	0.41±0.28	0.82
Pulm. vasodilator (%)	12/27(44)	46/147 (31)	0.18

Table 2. Hemodynamics of Fontan patients with Strong AVVR

	Strong AVVR (n=27)	Non (n=147)	P value
Cardiac indexes			
SVEDV (%)	132±69	102± 40	0.0023
SVESV (%)	66±42	49±24	0.0043
SVEF (%)	50±13	51±10	0.51
SVEDP (mmHg)	10.5±7.5	8.3±3.6	0.016
SVESP (mmHg)	92 ±19	91±17	0.74
Qs (L/min/m2)	3.3±1.3	3.4±1.4	0.58
NT-proBNP (pg/ml)	1156±2992	241± 367	0.014
Pulmonary indexes			
PCWP (mmHg)	9.4±5.8	6.8±2.7	0.00033
SVCP (mmHg)	13.4±5.7	12.1±2.8	0.076
(SVCP ≥ 15 mmHg)	11/27 (40)	30/147 (20)	0.041
Ao SatO2 (%)	91±6	92± 3	0.41

Table 3. Hepatic parameters in Fontan patients with Strong AVVR

	Strong AVVR (n=27)	Non (n=147)	p value
Plt (x104/μl)	20.8±8.9	22.4±8.6	0.37
T-bil (mg/dl)	1.0±0.4	0.9±0.4	0.36
GGT (IU/l)	136±105	66±58	0.00011
AST (IU/l)	35±13	36±12	
ALT (IU/l)	30±21	23±12	0.014
TP (g/dl)	6.6±1.1	6.8±0.7	0.14
Alb (g/dl)	4.2±0.7	4.4±0.5	0.046

Table 4. Hemodynamics of Fontan patients with mild AVVR

	mild AVVR (n=65)	No AVVR (n=82)	P value
Cath. age	12.2±10.0	10.5±10.9	0.35
Cardiac indexes			
SVEDV (%)	98±42	106± 37	0.23
SVESV (%)	48±24	50±24	0.58
SVEF (%)	50±9	52±10	0.25
SVEDP (mmHg)	8.1±3.7	8.4±3.5	0.62
SVESP (mmHg)	93 ±18	89±17	0.19
Qs (L/min/m2)	3.3±1.0	3.4±1.0	0.34
NT-proBNP (pg/ml)	185±167	287± 469	0.13
Pulmonary indexes			
PCWP (mmHg)	7.2±3.0	6.5±2.5	0.12
SVCP (mmHg)	11.9±2.6	12.3±2.9	0.34
(SVCP ≥ 15 mmHg)	10/65 (15)	20/82 (24)	0.17
Ao SatO2 (%)	92±3	92±4	0.82

Table 5. Hepatic parameters of Fontan patients with mild AVVR

	mild AVVR (n=65)	No AVVR (n=82)	p value
Plt (x104/μl)	21.5±8.3	23.1±8.8	0.27
T-bil (mg/dl)	1.0±0.4	0.8±0.4	0.13
GGT (IU/l)	86±73	50±27	0.0016
AST (IU/l)	36±15	35±10	0.59
ALT (IU/l)	24±16	21±8	0.10
TP (g/dl)	6.9±0.6	6.8±0.7	0.52
Alb (g/dl)	4.4±0.4	4.5±0.5	0.80

【Results】

Hemodynamics of Fontan patients with Strong AVVR (Table 2).
Ventricular volumes on end-diastole were significantly larger in Fontan patients with Strong AVVR than those without Strong AVVR; those on end-systole were also larger in Strong AVVR patients. Accordingly, ventricular ejection fractions were not different between two groups. Ventricular end-diastolic pressures were significantly elevated in Strong AVVR group. Consequently, levels of NT-proBNP were abundantly increased in Strong AVVR group. As for pulmonary performances, pressures of pulmonary capillary wedge were much elevated in Fontan patients with Strong AVVR. The rate of patients with high pressures of superior vena cava (≥ 15 mmHg) was significantly higher in Strong AVVR patients.
Hepatic parameters in Fontan patients with Strong AVVR (Table 3).
Platelet counts, which were decreased in patients with enlarged spleen, were not significantly different between Fontan patients with and witout Strong AVVR. Of 2 indexes (GGT levels and T-bil levels) which indicated degrees of liver congestion, GGT levels were much elevated in Strong AVVR patients. Levels of ALT, elevation of which suggested hepatic impairment, were significantly higher in Strong AVVR patients. Albumin levels , lowering of which indicated deterioration of liver function, fell in Strong AVVR group.
Hemodynamics of Fontan patients with mild AVVR (Table 4).
To investigate whether mild AVVR was connected with cardio-pulmonary circulation and hepatic function, we distributed 147 Fontan patients, who all did not hold Strong AVVR, into two groups, such as 65 patients with mild AVVR and 82 patients with no AVVR.
All cardiac performances, which included ventricular volumes, end-diastolic ventricular pressures, and levels of NT-proBNP, were not significantly different between Fontan patients with and without mild AVVR. Similarly, PCWP and SVCP were not more elevated in mild AVVR group than in no AVVR group.
Hepatic parameters of Fontan patients with mild AVVR (Table 5).
After excluding Strong AVVR patients, we compared liver indexes between Fontan patients with mild AVVR and those with no AVVR. Levels of GGT were significantly higher in mild AVVR patients than in no AVVR patients. However, the difference of ALT levels did not existed between two groups; that of Alb levels also did not exist between two groups.

【 Discussion】

Major findings.
First, Fonatn patients with Strong AVVR possessed pressure overloads and volume overloads on ventricle, although they had almost same ejection fraction. Moreover, they had hepatic impairment. Second, if Fontan patients had only Mild AVVR, they preserved as almost same cardiac functions as those with No AVVR did. Possibly, hpatocyte impairment faded away which subsisted between patients with and without Strong AVVR.
Hemodynamics in patients with AVVR.
Our study clearly showed cardiac loads were increased in Fontan patients with Strong AVVR, such as ventricular volume (expanded SVEDV), contraction force (decreased SVESV), diastolic function (elevated SVEDP), and whole cardiac loads (elevated NT-proBNP levels). However, there were no differences in internal remedies between Fontan patients with and without Strong AVVR. If we excluded Strong AVVR patients from the whole Fontan patients and compared cardiac functions employing rest patients without Strong AVVR, we obtained no differences in these cardiac indexes between mild AVVR group and no AVVR group. If Fontan patients owned Strong AVVR for years to come, these cardiac overloads would provoke collapse in frail Fontan circulation. We, if possible, should repair Strong AVVR to get up the point of mild AVVR. If we can not do so, we should at least tighten medical treatment.
Hepatic function in patients with AVVR.
Fontan patients with Strong AVVR possessed not only liver congestion (elevation of GGT and T-bil) but also hepatic impairment (ALT elevation) and function deterioration (Alb lowering). If Fontan patients, however, had only mild AVVR, they possessed only GGT elevation. The differences in other indexes which connote hepatic impairment or hepatic function deterioration disappeared between patients with mild AVVR and patients with no AVVR. From the perspective of liver function, we should repair Strong AVVR as soon as possible or we should intensify heart failure therapy.

Conclusion.
Young Fonatn patients with Strong AVVR possessed hepatic disorder as well as cardiac overloads. In case young Fontan patients had only Mild AVVR, they preserved as same cardiac and hepatic functions as those with No AVVR. We should perform Fontan with fenestration, when we predict Strong AVVR would leave after procedure. Otherwise we should attempt to repair Strong AVVR proactively, even if we found their ejection fraction did not fall.