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Venous Measurements as Predictors of Long-Term Fontan Complications: A Single-Center Echocardiographic Study

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ABSTRACT

Objective: This study aims to assess the impact of complications of the Fontan operation, such as protein-losing enteropathy and thrombosis, on patients' quality of life. We hypothesize that alterations in the diameter and flow of the inferior vena cava (IVC) and femoral vein (FV) are associated with these complications. The goal is to evaluate the influence of venous structural modifications on Fontan operation outcomes by analyzing Doppler time measurements of the IVC, FV, aorta (Ao), and femoral artery (FA).

Materials and Methods: We retrospectively analyzed the recorded images of patients who had undergone Fontan palliation at least two years prior to presentation at our outpatient clinic between January 2022 and January 2023. Patients with chest pain but no cardiac pathology served as controls. Demographic and physical examination data were collected retrospectively. In patients with a normal single-ventricular ejection fraction, we measured the widest IVC diameter and Doppler values, the descending aortic diameter in systole, the widest FV diameter and Doppler values, and the femoral artery diameter in systole.

Results: The study included 25 Fontan patients: 7 had an extracardiac Fontan, 4 had a fenestrated extracardiac Fontan, and 14 had an intra-extracardiac fenestrated Fontan. A significant difference (p=0.019) was found in the age at Fontan between patients with NYHA stages 1-2 and those with NYHA stages 3-4. A pathologic microalbumin/creatinine ratio (>15) was correlated with pre-Fontan pulmonary artery pressure >15 mmHg. The IVC/BSA (p=0.031) and FV/BSA ratios differed significantly between groups with and without complications, with lower ratios observed in the group with complications.

Conclusion: Age at Fontan palliation is a risk factor for complications. High pre-Fontan pulmonary pressure is associated with microalbuminuria. IVC/BSA and FV/BSA are inversely associated with mid- to long-term complications following Fontan palliation.

Keywords: Complication, congenital heart disease, echocardiography, femoral vein, Fontan operation, inferior vena cava.

INTRODUCTION

The Fontan operation, first described in 1971 by French physician Dr. Francis Fontan, significantly alters the hemodynamic profile of patients, affecting both the arterial and venous systems. This procedure improves oxygenation in patients with congenital heart disease who are not candidates for biventricular correction, thus enhancing their quality of life. The altered circulatory pattern, known as single-ventricle physiology, warrants further investigation due to its diverse physiological effects and consequences. The profound impact of the Fontan operation on hemodynamics has been well established after over five decades of clinical application in advanced centers.[1] Long-term investigation and monitoring of hemodynamic status in single-ventricle physiology are crucial for understanding patient mortality and morbidity. Complications are common in Fontan patients during long-term follow-up.[2]

Existing literature indicates a strong association between mortality and conditions such as osteoarthritis, protein-losing enteropathy, cirrhosis, and renal failure. Fontan-associated nephropathy, often identified by abnormal microalbumin-to-creatinine ratios, has recently garnered significant attention, although its specific markers remain unclear.[3,4] Studies report a 20% prevalence of nephropathy among young Fontan patients.[4-6] Although MRI and CT modeling have enhanced our understanding of hemodynamics involving surgical connections and energy loss,[7-9] evidence concerning the status of the inferior vena cava (IVC) and femoral vein (FV) in long-term prognosis remains scarce. While the relationship between IVC diameter and nephropathy development has been investigated, its overall prognostic significance remains unclear.[4,10] Therefore, this study aims to examine the potential correlation between inferior vena cava diameter and long-term complications following Fontan palliation.[11,12]

In vitro and computational models, including MRI and CT, have advanced our understanding of Fontan hemodynamics, focusing on surgical connections and energy loss.[7-9] However, research on the relationship between IVC and FV and long-term prognosis remains limited.[4,10] While IVC diameter is linked to nephropathy, its comprehensive prognostic significance is not fully understood. Although echocardiography effectively assesses ventricular function, non-invasive evaluation of venous and pulmonary circulation in single-ventricle patients remains challenging. Monitoring these circulatory changes is crucial due to serious risks such as Fontan-associated nephropathy.[1,2] However, the role of venous measurements in predicting and monitoring post-Fontan complications remains poorly defined, and their long-term clinical utility requires further investigation.[4,10]

KEY MESSAGES

- Unexpectedly, diminished IVC/BSA and FV/BSA ratios suggest that chronic metabolic effects, rather than elevated intravascular pressure, are the primary drivers of long-term Fontan complications.
- Angiography-measured pre-Fontan pulmonary artery pressures greater than 15 mmHg predict an increased risk of subsequent renal complications, as demonstrated by an association with pathological microalbuminuria.
- The study highlights the need for thorough, long-term monitoring of Fontan complications, such as protein-losing enteropathy, arrhythmia, and thrombosis, in patients with reduced IVC/BSA and FV/BSA ratios.

