Magnetic resonance lymphangiography in group 1 paediatric pulmonary arterial hypertension

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Abstract
Pulmonary hypertension could have thoracic lymphatic abnormalities caused by right ventricular failure. Since there is no description of such abnormalities, the purpose of this study was to investigate them with magnetic resonance. Prospective review magnetic resonance T2-weighted lymphangiography was performed between January 2017 and October 2019 through quantitative thoracic duct diameter, diameter index and qualitative lymphatic abnormalities types: 1 – little or none abnormalities, 2 – abnormalities in supraclavicular region, 3 – abnormalities extending into the mediastinum and 4 – abnormalities extending into the lung. Five patients with group 1 pulmonary arterial hypertension participated in this study. The mean age was 12.44 ± 4.92 years, three male and two female. The quantitative analysis yielded the following results: mean thoracic duct diameter of 2.92 ± 0.16 mm and thoracic duct index 2.28 ± 1.03 mm/m². Qualitative lymphangiography abnormalities were type 1 in three patients, type 2 in one, all with low-risk determinants, and type 3 in one with high-risk determinants and right ventricular failure. Magnetic resonance T2-weighted lymphangiography in group 1 paediatric pulmonary arterial hypertension allowed for the identification of the thoracic duct, which was used to perform both quantitative and qualitative analysis of thoracic lymphatic abnormalities, in particular when increased high-risk determinants and right ventricular failure were present. These features represent an extracardiac finding useful to understand systemic venous congestion impact on lymphatic system.

Keywords
thoracic duct, lymphatic abnormalities, pulmonary arterial hypertension

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Case report
Five paediatric patients with confirmed pulmonary arterial hypertension (PAH) were consecutively scanned with magnetic resonance T2-weighted lymphangiography for a period of 2 years and 10 months between January 2017 and October 2019, after Ethical Committee approval and informed consent forms collected.1,2 The purpose of such scanning was to describe thoracic duct (TD) and lymphatic abnormalities through T2-weighted cardiac magnetic resonance (CMR) lymphangiography with quantitative and qualitative data. Three patients were male and two female with mean age of 12.44 ± 4.92 (6.7–19) years. Three had idiopathic PAH, one was diagnosed with hereditary/familial PAH and one had PAH congenital heart disease (CHD) with persistent PAH after patent ductus arteriosus surgical repair. We reviewed existing clinical data including paediatric Functional Class (FC), six-minute walk test (6MWT), n-terminal pro-b-type natriuretic peptide, specific pulmonary hypertension (PH) treatment and risk determinants.1,3 Two patients had paediatric FC I, two had FC II and one FC IIIb. All except one completed the 6MWT with a mean of 522.75 ± 133.75 m. The patient who could not perform the 6MWT was due to dyspnoea. The mean values for the other measures were: 482.6 ± 720.4 pg/ml for NT-pro BNP, 52 ± 13.84 mmHg for cardiac catheterization (CC) pulmonary
artery pressure and 9.82 ± 3.29 WU·m² for Pulmonary Vascular Resistant Index. All patients had specific pulmonary artery hypertension treatment according to risk determinants.

Acquisition of CMR images was performed on a 3-Tesla scanner (Siemens Magneton Spectra – Erlanger, Germany), with a six-channel body coil, with ECG gating and respiratory navigator, without sedation/general anesthesia or external contrast agent enhancement. One patient, on subcutaneous treprostinil, required pump disconnection while performing CMR. Image acquisition started with T1-weighted anatomical thoracic orthogonal planes followed by coronal lymphangiography acquisition T2-weighted space steer sequence with respiratory navigator that enabled free breathing, repetition time/echo time 2500/650 ms, flip angle of 140° and voxel size of 1.1 x 1.1 x 1.1.4 mm for TD acquisition imaging in 4–6 min. Finally, True FISP at thoracic vertebra 1 or 2 level. Means and standard angle of 140° free breathing, repetition time/echo time 2500/650 ms, flip space steer sequence with respiratory navigator that enabled by coronal lymphangiography acquisition T2-weighted anatomical thoracic orthogonal planes followed by coronal lymphangiography acquisition T2-weighted space steer sequence with respiratory navigator that enabled free breathing, repetition time/echo time 2500/650 ms, flip angle of 140° and voxel size of 1.1 x 1.1 x 1.1.4 mm for TD acquisition imaging in 4–6 min. Finally, True FISP sequence real time cineangiography (GRAPPA, Siemens) was used to obtain right ventricle (RV) and left ventricle (LV) ejection fraction through two-dimensional reoriented short axis multi-sections. This methodology allowed us to perform CMR without breath hold, anesthesia or external contrast enhancement on these fragile PAH paediatric patients.

