10세 여아, 5세에 Fontan 수술, 좋은 혈역학 상태

- ACE inhibitor를 사용하지 않는다 -

동아대학교 의과대학 소아과학교실

이 영 석

Fontan circulation

SVC, IVC → flows passively to PA

Ventricle (pumps pul venous return to the systemic circ)

- lack of pul vent : pul blood flow – transpul pr grdient
- impaired contractility
- limited preload - abnormal diastolic function
- excessive afterload - systemic vascular resistance↑
- → CO↓
- → exercise capacity ↓ (central hemodynamics)

Reduced exercise capacity

Peripheral hemodynamics

Reduced blood supply of the working skeletal muscle

Attenuated post exercise O_2 resat of skeletal muscle

- impaired endothelium dependent vasodilation

Others

abnormal autonomic nervous system

abnormal ventilation-perfusion ratio

ACE inhibitor

improve clinical status, hemodynamics,

exercise capacity

systemic vascular resistance↓

improve vent diastolic dysfunction

Fontan patients

efficacy?

Pleural effusion

Mainwarning RD. *J Card Surg. 1995* n=40

6pts develop PE - renin↑, angiotensin II ↑

correlation with hosp stay

Thompson LD. *Cardiol Young. 2001* n=36(18:18)

pleural effusion vol↓, duration↓, readmission

Stewart JM. *JTCS. 1991* n=19

ANF↑, vasopressin ↑

Heragu N. *AJC. 1999* n=44

PE duration ↑

Gupta A. *JTCS. 2004* n=100

low preop sat, postop inf, small conduit, long bypass

ACEI-duration PE ↑

Activation of RAA system?

20pts (NYHA Ⅰ - Ⅱ), age 11yrs(4~22), post op 2yrs (0.5~6)

Table 3 Neurohormonal activity

	TCPC (n = 12)	*BDG (n = 8)*	*TCPC+BDG (n = 20)*	*Control (n = 33)*
Angiotensin II (pmol/l)	42 (24 to 109)*	40(14 to 97)*	42 (21 to 106)*	11 (8 to 15)
Renin (μU/ml)	182 (31 to 267)*	82 (39 to 202)*	129 (34 to 256)*	34 (27 to 41)
Aldosterone (pmol/l)	306 (111 to 778)*	111 (83 to 389)	278 (83 to 500)*	67 (56 to 117)
AVP (pmol/l)	1.2 (0.5 to 2.6)	2.2 (1.4 to 3.0)*	1.9 (0.6 to 2.6)*	0.7 (0.5 to 2.5)
ANF (pmol/l)	13 (6 to 17)*	20 (11 to 29)*	15 (9 to 22)*	6 (4 to 8)
BNP (pmol/l)	2.2 (1.8 to 3.4)*	1.6 (1.5 to 2.1)	2.0 (1.5 to 2.6)*	1.2 (1.0 to 1.9)

Inverse correlation between f/u interval and angiotensin Ⅱ, renin

Patients over the age of 15years ; late post-op phase

- normal neurohormone levels

Neurohymoral activation late after cavopulmonary connection. Heart 2000

Enalapril in Fontan patients

N=18 (14.5±6.2 yr, 4~19 yrs after Fontan, NYHA Ⅰ)

