

# Factors associated with renal dysfunction in adults with Fontan circulation

Ono H, Hayashi T, Kato H

National Center for Child Health and Development, Tokyo, Japan

## Introduction

- Fontan operation was reported for the first time in 1971. (*Fontan F. Thorax. 1971*)
- Approximately 350 Fontan operations are performed annually in Japan.
- It is not uncommon for adults with Fontan circulation to have multi-organ complications.
- Only a few studies have described the frequency and degree of renal dysfunction in adult Fontan patients.

## Purpose

- To elucidate factors associated with renal function in adult Fontan patients.

## Subject and methods

- We performed a retrospective chart review of 21 adult Fontan patients who had undergone postoperative cardiac catheterization for various indications.
- Renal function was evaluated by calculating estimated glomerular filtration rate (eGFR) based on serum creatinine level.
- Demographic data and laboratory results including platelet counts, serum levels of total bilirubin and gamma-glutamyltranspeptidase( $\gamma$ -GTP), plasma brain natriuretic peptide (BNP) concentration, and arterial oxygen saturation (SaO<sub>2</sub>) were collected.
- The hemodynamic measurements obtained by cardiac catheterization included central venous pressure (CVP), cardiac index (CI), and pulmonary vascular resistance (PVR).
- The correlation between eGFR and the aforementioned parameters was assessed with Pearson's correlation coefficient.
- Mann-Whitney's U test was used to compare eGFR between patient's groups dichotomized by the categorical demographic parameters.

## Results

### Patients' characteristics

- Age: 29.9  $\pm$  7.2 (21~45) years
- Sex: 13 males, 8 females
- Types of Fontan operation:
  - atriapulmonary artery anastomosis (APC) : 4 patients
  - extracardiac conduit : 8 patients (including 4 converted from APC)
  - lateral tunnel : 9 patients
- NYHA functional class: I<sup>o</sup> 19 patients, II<sup>o</sup> 1 patient, III<sup>o</sup> 1 patient
- Arrhythmia : 5 patients
- Patients treated with ACE inhibitor or ARB : 14 patients
- eGFR: 94.6  $\pm$  17.6 (62.9~137.9) ml/min/1.73m<sup>2</sup>
- Patients with renal dysfunction (eGFR < 90 ml/min/1.73m<sup>2</sup>): 9 patients (43%)

Renal dysfunction is mild and rarely symptomatic in adults with Fontan circulation.

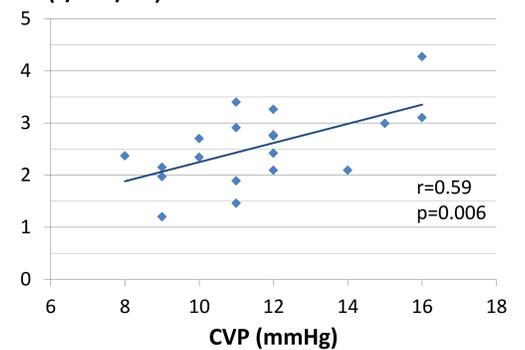
### Comparison of eGFR between patient's groups dichotomized by the categorical parameters

Categorical Variables	eGFR (ml/min/1.73m <sup>2</sup> )		p value
Sex	Male (n = 13) 90.2 $\pm$ 14.0	Females (n = 8) 101.6 $\pm$ 20.4	0.29
Types of Fontan operation	APC (n = 4) 93.8 $\pm$ 19.5	Other than APC (n = 17) 94.7 $\pm$ 17.1	0.89
NYHA functional class	Class I (n = 19) 96.2 $\pm$ 16.9	Class 2 or more (n = 2) 78.6 $\pm$ 15.7	0.25
Arrhythmia	Arrhythmia (n = 5) 87.2 $\pm$ 17.0	Without arrhythmia (n = 16) 96.8 $\pm$ 17.1	0.39
Medication	Treated with ACE inhibitor or ARB (n = 14) 97.4 $\pm$ 20.2	Without medication of ACE inhibitor nor ARB (n = 7) 88.9 $\pm$ 8.2	0.41