This study aims to investigate the potential correlation between venous measurements (inferior vena cava diameter and femoral vein diameter) and the occurrence of long-term complications, including protein-losing enteropathy, plastic bronchitis, thrombosis, and arrhythmia, in patients undergoing Fontan palliation. Additionally, we examined nephropathy, a chronic Fontan complication, by analyzing spot urine microalbumin/creatinine ratios and correlating these findings with venous diameter measurements (IVC, FV).

MATERIALS AND METHODS

We retrospectively collected data from images of Fontan patients acquired in the previous year. All patients had undergone Fontan palliation within the last 15 years and were seen in the outpatient clinic between January 2022 and January 2023 at the Ege University Faculty of Medicine, Department of Pediatric Cardiology. The study protocol was approved by Ege University Medical Research Ethics Committee (Approval Number: 23-9T/31, Date: 07.09.2023).

Data Collection

Patient data, including age, height, weight, body surface area (BSA), age at the time of operation, exercise capacity (according to the New York Heart Association classification), SpO_2, microalbumin/creatinine ratios, pre-Fontan pulmonary arterial pressure measured during conventional angiography, and complications such as protein-losing enteropathy, plastic bronchitis, thrombosis, and arrhythmia, were obtained from their medical records. Additionally, measurements of the inferior vena cava (IVC), femoral vein (FV), abdominal aorta, femoral artery, and Doppler times for the IVC and FV were retrospectively obtained from recorded echocardiography images.

Study Groups

There is no standard for inferior vena cava measurements, and in pediatric patients, these measurements vary with height and weight. Therefore, a control group was included. The control group consisted of patients presenting with chest pain and no cardiac pathology; their images were evaluated. Initially, measurements from Fontan patients were compared with those from the control group. Subsequently, the patient group was further divided into two subgroups: Fontan patients with complications and those without. Protein-losing enteropathy, plastic bronchitis, thrombosis, and arrhythmia were considered long-term complications arising during patient follow-up.[13] These measurements were then compared between these subgroups.

The exclusion criteria for the patient group were a history of thrombosis both preoperatively and during the first month, femoral vein thrombosis, low single-ventricle ejection fraction, and severe valvular insufficiency.

Additionally, the spot urine microalbumin/creatinine ratio, assessed during polyclinic visits in the Fontan patient group as a marker for chronic nephropathy, was retrospectively evaluated. While no patients presented with renal failure, those with abnormal microalbumin-to-creatinine ratios were classified as having renal dysfunction.[5,6]

Echocardiography

In patients with a normal single-ventricular ejection fraction on echocardiography, the widest inferior vena cava (IVC) diameter in the systolic phase, IVC Doppler measurements, and descending aortic diameter (Ao) measurements were evaluated using subxiphoid short-axis views with a GE Vivid e9 S5 probe (3-7 MHz frequency range). Additionally, the widest femoral vein diameter and Doppler measurements of femoral artery diameter were assessed during the systolic phase using a GE Vivid e9 L11 probe (12 MHz frequency).

Given the lack of standardization for vein measurements relative to age and weight in children, a solution was sought to eliminate the variability described above. This solution involved dividing the IVC and FV diameter measurements by body surface area (BSA). Furthermore, IVC was calculated as a proportion of the descending aorta (IVC/Ao) and as the ratio IVC/FV. The shortest distance at which the FV and IVC Doppler flow exhibited a zero line during the examination was documented. This value was designated as the "Vein Doppler Time." These values were then compared with the incidence of Fontan complications, including thrombosis, arrhythmias, and protein-losing enteropathy. BSA was calculated using the Mosteller formula.[14]

Statistical Analysis

Statistical analyses were performed using IBM SPSS 23.0 software (SPSS Inc., Chicago, IL, USA). The normality of continuous variables was assessed using the Shapiro-Wilk test. Descriptive statistics for normally distributed continuous variables are presented as mean±standard deviation, while non-normally distributed variables are reported as median with their first and third quartiles (median; Q1, Q3). Categorical variables are presented as frequencies. Appropriate analyses were conducted to compare groups. When continuous variables were not normally distributed, the Mann-Whitney U test was applied to compare distributions between groups. Fisher's exact test was used for categorical data. A p-value less than 0.05 was considered statistically significant.

