Blood Pressure in Adults with Congenital Heart Disease

Tomoaki Murakami¹, Yoko Horibata², Shigeru Tateno², Yasutaka Kawasoe² and Koichiro Niwa³

Abstract:

Background: We previously reported enhanced pressure wave reflection in adult patients with congenital heart disease, which can result in high systolic blood pressure. Although hypertension could cause significant damage to vulnerable systemic ventricles, few studies have reported on blood pressure in adults with congenital heart disease thus far. The purpose of this study was to investigate the incidence and risk factors associated with hypertension in adult patients with congenital heart disease.

Methods and Results: One-hundred and thirty-one adults with congenital heart disease were enrolled in this study. Brachial blood pressure was measured using an HEM-9000AI system (Omron Healthcare Co., Ltd., Kyoto, Japan). Patients with systolic/diastolic blood pressure ≥140/90 mmHg or those taking medication for hypertension were defined as hypertension. A systolic blood pressure ≥ +2 SD of systolic blood pressure in the age- and sex-matched general population was defined as high systolic blood pressure. The patients were aged 37.0 ± 15.0 years. Hypertension was observed in sixteen patients (16%), and logistic regression analysis revealed that the determinant of hypertension was age (years) (odds ratio [OR], 1.078; 95% confidence interval [CI], 1.029-1.129; p = 0.001). High systolic blood pressure was observed in twenty patients (20%). Logistic regression analysis revealed that the determinants of high systolic blood pressure were age (years) (OR, 1.072; 95% CI, 1.020-1.126; p = 0.016) and body mass index (kg/m²) (OR, 1.261; 95% CI, 1.054-1.508; p = 0.011). The body mass index in young patients (<30 years) with high systolic blood pressure was remarkably high (31.2 ± 3.0 kg/m²).

Conclusions: The incidence of high systolic blood pressure is high in adult patients with congenital heart disease. High systolic blood pressure is common in older patients and is associated with a high body mass index in young patients.

Key words: Hypertension, Body mass index, Cardiovascular disease, Congenital heart disease

Introduction

Systemic blood pressure gradually increases with age, and high blood pressure can cause potentially fatal conditions, such as ischemic heart disease and cerebral vascular disease. Owing to advances in surgical procedures and medical treatments, patients with congenital heart disease have a long life expectancy³. Since their hearts have been overloaded in some form or other since birth, their hearts are vulnerable to the effects of high blood pressure; however, few studies have reported on hypertension in adults with congenital heart disease.

We previously reported that pressure wave reflection is enhanced in adults with congenital heart disease². The enhancement of aortic pressure wave reflection elevates systolic blood pressure and is a well-known risk factor for cardiovascular diseases⁴. The prevalence of hypertension in pediatric patients who have had cardiac surgery was ten times higher than that of the general pediatric population⁵. However, patients with hypertension are scarce in the adult congenital heart disease clinic. One reason for this is that adult patients with congenital heart disease are generally still young. Therefore, the criteria for hypertension in the guidelines for the management of hypertension may not be able to identify patients with high blood pressure; it is possible that some patients had high blood pressure at the time of the study but had not yet been diagnosed with hypertension.

The purpose of this study was to clarify the incidence and

¹) Department of Pediatrics, Sapporo Tokushukai Hospital
²) Department of Adult Congenital Heart Disease, Chiba Cardiovascular Center
³) Department of Cardiology, St. Luke’s International Hospital
Corresponding author: Tomoaki Murakami, MD, murat@seagreen.ocn.ne.jp
Received: April 30, 2020, Accepted: March 24, 2021
Copyright © 2021 Japan Society for Vascular Failure
risk factors associated with high systolic blood pressure (≥ 2 SD of systolic blood pressure in age- and sex-matched general population) in adults with congenital heart disease.

**Material and Methods**

**Patients**

We enrolled 131 consecutive subjects aged ≥20 years who visited the Department of Adult Congenital Heart Disease, Chiba Cardiovascular Center. The exclusion criteria were as follows: (1) a history of atrial fibrillation or frequent supraventricular or ventricular premature beats for which accurate radial pressure waveforms could not be obtained by the system and (2) history of cardiac operation in the past 6 months. The brachial systolic blood pressure was measured twice, at 1- to 2-minute intervals, and we enrolled patients whose difference in brachial blood pressure was ≤ 5 mmHg. Patients with aortic tree obstruction were excluded, as were those with an ankle brachial pressure index of < 0.95. The systolic blood pressure ratio between the patients’ upper arms and ankles was also measured bilaterally using an ABI Form device (Omron Healthcare Co., Ltd., Kyoto, Japan) to confirm the patency of the artery and rule out obstruction of the aortic tree. One hundred patients who met the inclusion criteria were enrolled in this study (male, n = 63; mean age, 37.0 ± 15.0 years; range, 20-76 years). This study was conducted in accordance with the principles of the Declaration of Helsinki. All subjects provided informed consent, and the Ethics Committee of Chiba Cardiovascular Center approved the study protocol.

