

資料 9 : Fontan 術後に代表される先天性心疾患術後患者の心機能および循環動態 (大内秀雄)

Clinical Investigations

Determinants and prognostic value of albuminuria in adult patients with congenital heart disease



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Background The determinants and prognostic value of albuminuria remain unclear in patients with adult congenital heart disease (ACHD), especially in those with Fontan circulation (FC).

Methods We retrospectively reviewed 512 consecutive ACHD patients and investigated the determinants of urinary albumin-to-creatinine ratio (ACR) and albuminuria (MAU) and their association with all-cause mortality. Demographic data and laboratory and hemodynamic parameters were collected. Regression analysis and Cox proportional hazard models were used to identify the relationship between log ACR and variables, and clinical factors and all-cause mortality, respectively.

Results Body mass index, aortic systolic blood pressure (ASP), arterial oxygen saturation (SaO₂), glycated hemoglobin (HbA1c), B-type natriuretic peptide, and diuretic use were independently associated with log ACR. ASP, SaO₂, and HbA1c were independently associated with MAU ($P < .05$ -.0001). The prevalence of MAU was highest in unrepaired patients with low SaO₂ (50%; $P < .0001$). Log ACR and MAU were associated with exercise capacity and all-cause mortality ($P < .0001$ for both) independent of renal function. Patients with ACHD, MAU, and renal dysfunction ($n = 23$) had the highest risk of all-cause mortality, while those without MAU or renal dysfunction had the lowest risk ($P < .0001$). These prognostic values remained significant in separate analyses of Fontan and biventricular circulation ($P < .0001$).

Conclusions ASP, SaO₂, and HbA1c levels were independently associated with MAU in ACHD patients. MAU and log ACR were associated with all-cause mortality in patients with Fontan and biventricular circulation, independent of renal dysfunction. (*Am Heart J* 2023;263:15–25.)

Multiorgan interactions in heart failure pathophysiology have been highlighted. One typical pathophysiology is cardio-renal interaction in adults with congenital heart disease (ACHD).¹ Renal function is evaluated using both the estimated glomerular filtration rate (eGFR)

and the presence of albuminuria. In many diseases, such as hypertension, chronic kidney disease, and diabetes mellitus, as well as the general population,² albuminuria is associated with poor prognosis in a variety of diseases.^{3,4} Although cyanotic nephropathy has been recognized as a cause of albuminuria in patients with hypoxic ACHD,⁵ its clinical relevance in terms of its prognostic value of mortality has not been studied in a variety of ACHD patients, including patients with Fontan circulation (FC).^{6,7} There is a significant prognostic association between albuminuria and ACHD with biventricular circulation (BVC), whereas the association between albuminuria and adverse outcomes in FC patients has not been well studied.⁶ To this end, this study aimed to: (1) reconfirm the high prevalence of albuminuria by using the urine albumin-creatinine ratio (ACR) and identify the determinant factors in ACHD based on the hemodynamics; (2) establish the association of albuminuria with all-cause mortality in our large cohort of ACHD patients, and to identify differences in the prognostic values for all-cause mortality between those with FC and BVC.

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Abbreviation: ACHD, adult congenital heart disease; ACR, urinary albumin-to-creatinine ratio; ASP, aortic systolic blood pressure; BNP, B-type natriuretic peptide; BVC, biventricular circulation; Cr, 24-hour creatinine clearance; CVP, central venous pressure; GFR, glomerular filtration rate; eGFR, estimated glomerular filtration rate; eGFR_{cre}, estimated glomerular filtration rate using the Japanese cystatin C-based equation; FC, Fontan circulation; HbA1c, glycated hemoglobin; MAU, microalbuminuria and macroalbuminuria; MELD-XI, model for end-stage liver disease excluding international normalized ratio; ROC, receiver operator characteristic; SaO₂, arterial oxygen saturation.

Submitted December 16, 2022; accepted April 30, 2023

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0002-8703

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<https://doi.org/10.1016/j.ahj.2023.04.017>

Prevalence and clinical correlates and characteristics of “Super Fontan”

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Background Super-Fontan (SF) is an excellent phenotype of patients with Fontan circulation and normal exercise capacity. This study aimed to clarify the prevalence and clinical correlates and characteristics of SF.

Methods We reviewed 404 Fontan patients who had undergone cardiopulmonary exercise testing, and the results were compared with clinical profiles.

Results Seventy-seven (19%) patients had SF, and the postoperative prevalence at 5, 10, 15, 20, and ≥ 25 years was 16 (35%), 30 (39%), 18 (19%), 13 (14%), and 0 (0%), respectively. Compared with non-SF, SF patients were younger ($P < .001$) and were mostly men ($P < .05$). SF was characterized by a current high arterial blood pressure and oxygen saturation (SaO_2), low systemic ventricle (SV) end-diastolic pressure, favorable body composition, superior pulmonary function, preserved hepatorenal and hemostatic functions, and better glucose tolerance ($P < .05$ -.001). Pre-Fontan better SV function, low pulmonary artery resistance, and high SaO_2 were associated with current SF ($P < .05$ -.01). Furthermore, positive trajectory of exercise capacity and high daily activity during childhood were associated with current adult SF ($P < .05$). During the follow-up, 25 patients died, and 74 patients were unexpectedly hospitalized. There was no death in the SF group, and the rate of hospitalization was 67% lower than that of the non-SF group ($P < .01$ -.001).