RESULTS

Patient Demographics and Clinical Characteristics

The youngest participant was 5 years old, while the oldest was 19. The median age was 13 years (range 11–17 years), with 6 females and 19 males participating. The median weight and height percentiles were 14% (range: 6.55–26) and 44.83% (range: 14.92–67), respectively. Saturation values ranged from 82% to 95%, with a median of 91% (range: 90–94).

The diagnoses of the patients were as follows: tricuspid atresia, 9 (36%); pulmonary atresia, 6 (24%); large VSD with unbalanced ventricle, 4 (16%); hypoplastic left heart syndrome, 3 (12%); mitral atresia, 2 (8%); and Taussig–Bing anomaly, 1 (4%).

A total of 72% of patients underwent MBT shunt, with the procedure performed at a median of 2 months (IQR: 1.5–6.5 months). Pulmonary banding was performed in 12% (n=5) within a time frame of 0–3 months, with a median duration of 2 months. The Norwood procedure was performed in 8% (n=2) of cases, with a median time to surgery of 1.5 months (IQR: 0–2 months). All cases underwent the Glenn procedure, with a median age at the Glenn procedure of 11.5 months (IQR: 7–25 months). The Fontan procedure was performed at a median age of 54 months (IQR: 48–83 months). The median pulmonary artery pressure measured by angiography from the Glenn shunts before Fontan operations was 14 mmHg (IQR: 12–15 mmHg), with a minimum of 7 mmHg and a maximum of 18 mmHg.

Of the patients included in the study, seven underwent extracardiac Fontan surgery, four underwent fenestrated extracardiac Fontan surgery, and 14 underwent intra-extracardiac fenestrated Fontan surgery. Among patients with uncomplicated cases, 11 underwent a Fontan procedure with an additional fenestration.

Table 1. Comparison of measurements between the patient and control groups

Measurement	Patient group (n=25)	Control group (n=25)	p
IVC/BSA	9.85 (8.63–11.42)	8.49 (7.15–11.4)	0.12
Ao/BSA	7.83 (6.95–8.85)	8.06 (6.55–10.45)	0.33
IVC/Ao	1.28 (1.20–1.50)	1.09 (1.03–1.17)	**0.001**
FV/FA	1.41 (1.05–1.57)	1.16 (1.09–1.25)	**0.009**
IVC/FV	2.05 (1.73–2.44)	1.83 (1.45–2.02)	0.079
FV/BSA	4.96 (3.86–5.58)	4.38 (3.99–6.44)	0.97
FA/BSA	3.78 (3.51–4.12)	3.75 (3.48–5.41)	0.6

IVC: Inferior vena cava diameter; BSA: Body surface area; Ao: Abdominal aorta diameter; FV: Femoral vein diameter; FA: Femoral artery diameter.

Comparisons of Demographic Characteristics Between the Control and Patient Groups

Comparisons between the control and patient groups revealed that the control group included 25 participants (17 males, 8 females), and the patient group had an identical gender distribution. Median values for age were 11 years (range: 8–14) and 13 years (range: 11–17) (p=0.34); for weight, 42 kg (range: 29–49 kg) and 44 kg (range: 33–50 kg) (p=0.497); and for BSA, 1.32 m^2 (range: 1.03–1.44 m^2) and 1.36 m^2 (range: 1.13–1.47 m^2) (p=0.404).

Comparison of Patient and Control Groups

A comparison between the patient and control groups revealed that IVC/Ao and FV/FA ratios were significantly elevated in the patient group (p=0.001, r=0.57 and p=0.009, r=0.29; Table 1). The patient group exhibited higher IVC/Ao and FV/FA ratios. This finding aligns with expectations, as intravascular congestion that develops over time due to passive flow within the Fontan circuit could contribute to the observed differences. The lack of significant differences in other venous-arterial measurements suggests that the Fontan circulation maintains hemodynamics that approximate normal physiology.

Table 2. Comparison of Fontan age and NYHA staging

Measurement	NYHA stage 1-2 (n=21)	NYHA stage 3-4 (n=4)	p
Fontan age (months)	Median (Q1-Q3): 50 (48–57)	Median (Q1-Q3): 143 (121–151)	**0.019**

NYHA: New York Heart Association.

Fontan Operation Age and NYHA Staging

In accordance with the NYHA staging system, 19 patients were classified as stage 1, 2 patients as stage 2, 2 patients as stage 3, and 2 patients as stage 4. A comparison of the age at Fontan operation between NYHA stage 1-2 and stage 3-4 patients revealed that those who underwent the procedure at an older age (median 143 months) were subsequently classified as NYHA stage 3-4 (p=0.019, r=0.88) (Table 2). Furthermore, the age at which the Fontan operation was performed was evaluated for cases in which complications arose during the follow-up period. The Fontan operation was performed at a relatively advanced age (median 108 months) (p=0.018, r=0.30) (Table 3).