**Demographic characteristics**

To assess basic congenital heart diseases and comorbidities, data regarding the diagnosis of congenital heart diseases, history of surgery, New York Heart Association class, hypoxia status (SpO2 < 90%), cardiothoracic ratio on chest X-ray, medications, body mass index, and current smoking status were obtained from the patients’ medical records. The brachial blood pressure and radial pressure waveforms were recorded. Central systolic blood pressure was measured using an automated tonometric system (HEM-9000AI; Omron Healthcare Co., Ltd., Kyoto, Japan) after participants were seated on a chair for >5 min with their arms supported at heart level in an air-conditioned room. We used the brachial artery originating from the first branch of the aortic arch to measure brachial blood pressure. Patients with a systolic blood pressure of ≥ 140 mmHg and/or a diastolic pressure of ≥ 90 mmHg were defined as hypertensive. Patients who were prescribed antihypertensive drugs for the management of hypertension were also defined as hypertensive. All patients with hypertension met the criteria for hypertension at their previous visit 1-3 months prior. Patients whose systolic blood pressures over 2 or more SDs above those of the patients in the age- and sex-matched general population were considered to have high systolic blood pressure. The brachial blood pressure was measured, and central blood pressure was estimated using the HEM-9000 AI system, as previously reported by Takase et al. Given that the current study predominantly included young patients and the fact that isolated systolic hypertension in young patients can influence their brachial blood pressure, we measured the patients’ central systolic blood pressures and compared them with those of the general population.

**Biochemical analysis**

Peripheral blood was drawn after fasting for analysis of serum creatinine, total cholesterol, high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, triglycerides, hemoglobin A1c, and brain natriuretic peptide levels.

**Statistical analysis**

Quantitative variables are presented as mean ± SD. The Mann-Whitney test was used to analyze quantitative variables and the chi-square test was used to analyze qualitative variables. The relationship between hypertension or high systolic blood pressure and various clinical variables was analyzed to clarify whether the variables influenced blood pressure. Logistic regression analyses were performed following univariate analyses between hypertension or high systolic blood pressure and each variable. Because hypertension and high systolic blood pressure were strongly associated with patient age in this study, the participants were stratified into quartiles (Q) by age; with this approach, the youngest patients were assigned to Q1 and the oldest to Q4. Clinical and biochemical variables were compared between quartiles, and data were analyzed using one-way analysis of variance followed by Tukey’s multiple comparison test. Variables with p-values ≥ 0.05, as determined by univariate analyses, were excluded from the analysis. All statistical analyses were performed using SPSS 16.0J (SPSS Inc., Chicago, IL); p-values <0.05 were considered significant.

**Results**

Table 1 shows the demographic and clinical characteristics of the included patients. Although almost half of the patients were prescribed antihypertensive drugs (renin-angiotensin-aldosterone system blockers, beta blockers, diuretics and calcium antagonists), the medications were predominantly intended to treat heart failure and not hypertension (only four cases received treatment for hypertension). All diuretics used in this study were loop diuretics. Table 2 shows the basic diagnoses of several types of congenital heart diseases. The brachial systolic and diastolic blood pressures were 117.7 ± 20.1 mmHg and 69.7 ± 14.3 mmHg, respectively. The central systolic blood pressure was 119.9 ± 21.5 mmHg.

Hypertension was observed in 16 patients (16%). Table 3 shows the comparison of clinical and laboratory variables between patients with and without hypertension. Using univariate analyses, hypertension was associated with age and
Other one patient was 116 mmHg. The central systolic blood pressure of two patients was over +1 SD and that of the other one patient, the central systolic blood pressure was 116 mmHg, although his brachial systolic blood pressure was 146 mmHg. Because his brachial pulse pressure was wide (80 mmHg), his high systolic blood pressure could be due to the pulse pressure amplification. Therefore, our data suggest that brachial systolic blood pressure can be overestimated in young patients due to pulse pressure amplification.

The variables for each age quartile are presented in Table 7. The prevalence of high systolic blood pressure in Q4 was significantly higher than in Q1-3, although high systolic blood pressure was defined as systolic blood pressure ≥ +2 SD of that in the age- and sex-matched general population. In Q1 and Q2, among patients ≤30 years, the body mass index of patients with high systolic blood pressure was remarkably high (31.2 ± 3.0 kg/m² vs. 22.5 ± 2.5 kg/m² in patients aged > 30 years with high systolic blood pressure).

