Original Article

Evaluation of the diagnostic and prognostic potential of optical coherence tomography (OCT) of the pulmonary arteries during standardised right heart catheterisation in patients with pulmonary hypertension: a cross-sectional single-centre experience

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Background: Pulmonary hypertension (PH) is diagnosed based on an invasive evaluation of the mean pulmonary artery (PA) pressure. The morphological assessment of the pulmonary arteries was only recently not feasible. With the advent of optical coherence tomography (OCT)-imaging, an accessible tool allows to study PA morphology longitudinally. The primary hypothesis was that OCT distincts the PA structure of PH patients from control subjects. The secondary hypothesis was that PA wall thickness (WT) correlates with the progression of PH.

Methods: This is a retrospective monocentric study of 28 paediatric patients with (PH group) and without PH (control group) who had undergone cardiac catheterisation including OCT imaging of the PA branches. OCT parameters analysed were WT and the quotient of WT and diameter (WT/DM) and those were compared between the PH group and the control group. In addition, the OCT parameters were aligned with the haemodynamic parameters to evaluate the potential of OCT as a risk factor for patients with PH.

Results: WT and WT/DM in the PH group were significantly higher compared to the control group {WT: 0.150 [0.230, range (R): 0.100–0.330] *vs.* 0.100 [0.050, R: 0.080–0.130] mm, P<0.001; WT/DM: 0.06 [0.05] *vs.* 0.03 [0.01], P=0.006}. There were highly significant correlations between WT and WT/DM with the haemodynamic parameters mean pulmonary arterial pressure (mPAP) [Spearman correlation coefficient (r_s) =0.702, P<0.001; r_s=0.621, P<0.001], systolic pulmonary arterial pressure (sPAP) (r_s=0.668, P<0.001; r_s=0.658, P<0.001) and WT and pulmonary vascular resistance (PVR) (r_s=0.590, P=0.02). Also, there was a significant correlation between WT and WT/DM and the risk factors quotient of mPAP and mean systemic arterial pressure (mSAP) (mPAP/mSAP) (r_s=0.686, P<0.001; r_s=0.644, P<0.001) and pulmonary vascular resistance index (PVRI) (r_s=0.758, P=0.002; r_s=0.594, P=0.02).

Conclusions: OCT can detect significant differences in WT of the PA in patients with PH. Furthermore, the OCT parameters correlate significantly with haemodynamic parameters and risk factors for patients with PH. More investigations are required to evaluate to what extent the impact of OCT can contribute to the clinical care of children with PH.

Keywords: Pulmonary hypertension (PH); optical coherence tomography (OCT); wall thickness (WT); paediatric

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Introduction

Pulmonary hypertension (PH) in children is a rare disease (1-3). The diagnostic gold standard remains the right heart catheterisation (RHC) with the assessment of the haemodynamic parameters and acute vasodilator testing (4-6). Several prognostic parameters such as evidence of right ventricular failure, significantly elevated or rising N-terminal prohormone of brain natriuretic peptide (NT-pro-BNP), failure to thrive, mean right atrial pressure (mRAP), cardiac index (CI), mean pulmonary arterial pressure/mean systemic arterial pressure (mPAP/mSAP) and pulmonary vascular resistance index (PVRI) are used for risk assessment and are essential for therapeutic decisions (6,7). In contrast to adults, the diagnosis in paediatric patients often occurs in later stages (7) and disease progression remains unpredictable (8). Optical coherence tomography (OCT) is a relatively new imaging method in biomedical optics comparable to ultrasound but in contrast to ultrasound, the OCT uses light instead of sound. The physical principle of interferometry is based on the magnitude and echo time delay of infrared light to create high-resolution two- and three-dimensional images with approximately 10 to 20 (9-11). Compared to the limited resolution of intravascular ultrasound with about 100 to 200 µm, which results from the broader wavelength of sound compared to light, OCT enables a more detailed image acquisition and therefore is superior to intravascular ultrasound (9,12). Although intravascular application field of OCT in cardiology has mainly been the coronary arteries (13), its application in the pulmonary artery (PA) seems promising. Since 2010, several authors have reported on the safe use of OCT in the PA of adults and its potential to visualize morphologic changes in the PA vessel wall of patients with PH *in vivo*. The potential of PA OCT in PH to guide clinical decision making has been recognised (12,14-21). In 2018, Homma *et al.* showed for the first time that OCT is a promising tool for the evaluation of the PA wall even in children with PH (22). However, the data about OCT in the PA, especially in the paediatric population, is scarce. It was the primary hypothesis of this study that OCT imaging reveals a PA structure in patients with PH that is distinct from controls. The secondary hypothesis was that PA wall thickness (WT) correlates with the progression of PH (consider mPAP, sPAP, PVRI and CI). If changes in PA WT can reliably be assessed with OCT, OCT may become an additional clinical diagnostic and prognostic parameter for patients with PH which could improve clinical management and outcome of patients with PH. We present this article in accordance with the STROBE reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-22-421/rc).

Highlight box

Key findings

- In patients with pulmonary hypertension, the OCT revealed significantly higher WT and WT/DM and significant correlations with haemodynamic parameters such as mPAP, sPAP and PVR.

What is known, and what is new?

- OCT has mainly been used in the coronary arteries. The safe use of OCT in the PA of adult patients with PH *in vivo* was reported. However, the data about OCT in the PA, especially in the paediatric population, is scarce. This study confirms that OCT also detects morphological changes in the PA correlating with haemodynamic parameters in the paediatric population.

What is the implication, and what should change now?

- The impact of OCT can contribute to the clinical care of children with PH. Therefore, more investigations are required to evaluate to what extent the OCT can contribute to clinical care.