Venous Measurements and Complications

A statistically significant difference was found in the ratio of vein measurements to body surface area between the complication group and the non-complication group. The

Table 3. Comparison of measurements between the complicated and uncomplicated Fontan groups

Measurement	Uncomplicated Fontan group (n=17)	Complicated Fontan group (n=8)	p
Fontan age (months)	Median (Q1-Q3): 50 (48–57)	Median (Q1-Q3): 108 (47–148)	**0.018**
IVC/BSA	11.04 (8.91–12.3)	9.09 (8.56–9.91)	**0.031**
Ao/BSA	8.1 (7.0–8.88)	7.2 (5.53–7.68)	0.135
IVC/Ao	1.28 (1.22–1.41)	1.34 (1.14–1.55)	0.75
FV/FA	1.41 (1.07–1.57)	1.31 (1.01–1.53)	0.783
IVC/FV	2.04 (1.64–2.22)	2.27 (1.78–2.49)	0.44
FV/BSA	5.55 (4.59–6.49)	4.29 (3.58–5.06)	**0.021**
FA/BSA	3.93 (3.56–4.39)	3.58 (3.30–3.85)	0.05
IVC Doppler time (ms)	1321 (762–3000)	970 (637–1173)	0.204
Femoral vein Doppler time (ms)	2053 (1242–3000)	2815 (1481–3000)	0.736

IVC: Inferior vena cava diameter; BSA: Body surface area; Ao: Abdominal aorta diameter; FV: Femoral vein diameter; FA: Femoral artery diameter. The complicated Fontan group included patients with protein-losing enteropathy, plastic bronchitis, thrombosis, and arrhythmia.

Table 4. Comparison of measurements between groups stratified by pathological and normal microalbuminuria

Measurement	MCR normal (≤20 µg/ml) (n=18)	MCR high (≥20 µg/ml) (n=6)	p
Pre-Fontan pulmonary artery pressure measurement			**0.047**
<15 mmHg (n=11)	15 (62.5%)	1 (4.2%)	
≥15 mmHg (n=7)	3 (12.5%)	5 (20.8%)	
Fontan operation age (months; median, Q1-Q3)	81 (43–137)	57 (44–127)	0.77
IVC/BSA	10.8 (8.75–11.6)	10.4 (9.01–12)	0.93
Ao/BSA	7.81 (6.79–8.72)	9 (7.95–10.2)	0.36
IVC/Ao	1.42 (1.21–1.49)	1.21 (1.11–1.28)	0.21
FV/FA	1.31 (1.04–1.55)	1.6 (1.45–1.71)	0.8
IVC/FV	2.23 (1.79–2.56)	1.96 (1.68–2.16)	0.34
FV/BSA	5.09 (3.99–6.14)	5.83 (5.36–5.95)	0.5
FA/BSA	3.85 (3.57–4.28)	3.76 (3.14–3.94)	0.86

MCR: Microalbumin/creatinine ratio; IVC: Inferior vena cava diameter; BSA: Body surface area; Ao: Abdominal aorta diameter; FV: Femoral vein diameter; FA: Femoral artery diameter.

p-value for IVC/BSA was 0.031 (r=0.36), and for FV/BSA, it was 0.021 (r=0.54, Table 3). IVC/BSA and FV/BSA ratios were lower in patients with complications. We concluded that the other ratios—IVC/FV, IVC/Ao, FV/FA—and the IVC and FV Doppler time values could not be used to distinguish between complicated and uncomplicated cases.

In the patient cohort under investigation, observed complications included ventricular extrasystoles severe enough to warrant the initiation of antiarrhythmic therapy in one patient during the fourth year after the Fontan operation. A pacemaker was implanted in one patient following the onset of complete AV block. Three patients developed protein-losing enteropathy. Three patients are receiving continuous low-molecular-weight heparin and antiplatelet therapy due to a history of thrombosis.

Pre-Fontan Pulmonary Artery Pressure and Renal Dysfunction

In routine spot urine microalbumin/creatinine (MCR) tests performed at the outpatient clinic, MCR values above 20 mcg/ml were considered pathological. MCR was assessed in 23 of 24 Fontan patients; one patient's results were missing at the time of application. No statistically significant associations were found between pathological and normal MCR values in the patient group and the ratios of IVC/BSA, FV/BSA, IVC/Ao, and IVC/FV, nor with the age at which the Fontan operation was performed (Table 4).