### Discussion

This study demonstrated that high systolic blood pressure was common in adults with congenital heart disease (20%) because the high systolic blood pressure was defined as ≥ +2 SD (i.e., 2.3%) of that in the age- and sex-matched general population. Although one would expect fewer than three patients to have high systolic blood pressure in the present study, 20 patients were diagnosed with high systolic blood pressure. The prevalence is similar to that of hypertension in children after cardiac surgery (17%)\(^9\). This is understandable because the criteria for hypertension in children are defined as over the 95th percentile of the age-, sex-, and height-matched general population\(^9\). Considering that almost half of our patients had prescriptions for antihypertensive drugs, high systolic blood pressure was expected to be common in adults with congenital heart disease. However, it is difficult to recognize high systolic blood pressure in adults with congenital heart disease because patients with high systolic blood pressure do not necessarily meet the criteria for hypertension in the current guidelines. This may be because the majority of the patients in this study were young.

It has been reported that brachial systolic blood pressure can be overestimated in young patients due to pulse pressure amplification\(^7\). Most adults with congenital heart disease are still young; the age of our cohort was 37.0 ± 15.0 years. Therefore, we measured the central systolic blood pressure\(^8\). Among the 20 patients with high brachial systolic blood pressure, 17 of the patients also demonstrated high central systolic blood pressure of two patients in the other three patients was over +1 SD. Concerning the other one patient, the central systolic blood pressure was 116 mmHg, although his brachial systolic blood pressure was 146 mmHg. Because his brachial pulse pressure was wide (80 mmHg), his high brachial systolic blood pressure could be due to the pulse pressure amplification\(^7\). Therefore, our data suggest that high systolic blood pressure is common in adult patients with congenital heart disease. Moreover, the fact that the patients in this study not only had high brachial systolic blood pressure but also high central systolic blood pressure is significant given that central systolic blood pressure is more valuable compared to other blood pressure variables in predicting cardiovascular mortality\(^8-11\).

Logistic regression analysis of risk factors for high systolic blood pressure showed that age is a risk factor for high systolic blood pressure.

### Table 1. Demographic and clinical characteristics of participants

| Age (years) | 37.0 ± 15.0 |
| Sex (male/female) | 63/37 |
| Height (cm) | 164.0 ± 10.2 |
| Weight (kg) | 60.6 ± 14.2 |
| Body mass index (kg/m²) | 22.4 ± 4.2 |
| Current smokers | 9 (9%) |
| NYHA (I/II/III/IV) | 68/25/7/0 |
| CTR (%) | 52.5 ± 6.7 |
| BNP (pg/ml) | 69.2 ± 151.0 |
| Cyanosis | 18 (18%) |
| Open heart surgery | 77 (77%) |

Values are presented as mean ± standard deviation. BNP: Brain natriuretic peptide, CTR: Cardiothoracic ratio, RAAS: Renin-angiotensin-aldosterone system

### Table 2. Underlying Congenital Heart Disease Diagnoses

| Diagnosis | n = 100 |
| --- | --- |
| Tetralogy of Fallot | 25 |
| Single ventricle | 12 |
| Ventricular septal defect | 10 |
| Atrial septal defect | 10 |
| Aortic coarctation/interruption of the aortic arch | 8 |
| Complete transposition of the great arteries | 8 |
| Ebstein’s anomaly | 8 |
| Congenitally corrected transposition of the great arteries | 5 |
| Tricuspid atresia | 5 |
| Others | 9 |

### Table 4. Logistic regression analysis of risk factors for high systolic blood pressure

| Medication | Odds ratio (OR) | 95% confidence interval (CI) | p-value |
| --- | --- | --- | --- |
| RAAS inhibitors | 1.261 | 1.029-1.129 | 0.001 |
| Beta blockers | 1.156 | 1.001-1.329 | 0.053 |
| Diuretics | 1.115 | 0.973-1.278 | 0.167 |

Logistic regression analysis showed that the determinant of hypertension was age (years) (odds ratio [OR], 1.078; 95% confidence interval [CI], 1.029-1.129; p = 0.001) (Table 4). Considering that almost half of our patients had prescriptions for antihypertensive drugs, high systolic blood pressure was expected to be common in adults with congenital heart disease. However, it is difficult to recognize high systolic blood pressure in adults with congenital heart disease because patients with high systolic blood pressure do not necessarily meet the criteria for hypertension in the current guidelines. This may be because the majority of the patients in this study were young.

It has been reported that brachial systolic blood pressure can be overestimated in young patients due to pulse pressure amplification. Most adults with congenital heart disease are still young; the age of our cohort was 37.0 ± 15.0 years. Therefore, we measured the central systolic blood pressure. Among the 20 patients with high brachial systolic blood pressure, 17 of the patients also demonstrated high central systolic blood pressure of two patients in the other three patients was over +1 SD. Concerning the other one patient, the central systolic blood pressure was 116 mmHg, although his brachial systolic blood pressure was 146 mmHg. Because his brachial pulse pressure was wide (80 mmHg), his high brachial systolic blood pressure could be due to the pulse pressure amplification. Therefore, our data suggest that high systolic blood pressure is common in adult patients with congenital heart disease. Moreover, the fact that the patients in this study not only had high brachial systolic blood pressure but also high central systolic blood pressure is significant given that central systolic blood pressure is more valuable compared to other blood pressure variables in predicting cardiovascular mortality.

