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CARDIOVASCULAR IMAGING

ORIGINAL ARTICLE

Incidentally enhancing supraclavicular lymphatic convolutes in magnetic resonance angiography in patients with Fontan circulation

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PURPOSE
Fontan procedure and its modifications are the preferred approach to definitive palliation in univentricular hearts though often with short-term or long-term complications. It is believed that a dysfunction in lymphatic circulation is responsible for part of the complications. Occasionally, abnormal supraclavicular lymphatic vessel convolutes can be observed in contrast-enhanced magnetic resonance angiography (ceMRA). This study aims to determine the frequency of this phenomenon as well as a possible correlation with the functional status after Fontan procedure.

METHODS
CeMRA of 37 patients after Fontan surgery was retrospectively screened and grouped for the presence or absence of abnormal lymphatic convolute. An attempt was made to identify differences in the level of dysfunction of the Fontan circulation between the 2 groups.

RESULTS
In 6 of 37 patients (16%), an abnormal cervical lymphatic convolute was found in the cervical venous angle. The surrogate parameters for a malfunction of the Fontan circulation did not significantly differ between both groups.

CONCLUSION
This is the first description of cervical lymphatic vessels in Fontan patients enhancing incidentally in ceMRA, probably due to venous-to-lymphatic reflux. As the likelihood of various complications of Fontan circulation increases with the severity of lymphatic dysfunction, this observation could help to select patients who require closer monitoring or advanced lymphatic imaging.

Almost 50 years have passed since the conception of the Fontan palliation.[1] The technique allows patients with variants of the univentricular heart, one of the most severe heart defects, to survive well into adulthood. In principle, the initial Fontan operation and its numerous modifications recruit the single ventricle to the systemic circulation, whereas pulmonary perfusion takes place purely passively along the systemic venous to pulmonary venous pressure gradient by redirection of the caval veins to the pulmonary arteries. An evaluation of more than 1000 Fontan patients revealed a 10-year survival of 74% and 30-year survival of 43%.[2]

Late mortality is affected not only by cardiac complications, such as arrhythmias, impaired ventricular function and thromboembolism, but also by extracardiac complications such as bronchitis plastica, protein-losing enteropathy, and liver cirrhosis.[3] The pathogenesis of cardiac complications is largely known and is derived from the surgical technique and subsequent hemodynamics.[4] However, the etiology of extracardiac complications is still unclear in many aspects and cannot be entirely explained by cardiovascular conditions alone.

In recent years, there has been increasing evidence to suggest that a disturbance in lymphatic circulation would contribute to the above-mentioned problems.[5] Pathological alterations of the cervical, thoracic, and peripheral lymphatic pathways are therefore likely to be common in patients after Fontan palliation, although they have scarcely been studied to date. The lymphatic drainage can be visualized, either by direct, contrast-enhanced magnetic resonance (MR) lymphography or by T2-weighted, contrast-free MR lymphography[6,7] among other less frequently used techniques.

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During intravenous contrast-enhanced MR angiography (ceMRA), a vascular convolute in the supraclavicular region adjacent to the venous angle was noticed by chance in some of the T1-weighted images in our group of patients. This vascular convolute could be reliably identified as a lymphatic vascular convolute in T2-weighted images. This finding has not yet been presented in the literature. This study is intended to determine the frequency of this phenomenon as well as a possible correlation with the functional status after the Fontan procedure.

Methods

The study was approved by the local Ethics Committee of the University (decision number 501-20-ek) and was conducted according to the ethical standards of the Declaration of Helsinki and its amendments. Informed consent from the parents or the patients was obtained.

The cohort included patients after univentricular palliation using total cavopulmonary anastomosis who presented for regular follow-up at our tertiary care center between 2011 and 2016. A total of 37 patients, listed in the local cardiac magnetic resonance imaging (CMR) database, were retrospectively enrolled.

The details of the ceMRA acquisition have previously been published.[8] In summary, all examinations were performed on a 1.5 T scanner (Achieva, Philips Healthcare) in a supine position with a 5-channel surface coil. Contrast-enhanced, 3-dimensional, spoiled gradient echo MRA was acquired with a voxel size of $0.9 \times 0.9 \times 1.8$ mm. Gadobutrol (Gadovist, Bayer Schering Pharma) was used as an MR contrast agent at a dosage of 0.1 mmol/kg bodyweight. Three temporal phases of contrast enhancement were recorded: a pulmonary arterial phase triggered by care bolus detection in the superior vena cava, a systemic arterial phase about 20 s after arriving of the care bolus, and a delayed phase after another 90 s to visualize the venous distribution. During each phase, the entire field of view (usually extending from the neck to the upper abdomen) was screened for abnormal vascular convolutions by a pediatric radiologist with 10 years of experience in imaging of congenital heart disease. Patients were then assigned to 2 groups based on the presence or absence of an abnormal vascular formation.