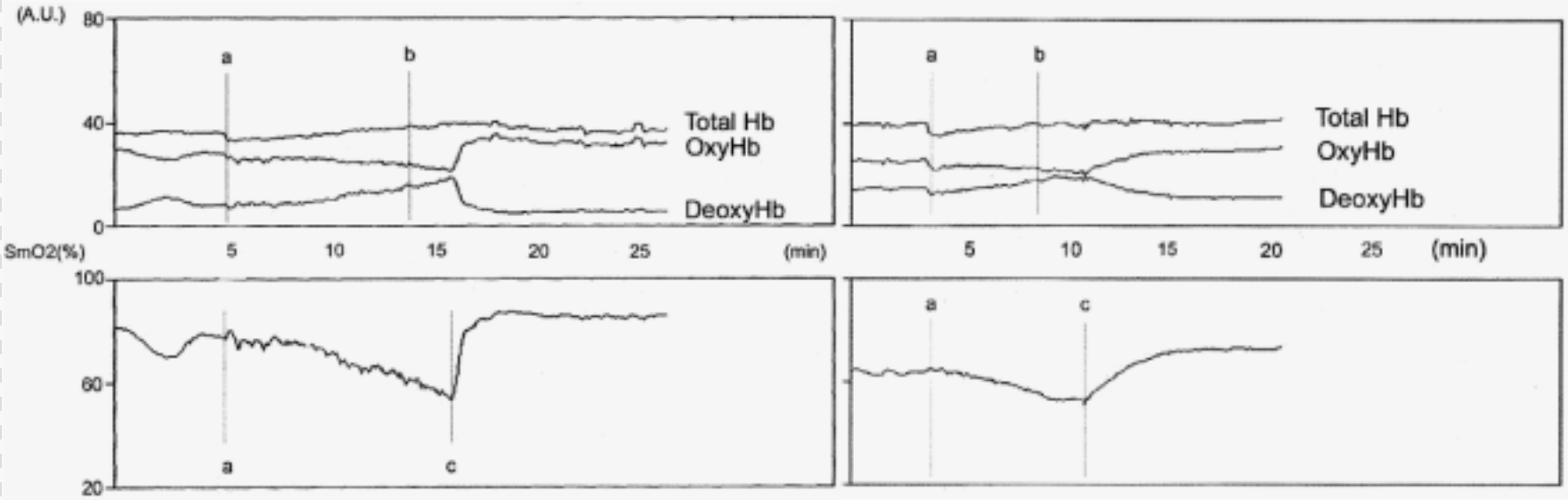
0.2~0.3mg/kg/d, max 15mg, 10weeks

Measurement	Enalapril	Placebo
Peak E velocity	0.73±0.21	0.74±0.26
Peak A velocity	0.55±0.16	0.52±0.18
Peak E/A ratio	1.35±0.31	1.47±0.48
IVRT	71.1±16.2	63.3±9.9

Enalapril does not enhance exercise capacity in patients after Fontan procedure. Circulation 1997

Measurement	Enalapril	Placebo
Heart rate at rest	88.9±13.8	86.9±12.6
Maximum heart rate	156±22	156 ±21
Maximum respiratory rate	52±11	52±9
Maximum systolic BP	135±21	143±16
Maximum diastolic BP	77±12	80±13
Cardiac output at rest	2.3±0.7	2.3±0.6
Maximum cardiac output	4.9±1.6	5.3±1.6
Cardiac index at rest	1.7±0.3	1.7±0.3
Maximum cardiac index	3.5±0.9	3.8±0.9
Cardiac index % change	102±34	125±34
Stroke volume index at rest	19.4±5.4	19.7±4.7
Maximum stroke volume index	23.8±7.3	26.1±7.6
Stroke volume index % change	18±27	28±21
Systemic vasc resist index at rest	37±14	40±9
Max systemic vasc resist index	24±7	21±10
Oxygen consumption at rest	5.3±1	5.2±1
Maximum oxygen consumption	18.3±9	20.5±7

Enalapril does not enhance exercise capacity in patients after Fontan procedure. Circulation 1997



normal **Fontan**

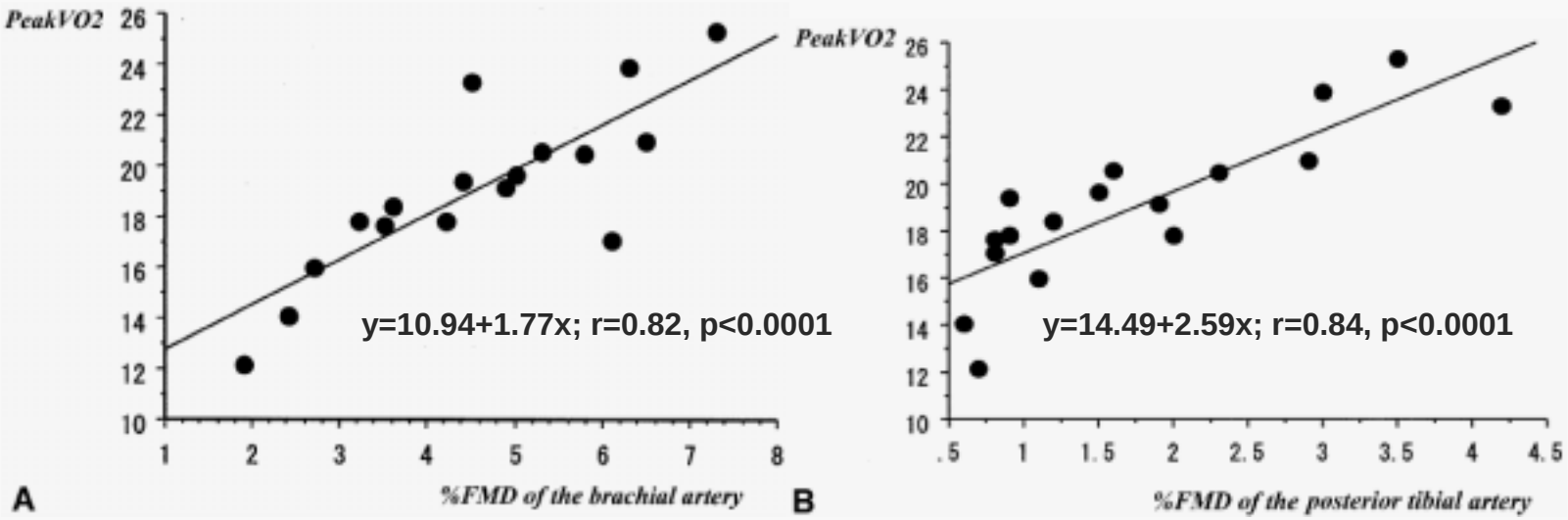
TABLE 4 Comparison of Skeletal Oxygenation During Exercise Using Near-Infrared Spectroscopy