Logistic regression analysis of risk factors for high systolic blood pressure showed that age is a risk factor for high systolic blood pressure.

BP in Adults with Congenital Heart Disease

Vascular Failure 2021; 4(2): 39-45
Table 3. Comparison of the Clinical and Biochemical Variables Between Patients with and without Hypertension

| Variables                          | Hypertension (+) (n = 16) | Hypertension (-) (n = 84) | p-value |
|-----------------------------------|---------------------------|---------------------------|---------|
| Brachial SBP (mmHg)               | 153.6 ± 15.2              | 111.0 ± 11.9              | <0.001  |
| Brachial DBP (mmHg)               | 90.1 ± 13.4               | 65.9 ± 10.7               | <0.001  |
| Age (years)                       | 50.1 ± 15.9               | 33.5 ± 12.5               | <0.001  |
| Sex (male/female)                 | 12/4                      | 51/33                     | 0.399   |
| Body mass index (kg/m²)           | 23.6 ± 4.3                | 22.2 ± 4.2                | 0.236   |
| Current smokers                   | 1 (6.3%)                  | 8 (9.5%)                  | 1.000   |
| Simple CHD                        | 6 (37.5%)                 | 15 (17.9%)                | 0.077   |
| Cyanosis                          | 0 (0%)                    | 18 (21.4%)                | 0.041   |
| Fontan circulation                | 0 (0%)                    | 14 (16.7%)                | 0.078   |
| History of open-heart surgery     | 11 (68.8%)                | 66 (78.6%)                | 0.392   |
| History of aortic surgery         | 1 (6.3%)                  | 9 (10.7%)                 | 0.585   |
| BNP (pg/mL)                       | 32.7 ± 31.9               | 76.7 ± 164.2              | 0.112   |
| Hemoglobin A1c (%)                | 5.4 ± 0.8                 | 5.1 ± 0.4                 | 0.118   |
| Chronic kidney disease            | 7 (43.8%)                 | 23 (27.4%)                | 0.236   |
| Total cholesterol (mg/dL)         | 210.3 ± 44.9              | 166.4 ± 35.8              | <0.001  |
| Low density lipoprotein           | 126.3 ± 33.4              | 96.1 ± 30.7               | 0.001   |
| High density lipoprotein          | 53.9 ± 22.8               | 49.9 ± 12.4               | 0.815   |
| Triglyceride (mg/dL)              | 190.5 ± 107.5             | 123.0 ± 90.1              | 0.005   |
| Drugs with antihypertensive action| 7 (43.8%)                 | 42 (50.0%)                | 0.787   |
| RAAS inhibitors                   | 5 (31.3%)                 | 30 (35.7%)                | 1.000   |
| Beta blockers                     | 2 (12.5%)                 | 28 (33.3%)                | 0.138   |
| Diuretics                         | 2 (12.5%)                 | 17 (20.2%)                | 0.730   |
| Calcium antagonists               | 2 (12.5%)                 | 0 (0%)                    | 0.001   |

Values are presented as mean ± standard deviation. BNP: Brain natriuretic peptide, CHD: Congenital heart disease, DBP: Diastolic blood pressure, RAAS: Renin-angiotensin-aldosterone system, SBP: Systolic blood pressure.

Table 4. Univariate and Multivariate Analysis of Factors Associated with Hypertension