The clinical, paraclinical, and functional parameters were taken from the electronic health record. If possible, the parameters obtained during the same hospital stay as the CMR examination were used. If these were not available, the closest possible time points to the CMR were chosen. The following variables were used for further analysis: ventricular function at CMR, central venous pressure (CVP) and transpulmonary pressure gradient from cardiac catheterization, maximum oxygen uptake from spiroergometry, and N-terminal pro-brain natriuretic peptide from blood samples.

Statistical analysis

Due to the limited sample size, normal distribution was not assumed. Therefore, the median along with minimal and maximal values are given and a non-parametric test was applied in order to assess the central tendency. Both groups were compared with respect to each of the parameters by using the Mann–Whitney *U* test. The level of significance was set to $P < .05$.

Results

The median age of the 37 patients enrolled in this retrospective study was 14.7 years (range: 6.8-53.8 years) with a gender ratio of 1.2 : 1 (male to female). At the ceMRA, 6 out of 37 (16%) Fontan patients were found to have an abnormal vascular convolute (Table 1). This was invariably located supraclavicular in the jugular vein angle. In 5 patients, the right cervical angle and in one of the patients the left angle were affected. None of the subjects exhibited a contrast enhancement of the intrathoracic lymph vessels. In the pulmonary arterial phase, the convolute was hardly delineable. In the systemic arterial phase, some patients already had a beginning of vascular enhancement in the venous angle. In the systemic venous phase, a peak in the size of the convolute was observed. The extent of the convolute was very heterogeneous in the subjects (Figure 1).

The comparison between the groups with and without an enhancing supraclavicular convolute did not reveal any

Main points

- Thoracic and cervical lymphatic anomalies in patients with Fontan circulation are common.
- These have been shown to be associated with a poorer function of the univentricular circulation.
- In some patients, cervical lymphatic convolute enhanced incidentally in magnetic resonance angiography.
- Fontan patients with the aforementioned phenomenon should be examined in more detail.

Table 1. Characteristics of the patients presenting with an abnormal lymphatic convolute

Panel	Age (years)	Diagnosis	Interval (years)	Other specifics
a	15	Unbalanced AVSD, DORV, DAA, heterotaxia, dextrocardia, asplenia	10	Embolization of a coronary fistula, MVR III, intrapulmonary shunts
b	24	DORV, large inlet-VSD, straddling of the TV, d-MGA, PS	18	Recurrent atrial flutter after several catheter ablations
c	18	Univentricular heart from right ventricular type, heterotaxia, dextrocardia, l-MGA, PA, MA, RAA	11	LPA stenosis with stent; intrapulmonary shunts
d	13	HLHS	10	LPA stenosis with stent; BAP of RPA
e	12	Unbalanced AVSD, TGA, PS, heterotaxia, asplenia	5	Prolonged right sided pleural effusion post Fontan; MVR III°
f	25	Tricuspid atresia, Fontan-Doty, conversion to TCPC with intraatrial tunnel, finally conversion to TCPC with extracardiac conduit	15	Recurrent atrial flutter

The first column corresponds to the illustration in Figure 1. Interval refers to the time interval after definitive Fontan palliation.
AVSD, atrioventricular septal defect; DORV, double outlet right ventricle; DAA, double aortic arch; VSD, ventricular septal defect; TV, tricuspid valve; MGA, malposition of the great arteries; PS, pulmonary stenosis; PA, pulmonary atresia; RAA, right aortic arch; HLHS, hypoplastic left heart syndrome; TGA, transposition of the great arteries; TCPC, total cavopulmonary anastomosis; MVR, mitral valve regurgitation; LPA, left pulmonary artery; BAP, balloon angioplasty; RPA, right pulmonary artery.