Post-processing, CMR was performed on a dedicated workstation (SyngoMR-Argus, Siemens) with a 1280-pixel-square-inch-resolution screen according to recommended report standardization. The CMR T2 lymphangiography TD quantification was done through major intensity projection (2D MIP) diameter (mm) and indexed to surface area (mm²/m²) on magnified image of three average measurements at thoracic vertebra 1 or 2 level. Means and standard deviations were calculated and yielded the following values as shown on Table 1. The CMR T2 lymphangiography 2D MIP mean TD diameter was 2.92 ± 0.16 mm and the mean TD index was 2.28 ± 1.03 mm²/m². Qualitative analysis was performed through three-dimensional volume rendered (3D VR) lymphatic reconstruction in order to establish lymphatic abnormality type: Type 1 – little or none, Type 2 – in supraclavicular region, Type 3 – extending into the mediastinum and Type 4 – extending into the lung. The qualitative 3D VR abnormalities were Type 1 in three patients, Type 2 in one and Type 3 in one (Table 1). CMR real-time cineangiography mean RV ejection fraction was 56.6 ± 9.02% and the mean LV ejection fraction was 64.2 ± 8.35% as shown on Table 1 as well. CMR T2 lymphatic abnormality Type 3 was present in the patient with increased NT-pro BNP, and 40% RV ejection fraction as part of high risk determinants (Fig. 1). These findings could be attributed to RV failure. The quantitative and qualitative analyses were performed by one CMR specialist (E.J., 24 years of experience).

Limitations of this study are small number of patients due to low incidence of PAH in paediatric population and lack of genetic study.

### Table 1. PAH patients demographics and CMR results.

| Age | Sex | Diagnosis | FC | 6MWT, m | Pro-BNP pg/ml | mPAP mmHg | PVRI WU.m² | TD mm | TD mm²/m² | EF % Type | RV | LV | T | R |
|-----|-----|-----------|----|--------|----------------|------------|-------------|--------|----------|--------|-----|-----|----|----|
| 12  | F   | HPAH      | II | 545    | 47             | 74          | 15.5        | 3.0    | 2.5      | 1      | 60 | 74 | S  | B  | L  |
| 19  | M   | IPAH      | I  | 643    | 21             | 42          | 10.6        | 3.0    | 1.7      | 1      | 66 | 72 | Ta | A  | L  |
| 6.7 | F   | IPAH      | IIb| 1887   | 51             | 6.8         | 3.0         | 4.2    | 3        | 40     | 60 | S  | B  | Tr | H  |
| 17  | M   | IPAH      | I  | 571    | 15             | 34          | 9.9         | 2.6    | 1.4      | 1      | 55 | 64 | S  | B  | L  |
| 7.5 | M   | PAH       | II | 332    | 443            | 59          | 6.3         | 3.0    | 1.6      | 2      | 62 | 51 | S  | B  | L  |

Note: Bottom line numbers represent mean ± standard deviation.
Cavopulmonary anastomosis, and recently, CMR T2 lymphangiography proved its utility before that procedure if a lymphatic Hraska decompression was necessary when lymphatic abnormality Type III or IV were present.2,9

PAH patients have RV afterload chronically increased and are at risk of developing RV failure. When RV failure occurs, right atrium and systemic venous pressure increases. As TD drains into systemic left jugular subclavian vein, patients with PAH with high-risk determinants and RV failure may have lymphatic abnormality not previously described with CMR T2 lymphangiography.

Conclusions
Magnetic resonance T2-weighted lymphangiography in group 1 paediatric PAH allowed for the identification of the TD, which was used to perform both quantitative and qualitative analyses of thoracic lymphatic abnormalities, in particular when increased high-risk determinants and RV failure were present. These features represent an additional extra cardiac finding useful to understand systemic venous congestion impact on the lymphatic system.

Consent to participate
Written informed consent to participate was obtained in all patients.

Consent to publish case report
All authors signed a consent for publication.

Conflict of interest
The author(s) declare that there is no conflict of interest.

Ethical approval
Local Institutional Ethic and Research Committee of Child and Adults statement accepted this research protocol due to the characteristic of this study (observational and prospective).

Guarantor
Not applicable.

Author contribution
E.J.: study conception, design, analysis, interpretation of data and drafting of manuscript; D.C. and J.P.F.: acquisition of data; A.P., I.J., C.K. and S.L.: critical revision; all authors approved the final version of the manuscript.

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