Six patients exhibited a pre-Fontan pulmonary artery pressure of ≥15 mmHg, as determined by catheter angiography. In these cases, the MCR was found to be pathological. A Chi-square analysis revealed a significant difference in the microalbumin/creatinine ratio in spot urine between the group with pre-Fontan Glenn shunt pressure <15 mmHg and the group with pressure ≥15 mmHg (p=0.047) (Table 4).

DISCUSSION

The Fontan procedure, while life-saving for patients with single-ventricle congenital heart disease, is associated with a spectrum of long-term complications that significantly impact morbidity and mortality.[15,16] These Fontan-associated diseases, such as protein-losing enteropathy, plastic bronchitis, liver disease, thrombosis, renal insufficiency, and arrhythmias, can ultimately lead to Fontan failure over time.[15,17] The chronic combination of elevated central venous pressure, non-pulsatile pulmonary blood flow, and a preload-deprived systemic ventricle contributes to this progressive deterioration.[18] This complex pathophysiology leads to chronic systemic venous hypertension and reduced cardiac output, driving peripheral stasis and congestion within the lymphatic system.[13] Persistent venous congestion, particularly affecting the inferior vena cava and its tributaries, often manifests as hepatomegaly, hepatic congestion, and fibrosis, potentially progressing to cirrhosis.[19,20] Indeed, a larger inferior vena cava diameter has been associated with elevated Fontan pressures and increased end-diastolic pressures, further exacerbating the risk of Fontan-associated liver disease.[21] These hemodynamic alterations also predispose Fontan patients to renal dysfunction, evidenced by increased microalbuminuria and decreased estimated glomerular filtration rate (eGFR).[4,5] Furthermore, microalbuminuria, a marker of renal injury, has a high incidence among Fontan patients.[11] The elevated central venous pressure characteristic of Fontan circulation can increase renal venous pressure and reduce renal perfusion pressure, thereby

contributing to the development of nephropathy.[10] Moreover, chronic hypoxemia, an additional factor in Fontan patients, can further impair renal function by promoting tubulointerstitial damage and subsequent proteinuria, a mechanism distinct from hepatorenal syndrome.[6] The persistent elevation of systemic venous pressure, an obligate feature of the Fontan circulation due to the absence of a sub-pulmonary ventricle, demonstrably decreases venous capacitance and compliance, thereby placing patients at increased risk of progressive renal dysfunction.[10,22] This sustained venous congestion also plays a critical role in the pathogenesis of protein-losing enteropathy and plastic bronchitis, conditions arising from lymphatic insufficiency and aberrant lymphatic channel formation, directly attributable to chronically elevated central venous pressures.[16]

It is crucial to monitor and assess the physical activity capacity of patients who have undergone Fontan palliation.[23] NYHA stage 2 or higher in Fontan operation cases is associated with increased mortality and the need for heart transplantation.[24] The findings of our study indicate that a later age at Fontan palliation is associated with an increased incidence of complications and reduced exercise capacity. This further underscores the importance of the age at which Fontan palliation is performed. Our findings show that the daily physical capacity of patients who underwent Fontan surgery aligns with NYHA stage 3-4 at a mean age of 143 months. The mean age at which Fontan palliation was performed in patients with complications was 108 months (9 years). In light of these findings, it is recommended that Fontan patients aged 9 years and older be monitored more closely for the development of complications, including arthritis, thrombosis, protein-losing enteropathy, plastic bronchitis, and microalbuminuria. Early diagnosis and treatment of potential complications will enhance patients' quality of life.

One of the most significant findings of our study is the association between microalbuminuria and a pre-Fontan pulmonary artery pressure of 15 mmHg or more, measured at the Glenn shunt during conventional angiography. Our analysis demonstrated a significant difference in the microalbumin/creatinine ratio between groups with pre-Fontan Glenn shunt pressure <15 mmHg and those with pressure ≥15 mmHg, with pathological microalbuminuria (MCR values above 20 mcg/ml) being significantly more prevalent in the latter group. This association is independent of the time elapsed since the operation. The presence of pathological MCR results serves as a critical indicator of future renal damage, a finding supported by literature that highlights microalbuminuria—highly prevalent in Fontan patients—as a marker of renal injury.[11] In a systematic review, T. Alsaied and colleagues further emphasized the significance of late mortality and renal injury.[25] Given that pre-Fontan pulmonary artery pressures exceeding 15 mmHg are significantly associated with pathological MCR, such elevated pressures are important for predicting the risk of subsequent renal injury and potential mortality.[19,25-27] Therefore, patients with pre-Fontan pulmonary artery pressure exceeding 15 mmHg should undergo periodic assessment of their microalbumin-to-creatinine ratio for early detection and management of renal complications.