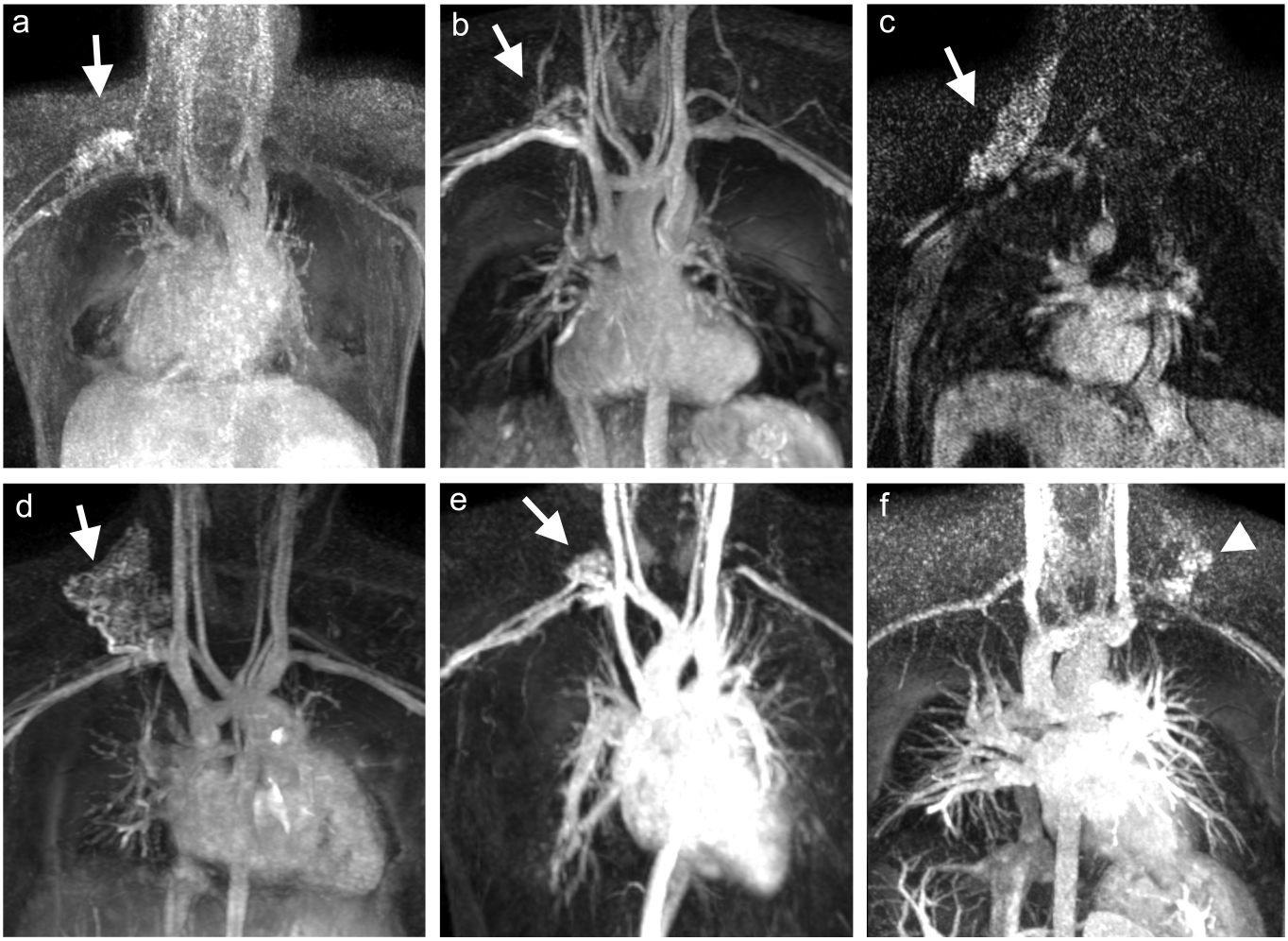

Figure 1. a-f. Contrast-enhanced magnetic resonance angiography (coronal maximum intensity projection) in 6 patients after Fontan procedure. In addition to the blood vascular system, an additional vascular convolute in the cervical venous angle is contrasted. In 5 patients **(a-e)**, the contrasted convolutes were located on the right (*white arrow*). Only in 1 subject **(f)**, the convolute was located on the left (*white arrowhead*). For characteristics of the individual patients see Table 1.