| Variables                          | Univariate Odds ratio | 95% CI           | p-value | Multivariate Odds ratio | 95% CI           | p-value |
|-----------------------------------|-----------------------|------------------|---------|-------------------------|------------------|---------|
| Age (years)                       | 1.088                 | (1.045–1.132)    | <0.001  | 1.078                   | (1.029–1.129)    | 0.001   |
| Sex (male)                        | 1.941                 | (0.577–6.532)    | 0.284   |                         |                  |         |
| Body mass index (kg/m²)           | 1.074                 | (0.955–1.208)    | 0.234   |                         |                  |         |
| Current smokers                   | 0.633                 | (0.074–5.444)    | 0.677   |                         |                  |         |
| Simple CHD                        | 1.932                 | (0.589–6.345)    | 0.190   |                         |                  |         |
| Cyanosis                          | -                     | -                | -       |                         |                  |         |
| Fontan circulation                | -                     | -                | -       |                         |                  |         |
| History of open-heart surgery     | 0.600                 | (0.185–1.950)    | 0.396   |                         |                  |         |
| History of aortic surgery         | 0.548                 | (0.065–4.655)    | 0.582   |                         |                  |         |
| BNP (pg/mL)                       | 0.991                 | (0.975–1.007)    | 0.248   |                         |                  |         |
| Hemoglobin A1c (%)                | 3.453                 | (1.058–11.263)   | 0.040   | 2.144                   | (0.585–7.859)    | 0.250   |
| Chronic kidney disease            | 2.063                 | (0.688–6.185)    | 0.196   |                         |                  |         |
| Total cholesterol (mg/dL)         | 1.029                 | (1.012–1.046)    | 0.001   | 1.027                   | (0.987–1.069)    | 0.191   |
| Low density lipoprotein           | 1.028                 | (1.028–1.046)    | 0.003   | 0.990                   | (0.949–1.034)    | 0.662   |
| High density lipoprotein          | 1.018                 | (0.983–1.054)    | 0.330   |                         |                  |         |
| Triglyceride (mg/dL)              | 1.006                 | (1.001–1.011)    | 0.021   | 1.003                   | (0.996–1.010)    | 0.383   |
| Drugs with antihypertensive action| 0.600                 | (0.200–1.800)    | 0.362   |                         |                  |         |
| RAAS inhibitors                   | 0.818                 | (0.260–2.577)    | 0.732   |                         |                  |         |
| Beta blockers                     | 0.286                 | (0.061–1.345)    | 0.113   |                         |                  |         |
| Diuretics                         | 0.563                 | (0.117–2.718)    | 0.475   |                         |                  |         |
| Calcium antagonists               | -                     | -                | -       |                         |                  |         |

BNP: Brain natriuretic peptide, CHD: Congenital heart disease, RAAS: Renin-angiotensin-aldosterone system

Systolic blood pressure, although high systolic blood pressure was defined by comparison with age- and sex-matched controls. Thus, aging can be considered a stronger risk factor for high systolic blood pressure in patients with congenital heart disease than in the general population. Recently, many studies have reported that cardiovascular diseases are
Table 5. Comparison of the Clinical and Biochemical Variables Between Patients with and without High Systolic Blood Pressure

| Variables                           | High systolic blood pressure (+) (n = 20) | High systolic blood pressure (-) (n = 80) | p-value |
|-------------------------------------|------------------------------------------|------------------------------------------|---------|
| Brachial SBP (mmHg)                 | 150.2 ± 15.2                             | 109.8 ± 10.7                             | < 0.001 |
| Brachial DBP (mmHg)                 | 89.1 ± 12.2                              | 64.9 ± 10.1                              | < 0.001 |
| Age (years)                         | 48.6 ± 17.7                              | 34.0 ± 12.8                              | 0.001   |
| Sex (male/female)                   | 14/6                                     | 49/31                                    | 0.607   |
| Body mass index (kg/m²)             | 24.7 ± 4.6                               | 21.8 ± 4.0                               | 0.014   |
| Current smoker                      | 1 (5.0%)                                 | 8 (10.0%)                                | 0.683   |
| Simple CHD                          | 6 (30.0%)                                | 15 (18.8%)                               | 0.269   |
| Cyanosis                            | 0 (0%)                                   | 18 (%)                                   | 0.019   |
| Fontan circulation                  | 4 (20.0%)                                | 10 (12.5%)                               | 0.387   |
| History of open-heart surgery       | 14 (70%)                                 | 63 (78.8%)                               | 0.406   |
| History of aortic surgery           | 2 (10.0%)                                | 8 (10.0%)                                | 1.000   |
| BNP (pg/mL)                         | 29.8 ± 29.4                              | 79.6 ± 167.8                             | 0.033   |
| Hemoglobin A1c (%)                  | 5.5 ± 0.7                                | 5.1 ± 0.3                                | 0.007   |
| Chronic kidney disease              | 7 (35.0%)                                | 23 (28.8%)                               | 0.585   |
| Total cholesterol (mg/dL)           | 209.8 ± 41.9                             | 164.4 ± 34.8                             | < 0.001 |
| Low density lipoprotein             | 128.5 ± 31.0                             | 94.0 ± 29.8                              | < 0.001 |
| High density lipoprotein            | 50.9 ± 21.0                              | 50.4 ± 12.4                              | 0.255   |
| Triglyceride (mg/dL)                | 213.8 ± 131.6                            | 114.1 ± 73.7                             | < 0.001 |
| Drugs with antihypertensive action  | 8 (40.0%)                                | 41 (51.3%)                               | 0.456   |
| RAAS inhibitors                     | 5 (25.0%)                                | 30 (37.5%)                               | 0.432   |
| Beta blockers                       | 3 (15.0%)                                | 27 (33.8%)                               | 0.171   |
| Diuretics                           | 2 (10.0%)                                | 17 (21.3%)                               | 0.348   |
| Calcium antagonists                 | 2 (10%)                                  | 0 (0%)                                   | 0.004   |

