Examination of Diffuse Myocardial Fibrosis in Pediatric and Young Adult Fontan Circulations: A Retrospective Cohort Study

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Background

- The Fontan procedure is a surgical intervention for various congenital heart defects. The result is a unique cardiopulmonary circuit with passive caval-pulmonary perfusion and a single systemic ventricle.
- Modern surgical techniques have driven 25-year survival as high as 85%, necessitating management of downstream complications of congestive hepatopathy, arrhythmias, heart failure and progression to heart transplant.
- Cardiac MR is the gold standard for monitoring parameters of ventricular function and offers quantitative measurement of myocardial fibrosis via native T1 and extracellular volume.

Methods

Aim: Employ cardiac MR to quantify myocardial fibrosis among Fontan and control patients to examine for any differences and to examine possible clinical correlates to these values.

- COMIRB approved retrospective cohort study established from patients with cardiac MR dated January 2019 to March 2022 as part of post-Fontan monitoring vs healthy volunteers. Chart reviewed for demographic and imaging data.
- Post-processing of imaging performed in Circle cvi42 to obtain myocardial native T1s and extracellular volume for the basal, middle and apical ventricle. Averaged to produce a global result.
- Statistical analysis of data was stratified by Fontan vs healthy control, field strength, and ventricular dominance.
- Correlates to patient demographics and functional status were calculated via Pearson correlation coefficients.

Figure 1. Cardiac MR 3D rendering of Fontan anatomy.

Results

Table 1. Demographics, CMR and CPET data for Controls and Fontans stratified by ventricular dominance.

Demographics	Controls (N=49)	Fontans (N=93)	p-value	DRV (N=45)	DLV (N=47)	p-value
Sex (% Male)	57%	60%	0.723	76%	47%	**0.0047**
Age (years)	14.7 ± 5.8	12.5 ± 7.5	**0.078**	9.8 ± 6.4	15.2 ± 7.6	**<.001**
Age at Fontan (months)	-	39.6 ± 13.6	-	39.9 ± 15.1	39.1 ± 12.2	0.785
Height (cm)	158.3 ± 22.3	139.9 ± 29.4	**<.001**	132.3 ± 30.8	148.3 ± 25.1	**0.008**
Weight (kg)	60.8 ± 27.1	47.7 ± 29.2	**0.010**	41.7 ± 27.8	54.2 ± 29.4	**0.039**
Hematocrit (%)	38.2 ± 7.9	46.5 ± 5.1	**<.001**	46.1 ± 5.5	46.9 ± 4.7	0.473
CMR Parameters						
EF (%)	57.4 ± 4.4	46.8 ± 9.3	**<.001**	44 ± 10.2	49.9 ± 6.7	**0.001**
EDV (mL)	135.1 ± 43.5	131 ± 70.3	0.707	140.6 ± 86	121.2 ± 51.2	0.190
EDVi (mL/m^2)	82.1 ± 15.4	102.5 ± 43	**0.002**	118 ± 41.7	83.9 ± 27.9	**<.001**
ESV (mL)	59.8 ± 21.2	72.5 ± 51.4	0.099	82.8 ± 65.4	61.6 ± 30.3	**0.048**
ESVi (mL/m^2)	36.1 ± 7.8	57.3 ± 36.5	**<.001**	69 ± 38.3	42.7 ± 19.1	**<.001**
Vent Massi (g/m^2)	47.2 ± 11	57 ± 44.8	0.187	80.6 ± 44	40.7 ± 12.6	**<.001**
CO (LPM)	5.4 ± 1.7	4.5 ± 1.6	**0.002**	4.5 ± 1.7	4.4 ± 1.5	0.684
CI (LPM/m^2)	3.3 ± 0.8	3.6 ± 1.3	0.163	4.2 ± 1.3	3.1 ± 1	**<.001**
APC Flow Aorta (%)	-	19.6 ± 12.5	-	21.9 ± 13.3	17.3 ± 11.4	0.122
APC flow PA (%)	-	24.6 ± 15.5	-	28.6 ± 16.5	20.5 ± 13.7	**0.035**
CPET Parameters						
Mean Time to CPET	-	121.3 ± 188.6	-	104.1 ± 148.8	101.6 ± 172.4	0.950
VO2 Max (LPM)	2.4 ± 0.7	1.3 ± 0.5	**<.001**	1.3 ± 0.5	1.3 ± 0.4	0.701
VO2 Maxi (mL/kg/min)	37.2 ± 9.8	26.5 ± 7.1	**<.001**	27.3 ± 6.3	26.2 ± 7.6	0.549
CMR Fibrosis Markers						
1.5T Global Native T1	981.4 ± 30.5	1031.6 ± 50.8	**<.001**	1040.9 ± 51.8	1023.1 ± 49.5	0.166
3T Global Native T1	1253.4 ± 48.7	1287.5 ± 58.6	**0.031**	1275.5 ± 68.5	1299.4 ± 46.3	0.289
Extracellular Volume	23.2 ± 2	26 ± 4	**<.001**	26.3 ± 4.1	25.4 ± 3.5	0.321