Patel et al.[10] demonstrated a significant association between a IVC/BSA ratio exceeding 1 cm/m^2 and the presence of pathological microalbuminuria, underscoring its utility as an indicator for evaluating late nephropathy. In contrast to these findings, our study did not find a significant correlation between the IVC/BSA ratio and the pathological microalbumin/creatinine ratio. This divergence may be attributable to inherent variability in IVC/BSA and femoral vein measurements in the pediatric population, particularly given dynamic growth parameters. The development of robust, standardized venous measurement protocols remains a critical challenge. Establishing clear and reliable reference values will necessitate comprehensive studies involving a substantial number of cases, precise delineation of physiological limits, and mitigation of subjective assessment biases. Further research is needed to refine diagnostic criteria and establish universal thresholds for venous parameters that reliably predict long-term Fontan complications, particularly in the context of renal dysfunction.[4]

Significant differences in the IVC/Ao and FV/FA ratios were observed between the patient and healthy control groups. Subsequent analysis, in which the patient group was further stratified into complication and no-complication subgroups and compared with the healthy control group, revealed that the healthy control group had lower IVC/Ao and FV/FA ratios. This observation not only suggests progressive venous congestion within the passive circulation of the Fontan shunt over time but also underscores a critical pathophysiological mechanism underlying many of the adverse long-term outcomes in these patients. This persistent venous congestion, particularly evident in the inferior vena cava and its tributaries, profoundly influences long-term hemodynamics and the overall prognosis in Fontan patients and contributes to the development of serious complications such as progressive renal dysfunction, protein-losing enteropathy, and plastic bronchitis.[10,16,22]

Our study revealed a statistically significant correlation between the IVC/BSA and FV/BSA ratios and the incidence of complications. In contrast to the existing literature, which often associates an increased indexed inferior vena cava (IVC) diameter with complications such as pathological

microalbuminuria,[10] we observed a paradoxical decrease in IVC/BSA and FV/BSA in complicated cases. This unexpected outcome suggests a unique pathophysiological mechanism within the Fontan circulation, characterized by chronically elevated systemic venous pressures and reduced cardiac output, leading to multifactorial complications.[13,22,28] We postulate that this decrease may serve as an early indicator of reduced intravascular volume in the venous compartment, potentially leading to compensatory redistribution of fluid into extravascular (or "third") spaces. Fluid shifts and issues with fluid balance are recognized challenges in Fontan patients,[29,30] often exacerbated by lymphatic dysfunction and multiorgan sequelae.[13,31] These changes could stem from mechanisms affecting metabolically compromised states, a known aspect of chronic Fontan physiology, which impacts various end organs, including the hepatic and renal systems.[18,19,26] The consistent, parallel alterations observed in both the femoral vein and inferior vena cava measurements strongly suggest that factors beyond isolated hemodynamic pressures, such as systemic metabolic effects and fluid balance dysregulation, significantly influence these venous parameters.

To achieve comprehensive conclusions regarding these venous measurements and ratios, further research is imperative, particularly with larger patient cohorts and the establishment of standardized measurement protocols, considering the complex and multifactorial nature of Fontan circulation.[13,32] We recommend longitudinal follow-up for every Fontan patient, with regular comparative assessments of IVC/BSA and FV/BSA ratios at each visit. This approach is critical for the early identification of these potentially subtle indicators of long-term complications.

Study Limitations

The present study is subject to several limitations. Although the cohort was relatively small, this reflects the rare nature of the disease under investigation. Future multi-center studies with larger sample sizes would strengthen the validity and generalizability of the findings. It was not feasible to measure current pulmonary artery and Fontan shunt pressures due to the absence of clinical indications for angiography, thus precluding their inclusion in this study. Furthermore, reliance on retrospectively collected microalbumin/creatinine ratios from spot urine samples obtained at clinical presentation constitutes an additional limitation

CONCLUSION

Effective long-term management following Fontan palliation is crucial for significantly improving patients' quality of life and reducing mortality rates. We strongly advocate for rigorous monitoring of patients aged nine years or older, with particular attention to complications such as protein-losing enteropathy, arrhythmia, thrombosis, and plastic bronchitis. Furthermore, patients presenting with a pre-Fontan pulmonary artery pressure of 15 mmHg, as measured by angiography, require diligent surveillance for renal complications using the microalbumin-to-creatinine ratio. Our findings underscore the importance of longitudinally tracking IVC/BSA and FV/BSA ratios: a decrease in these ratios—contrary to prior assumptions—emerged as a significant and unexpected indicator of potential future complications. This necessitates a re-evaluation of how these venous parameters are interpreted; a decrease in these ratios in any patient should now be regarded as a critical warning sign, potentially reflecting diminished intravascular volume and fluid accumulation in third spaces. Implementing such comprehensive monitoring strategies is vital for early detection and intervention, ultimately improving long-term outcomes for Fontan patients.