Table 2. Comparison of functional parameters in patients with abnormal convolutes in ceMRA against controls

	With convolute (n = 6)	Without convolute (n = 31)	*P*
Systemic EF (%)	41.1 (33-52)	49.9 (25-64)	.065
CI (L/min m^2)	2.93 (2.4-4.6)	3.11 (2.0-5.9)	.805
Lymphocytes (10^9/L)	0.31 (0.2-0.39)	0.27 (0.06-0.04)	.721
ALT (µmol/L)	0.46 (0.32-0.62)	0.55 (0.34-0.96)	.558
AST (µmol/L)	0.65 (0.39-1.02)	0.55 (0.34-0.87)	.507
gGT (µmol/L)	1.14 (0.91-1.52)	1.25 (0.64-1.56)	.857
proBNP (ng/L)	423 (93-1063)	260 (10-1232)	.331
tc-sO2 (%)	94.3 (92-97)	95.6 (87-99)	.118
TPG (mmHg)	4.5 (3-7)	5.4 (2-10)	.343
CVP (mmHg)	11.3 (7-15)	11.3 (6-18)	1.000
VO_2max (mL/min/kg)	24.4 (16.3-31.1)	26.9 (11.7-36.7)	.682

The median along with the minimum and maximum values is given. Though the level of significance was missed, there is a tendency toward lower LV-EF, higher proBNP, and increased CVP in patients with an abnormal lymphatic convolute.
EF, ejection fraction (LV-EF); CI, cardiac index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; gGT, gamma glutamyl transferase; proBNP, N-terminal pro-brain natriuretic peptide; tc-sO_2, transcutaneous oxygen saturation; TPG, transpulmonary gradient; CVP, central venous pressure; VO_2max, maximum oxygen uptake in spiroergometry.

significant differences in age (median age 16.6 years vs. 14.6 years, P = .481), gender (male to female ratio 4 : 2 vs. 15 : 16, P = .661), the investigated cardiopulmonary functional parameters, or laboratory findings (Table 2). None of the individuals suffered from bronchitis plastica or protein-losing enteropathy.

Discussion

To the best of our knowledge, this is the first time that contrast enhancement of abnormal cervical convolutes has been demonstrated in almost every sixth patient in a cohort of Fontan patients. It can be assumed with confidence that these findings represent lymphatic vessels comparing lymphatic convolutes described several times by T2-lymphography.[9,10]

It is not yet completely evident why lymphatic vessels are contrasted after intravenous administration of a contrast

medium. A lymphatic elimination of gadolinium that has diffused into the interstitial space is unlikely since a part of the bundle is already visible in the systemic arterial phase. A fistula between arterioles and lymphatic vessels in the neck region is likewise unlikely, since the marked pressure gradients across the arterial and lymphatic system would have led to a more pronounced dilatation of the lymphatic vessels. In our opinion, the most plausible scenario is a slow retrograde contrast flow into the cervical lymphatic ducts at the venous angle.

Such backflow should in fact be prevented by a valve in the lymphatic vessels near the junction in the venous angle, especially because the influx of blood into the lymphatic vessel can trigger the formation of thrombi.[11] The lymphatic outflow from the thoracic duct into the cervical venous angle happens passively, facilitated by the pressure relations which vary with the respiratory cycle and the heartbeat. With regard to Fontan circulation, the CVP is distinctly elevated, ideally to 12-15 mmHg[5] and shows no decline during the atrial filling phase. Both of these factors hinder the passive outflow from the thoracic duct. It is conceivable that the high CVP may lead to a dilatation of the lymphatic vessels and thus to incompetence of the lymphatic valves. This would resemble the well-known venous valve insufficiency in varicosis. This might only occur when CVP is further increased through power injection of the contrast agent.

It is reasonable to assume that there is a correlation between the degree of lymphatic congestion and the extent of valve insufficiency. Patients with such a convolute in our group tend to present with a rather poor functional status of the Fontan circulation. This is concordant with the systematic study by Biko et al., who were able to correlate the degree of lymphatic congestion with the severity of complications after the Fontan procedure.[9] The level of significance in our study was missed, probably due to the small number of affected subjects (n = 6).

Besides the fact that these anomalies in the ceMRA in Fontan patients have never been reported in the literature, the relevance of these observations arises from the following practical considerations: Both T2-weighted lymphography and direct contrast-enhanced lymphography are technically challenging and, unlike ceMRA, have not yet been implemented in routine CMR follow-up after Fontan procedure.[12] An observation of the lymphatic phenomena in ceMRA could support the selection of patients for this specific lymphographic imaging. The assessment of an abnormal lymphatic status is of particular relevance because interventional[9,13] and surgical[14] therapies with positive outcome have been reported.

In conclusion, even though the study has limitations due to its retrospective nature and the relatively small number of cases, the mere first-time description of this phenomenon in the ceMRA is a relevant report. This is all the more true as it forms a piece in the mosaic of the overall picture of lymphatic dysfunction in Fontan patients that has emerged over the last few years.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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