Values are presented as mean ± standard deviation. BNP: Brain natriuretic peptide, CHD: Congenital heart disease, DBP: Diastolic blood pressure, RAAS: Renin-angiotensin-aldosterone system, SBP: Systolic blood pressure

Table 6. Univariate and Multivariate Analyses of Factors Associated with High Systolic Blood Pressure

| Variables                           | Univariate Odds ratio 95% CI | Multivariate Odds ratio 95% CI | p-value |
|-------------------------------------|-----------------------------|------------------------------|---------|
| Age (years)                         | 1.063 (1.028–1.099)         | 1.072 (1.020–1.126)          | < 0.001 |
| Sex (male)                          | 1.476 (0.513–4.247)         |                              | 0.470   |
| Body mass index (kg/m²)             | 1.159 (1.033–1.300)         | 1.261 (1.054–1.508)          | 0.011   |
| Current smokers                     | 0.474 (0.056–4.024)         |                              | 0.474   |
| Simple CHD                          | 1.333 (0.422–4.215)         |                              | 0.624   |
| Cyanosis                            |                             |                              |         |
| History of open-heart surgery       | 0.630 (0.210–1.884)         |                              | 0.408   |
| History of aortic surgery           | 0.986 (0.193–5.051)         |                              | 0.987   |
| BNP (pg/mL)                         | 0.986 (0.970–1.003)         |                              | 0.117   |
| Hemoglobin A1c (%)                  | 6.357 (1.649–24.504)        | 4.338 (0.874–21.539)         | 0.073   |
| Chronic kidney disease              | 1.334 (0.472–3.770)         |                              | 0.586   |
| Total cholesterol (mg/dL)           | 1.032 (1.015–1.050)         | < 0.001 (0.993–1.088)        | 0.094   |
| Low density lipoprotein             | 1.035 (1.016–1.054)         | < 0.001 (0.924–1.024)        | 0.289   |
| High density lipoprotein            | 1.002 (0.968–1.038)         |                              | 0.895   |
| Triglyceride (mg/dL)                | 1.01 (1.004–1.015)          | 1.007 (0.999–1.016)          | 0.087   |
| Drugs with antihypertensive action  | 0.512 (0.185–1.418)         |                              | 0.198   |
| RAAS inhibitors                     | 0.556 (0.182–1.684)         |                              | 0.299   |
| Beta blockers                       | 0.346 (0.093–1.286)         |                              | 0.113   |
| Diuretics                           | 0.412 (0.087–1.952)         |                              | 0.264   |
| Calcium antagonists                 |                             |                              |         |

BNP: Brain natriuretic peptide, CHD: Congenital heart disease, RAAS: Renin-angiotensin-aldosterone system

frequent in adults with congenital heart disease, even in patients with lower complexity congenital heart disease\textsuperscript{14-17). One of the reasons for the high prevalence of cardiovascular diseases may be the increased incidence of high systolic blood pressure associated with aging. The reason that older patients with congenital heart disease develop hypertension
Table 7. Clinical and Biochemical Variables of Each Age Quartile