Ethics Committee Approval: Ethics committee approval was obtained from Ege University Medical Research Ethics Committee (Approval Number: 23-9T/31, Date: 07.09.2023).

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REFERENCES

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971;26(3):240-8. [CrossRef]
2. Ohuchi H, Yasuda K, Miyazaki A, Iwasa T, Sakaguchi H, Shin O, et al. Comparison of prognostic variables in children and adults with Fontan circulation. Int J Cardiol 2014;173(2):277-83. [CrossRef]
3. Alsaied T, Bokma JP, Engel ME, Kuijpers JM, Hanke SP, Zuhlke L, et al. Predicting long-term mortality after Fontan procedures: A risk score based on 6707 patients from 28 studies. Congenit Heart Dis 2017;12(4):393-8. [CrossRef]

4. Van den Eynde J, Westenberg JJM, Hazekamp MG, Lamb HJ, Jongbloed MRM, Wentzel JJ, et al. Noninvasive Advanced Cardiovascular Magnetic Resonance-Derived Fontan Hemodynamics Are Associated With Reduced Kidney Function But Not Albuminuria. J Am Heart Assoc 2024;13(3):e033122. [CrossRef]
5. Khuong JN, Wilson TG, Grigg LE, Bullock A, Celermajer D, Disney P, et al. Fontan-associated nephropathy: Predictors and outcomes. Int J Cardiol 2020;306:73-7. [CrossRef]
6. Muraoka M, Nagata H, Yamamura K, Sakamoto I, Ishikita A, Nishizaki A, et al. Long-Term Renal Involvement in Association with Fontan Circulation. Pediatr Cardiol 2024;45(2):340-50. [CrossRef]
7. Loke YH, Kim B, Mass P, Opfermann JD, Hibino N, Krieger A, et al. Role of surgeon intuition and computer-aided design in Fontan optimization: A computational fluid dynamics simulation study. J Thorac Cardiovasc Surg 2020;160(1):203-12.e2. [CrossRef]
8. Dasi LP, Krishnankuttyrema R, Kitajima HD, Pekkan K, Sundareswaran KS, Fogel M, et al. Fontan hemodynamics: importance of pulmonary artery diameter. J Thorac Cardiovasc Surg 2009;137(3):560-4. [CrossRef]
9. Ryu K, Healy TM, Ensley AE, Sharma S, Lucas C, Yoganathan AP. Importance of accurate geometry in the study of the total cavopulmonary connection: computational simulations and *in vitro* experiments. Ann Biomed Eng 2001;29(10):844-53. [CrossRef]
10. Patel S, Anne P, Somerfield-Ronek J, Du W, Zilberman MV. Inferior Vena Cava Diameter Predicts Nephropathy in Patients Late After Fontan Palliation. Pediatr Cardiol 2020;41(4):789-94. [CrossRef]
11. Anne P, Du W, Mattoo TK, Zilberman MV. Nephropathy in patients after Fontan palliation. Int J Cardiol 2009;132(2):244-7. [CrossRef]
12. Byrne RD, Weingarten AJ, Clark DE, Huang S, Perri RE, Scanga AE, et al. More than the heart: Hepatic, renal, and cardiac dysfunction in adult Fontan patients. Congenit Heart Dis 2019;14(5):765-71. [CrossRef]
13. Mazza GA, Gribaudo E, Agnoletti G. The pathophysiology and complications of Fontan circulation. Acta Biomed 2021;92(5):e2021260.
14. Mosteller RD. Simplified calculation of body-surface area. N Engl J Med 1987;317(17):1098. [CrossRef]
15. Ordonez MV, Biglino G, Bedair R. Routine surveillance of patients post Fontan palliation: lessons learnt from cardiac catheterisation. J Congenit Cardiol 2021;5:3. [CrossRef]
16. de Lange C. Imaging of complications following Fontan circulation in children - diagnosis and surveillance. Pediatr Radiol 2020;50(10):1333-48. Erratum in: Pediatr Radiol 2020;50(10):1478. [CrossRef]
17. Kawasaki Y, Sasaki T, Kobayashi D. Hemodynamic Profiling Using a Cardiac Index-Systemic Vascular Resistance Plot in Patients with Fontan Circulation. Congenital Heart Disease 2023;18(4):431. [CrossRef]
18. van Hassel G, Groothof D, Douwes JM, Hoendermis ES, Liem ET, Willems TP, et al. Deterioration in Renal Function in Patients With a Fontan Circulation and Association With Mortality. JACC Adv 2024;3(12):101399. [CrossRef]
19. Rychik J, Atz AM, Celermajer DS, Deal BJ, Gatzoulis MA, Gewillig MH, et al.; American Heart Association Council on Cardiovascular Disease in the Young and Council on Cardiovascular and Stroke Nursing. Evaluation and Management of the Child and Adult With Fontan Circulation: A Scientific Statement From the American Heart Association. Circulation 2019;140(6):e234-84. [CrossRef]
20. El-Sisi A, Taha AH, Sheba M, Hanna B, Alem SA, Mostafa FAZ, et al. Prevalence of hepatic dysfunction in paediatric patients with Fontan circulation. Pediatria Polska 2024;99(2):105-10. [CrossRef]
21. Gunsaulus M, Wang L, Haack L, Christopher A, Feingold B, Squires J, et al. Cardiac MRI-Derived Inferior Vena Cava Cross-Sectional Area Correlates with Measures of Fontan-Associated Liver Disease. Pediatr Cardiol 2024;45(4):909-20. [CrossRef]
22. Heying R, d'Udekem Y, Gewillig M, Rychik J. Editorial: The Fontan circulation: Problems and solutions. Front Pediatr 2022;10:1087739. [CrossRef]
23. Hedlund ER, Lundell B, Söderström L, Sjöberg G. Can endurance training improve physical capacity and quality of life in young Fontan patients? Cardiol Young 2018;28(3):438-46. [CrossRef]
24. Meyer SL, St Clair N, Powell AJ, Geva T, Rathod RH. Integrated Clinical and Magnetic Resonance Imaging Assessments Late After Fontan Operation. J Am Coll Cardiol 2021;77(20):2480-9. [CrossRef]
25. Alsaied T, Bokma JP, Engel ME, Kuijpers JM, Hanke SP, Zuhlke L, et al. Factors associated with long-term mortality after Fontan procedures: a systematic review. Heart 2017;103(2):104-10. [CrossRef]
26. Rathgeber SL, Lam C, Harris KC, Grewal J. Hepatic and Renal Consequences of Single-Ventricle Physiology Palliated With the Fontan Operation. Can J Cardiol 2022;38(7):1002-11. [CrossRef]
27. Pundi KN, Johnson JN, Dearani JA, Pundi KN, Li Z, Hinck CA, et al. 40-Year Follow-Up After the Fontan Operation: Long-Term Outcomes of 1,052 Patients. J Am Coll Cardiol 2015;66(15):1700-10. [CrossRef]