### Correlation between eGFR and the numerical parameters

Numerical parameters	Measurements	Univariate analysis		Multivariate analysis		
		Correlation coefficient (r)	P value	$\beta$	Standard error	P value
Age (years)	29.9 $\pm$ 7.2	-0.513	0.017	-0.02	0.67	0.976
Age at the initial Fontan operation (years)	8.9 $\pm$ 5.1	-0.151	0.068			
Time interval since Fontan operation (years)	20.3 $\pm$ 4.5	-0.548	0.010	-1.59	0.94	0.106
Platelet counts ( $\times 10^9/L$ )	140 $\pm$ 37	0.670	0.763			
Total bilirubin (mg/dL)	1.1 $\pm$ 0.5	-0.397	0.075			
$\gamma$ GTP (U/mL)	120.5 $\pm$ 98.3	-0.173	0.454			
BNP (pg/mL)	67.8 $\pm$ 142.6	-0.400	0.072			
SpO <sub>2</sub> (%)	92.1 $\pm$ 3.6	-0.258	0.258			
Ejection fraction (%)	50.5 $\pm$ 9.1	0.131	0.572			
CVP (mmHg)	11.6 $\pm$ 2.2	0.563	0.008	1.13	1.70	0.515
CI (L/min/m <sup>2</sup> )	2.5 $\pm$ 0.7	0.605	0.004	12.56	5.65	0.039
Rp (Wood U $\cdot$ m <sup>2</sup> )	1.9 $\pm$ 1.0	-0.122	0.600			

### CI (L/min/m<sup>2</sup>)



Cardiac index (CI) is the sole parameter that independently correlate with eGFR in adult Fontan patients.

## Discussion

### Common abdominal organ complications of Fontan circulation

- Protein losing enteropathy
- Cirrhosis, hepatocellular carcinoma
- Hypersplenism (thrombocytopenia)

### Pathophysiology of complications of Fontan circulation

#### <Cardiac problems>

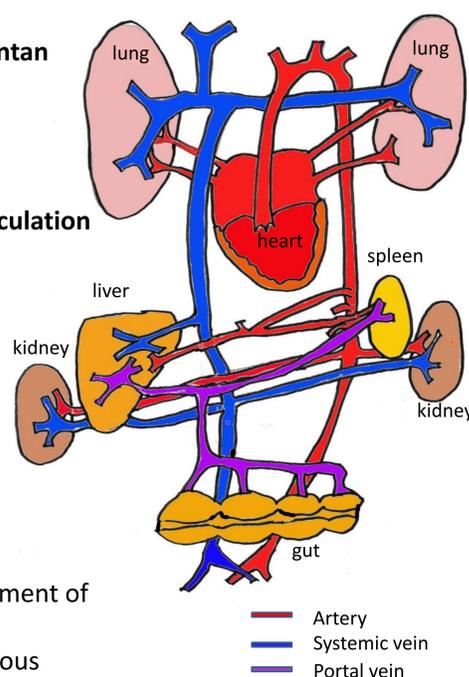
- Arrhythmia
- Atrioventricular valve regurgitation
- Systemic ventricle failure
- History of multiple operation

#### <Hemodynamic problems inherent in Fontan circulation>

- Pulseless pulmonary arterial blood flow
- Elevated venous pressure
- Low oxygenation

⇒ All of these factors contribute to the development of end-organ dysfunction in Fontan circulation.

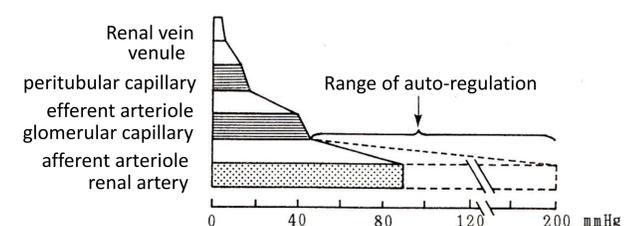
⇒ Especially, elevated infracardiac systemic venous pressure and portal venous pressure leads to a decreased perfusion pressure of the gastrointestinal system, the liver, and the spleen (normal portal vein pressure is below 15mmHg).



— Artery  
— Systemic vein  
— Portal vein

### Why renal dysfunction is mild and rarely symptomatic in Fontan patients in contrast to liver dysfunction?

- All of the blood perfusing the kidneys passes through the glomeruli, where it is subject to filtration and urine is produced. Pressure gradient across a glomerulus affects the amount of urine produced.
- Blood pressure in glomerular capillary and efferent arteriole is approximately 45 mmHg, which is much higher than that in all other capillary beds in the human body.
- Therefore, an elevation of renal venous pressure by 5~10 mmHg as a result of Fontan circulation would minimally impair glomerular filtration.
- Our study demonstrated that eGFR correlates with cardiac index (CI) but not with a elevation of CVP in adult Fontan patients, highlighting that a high blood flow is necessary for glomerular filtration.



## Conclusions

- In contrast to liver dysfunction which is common in adult Fontan patients, renal dysfunction is mild, if any, and rarely symptomatic.
- Cardiac index (CI), but not a elevation of central venous pressure (CVP), is an independent factor that affects eGFR in adult Fontan patients.
- The degree of renal dysfunction is associated with hemodynamic integrity of Fontan circulation that is reflected in CI, which highlights that a high blood flow is essential for glomerular filtration.
- Since blood pressure in glomerular capillary is much higher than other capillary beds in the human body, an elevation of renal venous pressure in Fontan circulation would only minimally impair renal function.