Association of Lymphatic Abnormalities by T2-weighted MRI with Late Complications After Fontan Operation

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Background

T2-weighted (T2w) Magnetic Resonance Imaging (MRI) can be used to assess for lymphatic abnormalities among single ventricle patients. While studies have shown an association between lymphatic patterns on T2w MRI and early Fontan outcomes, robust data linking lymphatic abnormalities to long-term Fontan outcomes are sparse. The primary objective of this study is to determine if lymphatic abnormalities assessed by T2w MRI in Fontan patients are associated with long-term adverse outcomes. The secondary objective is to investigate the association between T2w lymphatic abnormalities and clinical and hemodynamic parameters.

Methods

We performed a retrospective review of all patients with Fontan circulation who underwent cardiac MRI between June 2018 and May 2024 at Children's Hospital Los Angeles (CHLA IRB exempt *#CHLA-24-00009-AM001*). T2w MRI images were classified by abnormal lymphatic channel hyperintensity in the neck and chest, ranging from type 1 (minimal lymphatic channels in the mediastinum or neck) to type 4 (involvement of supraclavicular, mediastinal, and lung parenchyma). Demographic and clinical data were collected. Clinical outcome data collected included presence of lymphatic complications, heart transplant listing, and death.

Results

A total of 119 patients were included. The mean age and time from Fontan at T2w MRI were 13.6±3.9 years and 10.1±3.9 years, respectively. Mean follow-up after Fontan operation was 12.1±3.9 years. Majority of the patients were male (57.1%), had a dominant morphologic right ventricle (RV) (52.8%), and had normal systolic ventricular function (52.5%). Approximately two-thirds (67.2%) were categorized as having type 1 or 2 lymphatic pattern, 28.6% as type 3, and 4.2% as type 4. There was a significant association between lymphatic pattern and gender, with 100% of type 4, 38.2% of type 3, and 42.3% of type 1-2 being females (p=0.0328). Lymphatic pattern did not have a significant association with systolic ventricular function, Fontan pressure, pulmonary vascular resistance, presence of plastic bronchitis, or history of chylothorax. While lymphatic pattern was not associated with ventricular morphology, all 5 patients with type 4 perfusion had a systemic morphologic RV. Lymphatic pattern was not associated with fibrosis on liver biopsy but was associated with liver extracellular volume (ECV) fraction (type 1-2: 41.9±4.7, type 3: 42.1±4.5, type 4: 50.4±6.0, p=0.0008). There was a significant association between lymphatic pattern and presence of protein-losing enteropathy (PLE), with 20% of type 4, 5.9% of type 3, and 1.3% of type 1-2 having PLE (p=0.046). Lymphatic pattern was also associated with heart transplant listing. 40% of type 4, 5.9% of type 2, and 2.5% of type 1-2 were listed for transplant (p=0.0127). There was only one death during the follow-up period.

Conclusion

Type 3 and type 4 lymphatic perfusion patterns were present in nearly one-third of Fontan patients and all patients with type 4 pattern had a morphologic RV. Lymphatic pattern was associated with both presence of PLE and heart transplant listing. While lymphatic pattern was not associated with hemodynamic variables or ventricular function, there was a significant association with hepatic ECV.

Table 1.

Demographics and Clinical Variables among Children with Type 1 or 2, Type 3, or Type 4 Lymphatic Abnormalities on T2-weighted MRI

Variable		Type 1 or 2 (n=80)	Type 3 (n=34)	Type 4 (n=5)	P-Value
Gender					0.0328
	Male	47 (58.8)	21 (61.8)	0 (0)	
	Female	33 (42.3)	13 (38.2)	5 (100)	
MRI function					0.6024
	Normal	41 (51.9)	19 (55.9)	2 (40.0)	
	Mild	16 (20.3)	4 (11.8)	2 (40.0)	
	Mod-Severe	22 (27.9)	11 (32.4)	1 (20.0)	
Liver Biopsy					0.359
	Low grade fibrosis (1-2)	32 (72.7)	16 (72.3)	1 (33.3)	
	High grade fibrosis (3-4)	12 (27.3)	6 (27.3)	2 (66.7)	
History of Fenestration					0.1102
	Yes	8 (10.0)	2 (5.9)	2 (40.0)	
	No	72 (90.0)	32 (94.1)	3 (60.0)	
Ventricular morphology					0.1839
	RV	43 (53.8)	16 (47.1)	5 (100)	
	LV	35 (43.8)	18 (52.9)	0 (0)	
	Unknown	2 (2.5)	0 (0)	0 (0)	
Norwood as first operation					0.6621
	Yes	33 (41.3)	12 (35.3)	1 (20.0)	
	No	47 (58.8)	22 (64.7)	4 (80.0)	
Heterotaxy					0.2278
	Yes	15 (18.8)	4 (11.8)	2 (40.0)	
	No	65 (81.3)	30 (88.2)	3 (60.0)	
Plastic Bronchitis					0.0826
	Yes	1 (1.3)	0 (0)	1 (20.0)	
	No	79 (98.8)	34 (100)	4 (80.0)	
PLE					0.0461
	Yes	1 (1.3)	2 (5.9)	1 (20.0)	
	No	79 (98.8)	32 (94.1)	4 (80.0)	
Chylous Effusions					0.1967
	Yes	4 (5.1)	5 (15.2)	0 (0)	
	No	74 (94.9)	28 (84.9)	5 (100.0)	

Transplant Eval				0.0037
Yes	4 (5.0)	3 (8.8)	3 (60.0)	
No	76 (95)	31 (91.2)	2 (40.0)	
Transplant Listing				0.0127
Yes	2 (2.5)	2 (5.9)	2 (40.0)	
No	78 (97.5)	32 (94.1)	3 (60.0)	
Death				0.6723
Yes	1 (1.3)	0 (0)	0 (0)	
No	79 (98.8)	34 (100)	5 (100.0)	
Lymphatic failure, transplant listing, or death				0.0252
Yes	4 (5.0)	3 (8.8)	2 (40.0)	
No	76 (94.0)	31 (91.2)	3 (60.0)	
Transplant listing, or death				0.0219
Yes	3 (3.8)	2 (5.9)	2 (40.0)	
No	77 (96.3)	32 (94.1)	3 (60.0)	

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