AAPC, aortopulmonary collateral; BP, blood pressure; BSA, Body Surface Area; CMR, cardiac magnetic resonance; CO, cardiac output; CI, cardiac output indexed; CPET, cardiopulmonary exercise test; DRV, dominant right ventricle; DLV, dominant left ventricle; EDV, end diastolic volume; EDVi, end diastolic volume indexed; EF, ejection fraction; ESV, end systolic volume; ESVi, end systolic volume indexed; HCT, Hematocrit; QPi, pulmonary flow indexed; RPi, pulmonary resistance indexed; VEDP, ventricular end diastolic pressure; Vent Massi, ventricular mass indexed.

Table 2. ECV Correlations to Demographics and Functional Status

	Fontans	DRV	DLV
Age	-0.35**	-0.30*	-0.35*
Age at Fontan	0.09	0.02	0.00
Hematocrit	-0.51**	-0.55**	-0.45*
Systolic BP	-0.26*	-0.28	-0.03
Diastolic BP	-0.39**	-0.35*	-0.35*
EF	0.09	0.19	-0.10
EDV	-0.28*	-0.28	-0.37*
EDV (i)	-0.06	-0.23	-0.06
ESV	-0.22*	-0.26	-0.27
ESV (i)	-0.07	-0.23	-0.01
Vent Mass (inc	0.27*	0.31	0.03
CO	-0.20	-0.08	-0.39*
CO (i)	0.25*	0.22	0.13
APC Aorta	0.20	0.17	0.17
APC PA	0.26*	0.14	0.22
VEDP	0.01	0.57*	-0.39
Q_p(i)	-0.14	-0.19	-0.10
Fick CO (i)	0.36*	0.25	0.46*
R_p(i)	0.02	0.10	0.26
Vo2 Max	-0.28*	-0.08	-0.35*
VO2 max (i)	0.03	0.08	0.05

* or ** denotes significance for p<.05 or p<.001, respectively

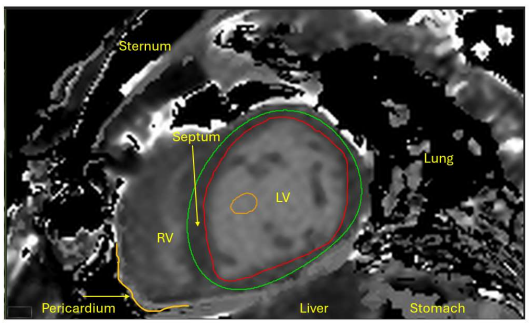

Figure 2. T1 mapping through cardiac apex with labelled anatomy.

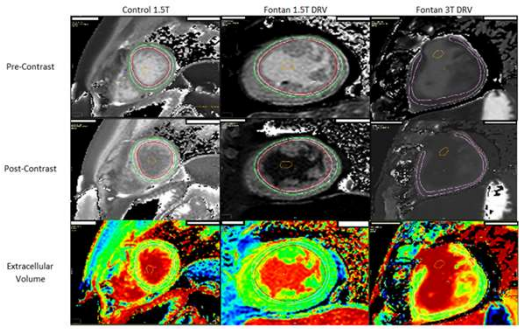

Figure 3. Examples of post-processing in cvi42.

Results/Discussion

- Fontan cohort of 93 patients (45 DRV, 47 DLV, 1 combined) showed significant difference when compared to the control cohort (N=49) with EF, CO, and VO2 max markedly reduced among the Fontans.
- Native T1 and ECV were significantly and diffusely elevated among the Fontans.
- Some demographics differences were present between DRV and DLV but there were no significant differences in fibrotic markers.
- Significant inverse correlation to ECV was noted with age, hematocrit, diastolic BP and VO2 max.

Conclusions

- Markers of myocardial fibrosis were elevated among the Fontan cohort compared to healthy controls.
- Fontan patients were shown to have a reduced exercise tolerance as measured by VO2 max.
- A negative correlation between ECV and VO2 max was observed across the Fontan group, suggesting a possible relationship between myocardial fibrosis and impaired exercise tolerance.

Limitations

- Sedation is not routinely used for pediatric CMR screening and is thus limited by patients' ability to cooperate and breath-hold.
- Similar limits on contrast administration and obtaining hematocrits in healthy volunteers.
- Strain measurements were not incorporated into the present study but could be of future interest.

Disclosures

- The authors have no disclosures.