| Variables                           | Age quartile | p-value   |
|------------------------------------|--------------|-----------|
|                                    | Q1 (n = 25)  | Q2 (n = 25) | Q3 (n = 25) | Q4 (n = 25) |
| Age (years)                        | 22.4 ± 1.7** | 28.0 ± 1.8* | 38.1 ± 4.2* | 59.0 ± 9.5* |
| Hypertension                       | 2 (8%) §     | 0 (0%) §    | 2 (8%) §    | 12 (48) *   |
| High systolic blood pressure       | 3 (12%) §    | 2 (8%) §    | 3 (12%) §   | 12 (48) *   |
| Brachial SBP (mmHg)                | 113.1 ± 16.2‡ | 114.4 ± 13.7§ | 113.1 ± 14.2§ | 130.7 ± 27.7* |
| Brachial DBP (mmHg)                | 67.1 ± 13.9‡ | 65.4 ± 11.5§ | 68.6 ± 9.8  | 78.0 ± 17.9* |
| Sex (male/female)                  | 19/6         | 19/6       | 12/13       | 13/12       |
| Body mass index (kg/m²)            | 22.8 ± 4.7   | 22.3 ± 3.5  | 22.5 ± 5.4  | 22.0 ± 3.2  |
| Current smoker                     | 1 (4%)       | 5 (20%)     | 2 (8%)      | 1 (4%)      |
| Simple CHD                         | 2 (8%)       | 6 (24%)     | 4 (16%)     | 9 (36%)     |
| Cyanosis                           | 3 (12%)      | 5 (20%)     | 5 (20%)     | 5 (20%)     |
| Fontan circulation                 | 6 (24%)      | 4 (16%)     | 4 (16%)     | 0 (0%)      |
| History of open-heart surgery      | 22 (88%) §   | 22 (88%) §  | 19 (76%)    | 14 (56%) *  |
| History of aortic surgery          | 4 (16%)      | 2 (8%)      | 4 (16%)     | 0 (0%)      |
| BNP (pg/mL)                        | 52.2 ± 129.3 | 95.9 ± 244.0| 46.3 ± 46.1 | 84.3 ± 121.6|
| Hemoglobin A1c (%)                 | 5.1 ± 0.4    | 5.0 ± 0.2   | 5.2 ± 0.4   | 5.4 ± 0.7   |
| Chronic kidney disease             | 4 (16%)      | 5 (20%)     | 9 (36%)     | 12 (48%)    |
| Total cholesterol (mg/dL)          | 161.9 ± 37.6‡| 160.7 ± 32.6§| 178.7 ± 34.9| 191.8 ± 49.2*|
| Low density lipoprotein            | 93.4 ± 31.6  | 94.9 ± 24.7 | 104.2 ± 32.4| 110.9 ± 40.0|
| High density lipoprotein           | 48.6 ± 12.5  | 46.2 ± 8.2  | 54.1 ± 17.2 | 53.5 ± 17.0 |
| Triglyceride (mg/dL)               | 128.3 ± 99.0 | 124.9 ± 79.1| 131.5 ± 104.0| 148.8 ± 102.2|
| Drugs with antihypertensive action | 12 (48%)     | 14 (56%)    | 10 (40%)    | 13 (52%)    |
| RAAS inhibitors                    | 8 (32%)      | 13 (52%)    | 6 (24%)     | 8 (32%)     |
| Beta blockers                      | 7 (28%)      | 10 (40%)    | 6 (24%)     | 7 (28%)     |
| Diuretics                          | 3 (12%)      | 3 (12%)     | 3 (12%)     | 9 (36%)     |
| Calcium antagonists                | 0 (0%)       | 0 (0%)      | 0 (0%)      | 2 (8%)      |

Values are presented as mean ± standard deviation. BNP: Brain natriuretic peptide, CHD: Congenital heart disease, DBP: Diastolic blood pressure, RAAS: Renin-angiotensin-aldosterone system, SBP: Systolic blood pressure. *p < 0.05 vs Q1, †p < 0.05 vs Q2, ‡p < 0.05 vs Q3, §p < 0.05 vs Q4.

is uncertain; however, other factors may play a role given that both cyanosis and cardiac surgery can impair renal function. Further studies with a larger sample size are needed to clarify the pathogenic mechanism of high blood pressure in adults with congenital heart disease.

Logistic regression analysis demonstrated that a high body mass index was a risk factor for high systolic blood pressure. In Q1 and Q2 (age ≤30 years), the body mass index in patients with high systolic blood pressure was remarkably high (31.2 ± 3.0 kg/m² vs. 22.5 ± 2.5 kg/m² in patients aged >30 years with high systolic blood pressure). Therefore, even in young patients, appropriate control of body weight could be an important factor in maintaining a healthy blood pressure and may inhibit cardiovascular events associated with systemic ventricular failure. It has been reported that tight control of risk factors could improve the cardiovascular outcomes in patients with aortic coarctation; thus, rigid body weight control may improve patient prognosis. Further research is needed to establish the optimal blood pressure levels for adult patients with congenital heart disease.

Recently, the SPRINT study proved that strict blood pressure control compared to the recommended blood pressure level in current guidelines diminished the incidence of cardiovascular events. Adult patients with congenital heart disease have systemic ventricles that are variously over-loaded (volume overload, pressure overload, cyanosis) from birth, stressed by surgical procedures and could be anatomically right ventricle. Therefore, hypertension is a disadvantage to vulnerable systemic ventricles, and early determination of risk factors for hypertension is essential along with early intervention.

Cyanosis was not a determinant of hypertension or high systolic blood pressure according to logistic regression analysis, and none of the patients with cyanosis demonstrated hypertension or high systolic blood pressure. It is well known that cyanosis-induced polycythemia elevates the shear stress of endothelial cells, which leads to vasodilation due to the increased production of nitric oxide and prostaglandins. Anti-atherogenic changes in lipoproteins have been reported in adults with cyanotic congenital heart disease. However, further studies are needed to establish the relationship between cyanosis and blood pressure.

Limitations

This study has several limitations, such as the fact that it was a small, single-center study. Given that the hemodynamics varied among patients with congenital heart disease, it was difficult to evaluate the influence of hemodynamic load on blood pressure. Moreover, owing to recent progress in pediatric cardiology and pediatric cardiac surgery, the influence of hemodynamics and surgery may vary between...
young and aged patients. Lastly, this study did not evaluate the relationship between high systolic blood pressure and prognosis.