28. van De Bruaene A, Claessen G, Salaets T, Gewillig M. Late Fontan Circulatory Failure. What Drives Systemic Venous Congestion and Low Cardiac Output in Adult Fontan Patients? Front Cardiovasc Med 2022;9:825472. [CrossRef]
29. Ven JPG van der, Kamphuis VP, Bosch E, Gnanam D, Monteros CTE de L, Bogers AJJC, et al. Cardiac Function and Serum Biomarkers throughout Staged Fontan Palliation: A Prospective Observational Study. J Cardiovasc Dev Dis 2023;10(7):289. [CrossRef]
30. Luppes VAC, Willems A, Hazekamp MG, Blom NA, Ten Harkel ADJ. Fluid Overload in Pediatric Univentricular Patients Undergoing Fontan Completion. J Cardiovasc Dev Dis 2023;10(4):156. [CrossRef]
31. Castellanos DA, Ahmad S, St Clair N, Sleeper LA, Lu M, Schidlow DN, et al. Magnetic resonance three-dimensional steady-state free precession imaging of the thoracic duct in patients with Fontan circulation and its relationship to outcomes. J Cardiovasc Magn Reson 2023;25(1):28. [CrossRef]
32. Baroutidou A, Karagiannidis AG, Dimitroulas T, Kamperidis V, Ziakas A, Dimopoulos K, et al. Pathophysiology of endothelial dysfunction in Fontan circulation: from bench to bedside and back again. Angiogenesis 2025;28(4):45. [CrossRef]