Conclusions The prevalence of SF gradually decreased over time. SF was characterized by preserved multi-end-organ function and an excellent prognosis. Pre-Fontan hemodynamics and post-Fontan childhood daily activity were associated with being adult SF. (Am Heart J 2023;263:93–103.)

Patients with Fontan circulation exhibit lower exercise capacity than their normal healthy peers, which is strongly associated with high morbidity and mortality.¹ Thus, exercise training could be one of the therapeutic strategies, and several studies with exercise interventions have been conducted and the beneficial effect of improving exercise capacity has been demonstrated.² On the other hand, Fontan patients with normal exercise capacity ($\geq 80\%$ predicted normal value) have been defined as “Super-Fontan (SF)”³; they are an excellent clinical phenotype that should be the optimal therapeutic target in our practice.

Several studies have investigated the clinical characteristics of SF patients.^{3–6} These studies have found that SF has a prevalence of 10% to 20%, and that patients are typ-

ically young, non-obese, have an active daily life, a better hepatic function, and no history of hospitalization. However, to date, no studies have comprehensively clarified the clinical characteristics of SF, including the hemodynamics and multi-end-organ function. Furthermore, there is no data on the significance of pre-Fontan hemodynamics and past history of daily physical activity during childhood⁷ in predicting adult SF outcomes.

Accordingly, the aim of our study was to clarify the following clinical characteristics of SF in terms of the cross-sectional and longitudinal aspects: (1) prevalence of SF, (2) associations of current SF status with current hemodynamics and pre-Fontan hemodynamics, current multi-end-organ function, trajectory of exercise capacity,⁷ and daily physical activity during childhood determined in our previous study.⁸ Our findings could provide detailed clinical profiles of SF and useful information for establishing a better management strategy for these patients.

Methods

Subjects

We retrospectively reviewed 414 Fontan patients who had undergone cardiopulmonary exercise testing (CPX) between April 2005 and October 2021 in our hospital.

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Submitted December 17, 2022; accepted May 15, 2023

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0002-8703

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<https://doi.org/10.1016/j.ahj.2023.05.010>



Pulmonary Arteriovenous Fistulae After Fontan Operation: Incidence, Clinical Characteristics, and Impact on All-Cause Mortality

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OPEN ACCESS

Edited by:

Matthias Sigler,
University of Göttingen, Germany

Reviewed by:

Gianfranco Butera,
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(IRCCS), Italy
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Erasmus University Rotterdam,
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Specialty section:

This article was submitted to
Pediatric Cardiology,
a section of the journal
Frontiers in Pediatrics

Received: 22 May 2021

Accepted: 28 February 2022

Published: 09 June 2022

Citation:

Ohuchi H, Mori A, Nakai M,
Fujimoto K, Iwasa T, Sakaguchi H,
Kurosaki K and Shiraishi I (2022)
Pulmonary Arteriovenous Fistulae
After Fontan Operation: Incidence,
Clinical Characteristics, and Impact
on All-Cause Mortality.
Front. Pediatr. 10:713219.
doi: 10.3389/fped.2022.713219

Background: The Fontan operation is a surgical procedure used in children with univentricular hearts. Pulmonary arteriovenous fistulae (PAVF) is a major complication after a Fontan operation. However, the incidence and related clinical pathophysiology of PAVF remain unclear.

Purpose: This study aimed to clarify the incidence of PAVF, its clinical characteristics, and its influence on all-cause mortality.

Methods and Results: We serially assessed the presence of PAVF using pulmonary artery angiography and/or contrast echocardiography during catheterization in 391 consecutive patients who underwent the Fontan procedure and compared the results with the Fontan pathophysiology and all-cause mortality. PAVF developed in 36 patients (9.2%), including 30 diffuse- and six discrete-PAVF types. The PAVF-free rates at 1, 5, 10, 15, 20, and ≥ 25 years after Fontan operation were 97, 96, 93, 88, 87, and 83%, respectively. The mean arterial blood oxygen saturation (SaO_2) in patients with diffuse PAVF at each corresponding postoperative stage were 90, 91, 91, 91, 89, and 88%, respectively, indicating lower SaO_2 levels than those in patients without PAVF (all $p < 0.01$). However, there was no difference in the SaO_2 levels between patients with discrete PAVF and those without PAVF. During a median follow-up period of 2.9 years after the last catheterization, 31 patients, including 12 patients with PAVF, died. Patients with PAVF, especially those with diffuse PAVF, had a higher mortality rate ($p = 0.01$) than those without PAVF (hazard ratio: 3.6, 95% confidence interval: 1.6–7.8, $p = 0.0026$).

Conclusion: Patients who underwent Fontan surgery had an increased incidence of PAVF as they aged. Discrete PAVF did not influence SaO_2 or mortality, whereas the presence of diffuse PAVF caused hypoxia and was associated with all-cause mortality.

Keywords: Fontan operation, pulmonary arteriovenous fistulae, arterial oxygen saturation, heart failure, mortality