**Conclusions**

The incidence of high systolic blood pressure is high in adults with congenital heart disease, in aged patients, and is associated with a high body mass index in young patients. Further research is needed to clarify the causes and influences of high systolic blood pressure.

**Conflicts of Interest**

None

**Names of Grants**

None

**References**

1. Shiina Y, Toyoda T, Kawasoe Y, Tateno S, Shirai T, Wakisaka Y, et al. Prevalence of adult patients with congenital heart disease in Japan. Int J Cardiol 2011; 146: 13-6.

2. Murakami T, Tateno S, Kawasoe Y, Niwa K. Aortic surgery is one of the risk factors for enhancement of pressure wave reflection in adult patients with congenital heart disease. Int J Cardiol 2014; 175: 451-4.

3. Shiina Y, Murakami T, Kawamatsu N, Niwa K. Aortopathy in adults with tetralogy of Fallot has a negative impact on the left ventricle. Int J Cardiol 2017; 228: 380-4.

4. Aging. Nichols WW, O’Rourke MF, Vlachopoulos C, editors. McDonald’s Blood Flow in Arteries. 6th edn. London, Great Britain: Hodder Arnold; 2011. p. 411-46.

5. Greenberg JH, Zappitelli M, Devarajan P, Thiessen-Philbrook HR, Krawczeniuk C, Li S, et al. TRIBE-AKI Consortium. Kidney outcomes 5 years after pediatric cardiac surgery: the TRIBE-AKI Study. JAMA Pediatr 2016; 170: 1071-8.

6. Takase H, Dohi Y, Kimura G. Distribution of central blood pressure values estimated by Omron HEM-9000AI in Japanese general population. Hypertens Res 2013; 36: 50-7.

7. O’Rourke MF, Adj A. Guidelines on guidelines: focus on isolated systolic hypertension in youth. J Hypertens 2013; 31: 649-54.

8. O’Rourke MF, Adj A. Isolated systolic hypertension in the young: a need for clarity, Reply. J Hypertens 2013; 31: 1913-4.

9. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004; 114(suppl 4th report): 555-76.

10. Wang KL, Cheng HM, Chuang SY, Spurgeon HA, Ting CT, Lakatta EG, et al. Central or peripheral systolic or pulse pressure: which best relates to target organs and future mortality? J Hypertens 2009; 27: 461-7.

11. Roman MJ, Devereux RB, Kizer JR, Lee ET, Galloway JM, Ali T, et al. Central pressure more strongly relates to vascular disease and outcome than does brachial pressure: the Strong Heart Study. Hypertension 2007; 50: 197-203.

12. Pini R, Cavallini MC, Palmieri V, Marchioni N, Bari MD, Devereux RB, et al. Central but not brachial blood pressure predicts cardiovascular events in an unselected geriatric population: the ICARe Dicomano Study. J Am Coll Cardiol 2008; 25: 2329-32.

13. Williams B, Lacy PS, Thom SM, Cruickshank K, Stanton A, Collier D, et al; CAFE investigators; Anglo-Scandinavian Cardiac Outcomes Trial Investigators; CAFE Steering Committee and Writing Committee. Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: principal results of the Conduit artery Function Evaluation (CAFE) study. Circulation 2006; 113: 1213-25.

14. Wang T, Chen L, Yang T, Huang P, Wang L, Zhao L, et al. Congenital heart disease and risk of cardiovascular disease: A meta-analysis of cohort studies. J Am Heart Assoc 2019; 8: e012030.

15. Saha P, Potiny P, Rigdon J, Morello M, Tchandjieu C, Romfh A, et al. Substantial cardiovascular morbidity in adults with lower-complexity congenital heart disease. Circulation 2019; 139: 1889-99.

16. Bauer UMM, Körtten MA, Diller GP, Helm P, Baumgartner H, Ewert P, et al. Cardiovascular risk factors in adults with congenital heart defects—recognized but not treated? An analysis of the German National Register for Congenital Heart Defects. Int J Cardiol 2019; 277: 79-84.

17. Videbæk J, Laursen HB, Olsen M, Hofsten DE, Johnsen SP. Long-term nationwide follow-up study of simple congenital heart disease diagnosed in otherwise healthy children. Circulation 2016; 133: 474-83.

18. Roifman I, Therrien J, Ionescu-Ittu R, Pilote L, Guo L, Kotowycz MA, et al. Coarctation of the aorta and coronary artery disease: fact or fiction? Circulation 2012; 126: 16-21.

19. SPRINT Research Group, Wright JT Jr, Williamson JD, Whelton PK, Snyder JK, Sink KM, et al. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med 2015; 373: 2103-16.

20. Fyfe A, Perloff JK, Niwa K, Child JS, Miner PD. Cyanotic congenital heart disease and coronary artery atherogenesis. Am J Cardiol 2005; 96: 283-90.