	Fontan Patients (n = 50)	Control Subjects (n = 15)	p Value
Exercise hyperemic reaction (AU) (Δtotal hemoglobin)	4.8 ± 3.8	8.9 ± 4.1	<0.001
Postexercise oxygen resaturation (%)	31.3 ± 15.4	39.9 ± 8.7	<0.01
Muscle oxygen extraction (%)	15.0 ± 9.8	24.7 ± 8.7	<0.001

Skeletal muscle hemodynamics and endothelial fx in pt after Fontan AJC 2004

Flow mediated vasodilation

	Fontan	Control
Brachial a	4.5±1.5%	8.4±2.0%
Post tibial a	1.7±1.3%	6.0±2.0%



Skeletal muscle hemodynamics and endothelial fx in pt after Fontan AJC 2004

Cardiac autonomic nervous activity?

TABLE 2. Comparison of Cardiac Autonomic Nervous Activity Among the Study Groups

	Groups					
Variables	APC	n	TCPC	n	Control	n
Log HF	1.1±0.7‡	18	1.4±0.5‡	45	2.5±0.5	40
Log LF	1.4±0.5‡	18	1.7±0.5‡	45	2.5±0.4	40
BRS, ms/mm Hg	3.1±3.1‡	18	3.2±3.1‡	40	17.1±6.0	44
α, bpm	11±8‡	8	16±12‡	19	48±12	11
H/M	1.6±0.4‡	13	1.8±0.4‡	26	2.9±0.6	14
β, bpm	27±13	8	28±11	19	24±7	11
NE, pg/mL	266±181†	18	229±130*	45	160±72	44

Severely impaired cardiac autonomic nervous activity after Fontan. Circulation 2001

TABLE 4. Change in Cardiac Autonomic Nervous Activity Before and After ACEI Therapy and in Those During Follow-Up Without ACEI Therapy

ACEI Status/Variables	Before	n	After	n	*P*
With ACEI					
Log HF	0.9±0.6	10	1.2±0.4	10	NS
BRS, ms/mm Hg	2.1±1.6	10	2.3±2.1	10	NS
NE, pg/mL	231±137	10	279±268	10	NS
ANP, pg/mL	120±80	10	162±219	10	NS
BNP, pg/mL	139±153	10	159±252	10	NS
Without ACEI					
Log HF	1.2±0.6	8	1.3±0.5	8	NS
BRS, ms/mm Hg	2.6±2.3	8	3.3±1.5	8	NS
NE, pg/mL	173±70	8	299±223	8	NS
ANP, pg/mL	70±39	8	76±49	8	NS
BNP, pg/mL	50±29	8	58±47	8	NS

Severely impaired cardiac autonomic nervous activity after Fontan. Circulation 2001

Medication of ACEI

		N	f/u	%	
JTCS	1997	327	5.4	16.8	no med 37.9%
AJC	2004	36	15	9	Warf 91%
Circ	2003	22	13	27.3	Warf 81.8%
Circ	2004	97	8	8.2	FC Ⅰ-0, Ⅱ-3, Ⅲ-5

Conclusion

1. There is no benefit to use ACE inhibitor to healthy Fontan patients.
2. Decreased exercise capacity depends on many mechanisms.
3. Further study is needed to clarify that ACEI administration benefits the Fontan patients.