Methods

Study population and ethic aspects

This retrospective, monocentric, cross-sectional study from the Department of Paediatric Cardiology and Intensive Care of the Ludwig-Maximilians-University in Munich has used OCT during standardised RHC for evaluation of the PA wall. All OCT assessments of the PA were performed between February 2016 and April 2019 fulfilling the following inclusion criteria: (I) RHC in the PA with a pulsatile flow; (II) documented mPAP during RHC; (III) sufficient quality of the OCT records [(i) clear delineation of the luminal and abluminal border of WT in three locations of the vessel wall circumference in at least three cross-sections of the OCT record and (ii) complete imaging of the vessel wall circumference in at least three cross-sections of the OCT record to measure the inner diameter (DM)]. Except for one subject who was examined twice, all subjects were examined once during the study period. Detailed selection of patients can be found in *Figure 1*.

According to the current recommendation of the 6th World Symposium on Pulmonary Hypertension in Nizza 2018 (6), all patients were stratified into two subgroups: patients with PH (PH group) [mPAP >20 mmHg and pulmonary vascular resistance (PVR) ≥3 WU] and patients without PH (control group) (mPAP ≤20 mmHg and PVR <3 WU). Two subjects were allocated to the PH group based on mPAP only because

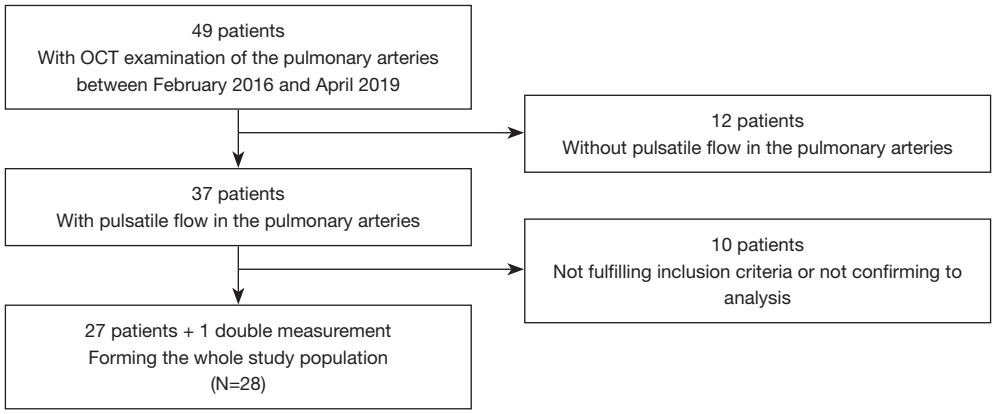

Figure 1 Selection of patients. OCT, optical coherence tomography.

PVR was not feasible. One of the control subjects was allocated to the control group although the mean right- and left-sided mPAP was 21 mmHg, one of the two measurements only showed mPAP <20 mmHg. This study was approved by the local Ethics Committee at the Medical Faculty of the Ludwig-Maximilians-University of Munich (project number: 18-516) and conformed to the ethical guidelines of the Declaration of Helsinki (as revised in 2013). For all subjects, written informed consent was obtained. For minor patients, the consent of the legal guardian was obtained.

Analysis of the OCT records

Analysis of the OCT records was a standardised procedure performed by one observer with the medical imaging software QIvus (Version 3.0) (23). From each OCT record, the section consisting of three consecutive cross-sections with the highest image quality and the most distal localisation in the PA branch were obtained for the analysis. In the cross-sections, DM was measured semiautomatically (operator involvement was required) once and WT was measured manually three times in three different pulmonary arterial wall locations (*Figure 2*). The arithmetic mean of WT and WT/DM were allocated per cross-section. Subsequently, the final average of DM, WT and WT/DM of all three cross-sections was specified and analysed. WT is the distance between the intima and the approximate outer limit of the media, identified through the vessel wall's highly reflective layer. Twenty-three of the 28 OCT records were analysed again by the same observer blinded to diagnosis.

Data acquisition and statistical analysis

OCT image acquisition is a standardized procedure according to the international standards of OCT in the coronary arteries (13,24,25). In our study, OCT was performed transvenously using a 6 French sheath and a 6 French right or left coronary guiding catheter. A 0.014' coronary guidewire (Asahi Sion® Blue, ASAHI INTECC USA INC.) was introduced into the peripheral pulmonary arteries allowing for introducing of the 2.6 French OCT catheter of Terumo in a monorail technique. For imaging, a contrast injection with approximately 15 mL of contrast medium was performed, and simultaneously the OCT image acquisition was started. During RHC and OCT, no patient of the study showed any complications.

Patient data and parameters assessed during RHC (demographic data, haemodynamic parameters and technical and assessed OCT data) were documented using Microsoft Excel (Version 2160) (26). Statistical analysis was performed using IBM SPSS Statistics (Version 26.0) (27). All variables were tested for normal distribution with Kolmogorov-Smirnov-test and Shapiro-Wilk-test and by visual inspection of the respective histograms and QQ-plots. To compare the characteristics of the PH group and the control group, Mann-Whitney-U-test and *T*-test were used for non-parametric and parametric variables. Variables with less than ≤7 cases (n) in one group were not considered for group comparison. For correlation analysis of non-parametric and parametric variables, Spearman correlation coefficient (r_s) and Pearson correlation coefficient (r_p) were calculated. To analyse the reproducibility of OCT measurements in the PA, two independent OCT images were analysed by one observer. Then, the intraclass correlation coefficient (ICC) (28) ("model": two-way mixed model, "type": single-measurement, "definition": absolute-agreement) was calculated and a Bland Altman plot (29) was created. All results presented in mean ± standard deviation (m ± SD) (parametric variables) or median and range [med (R)]

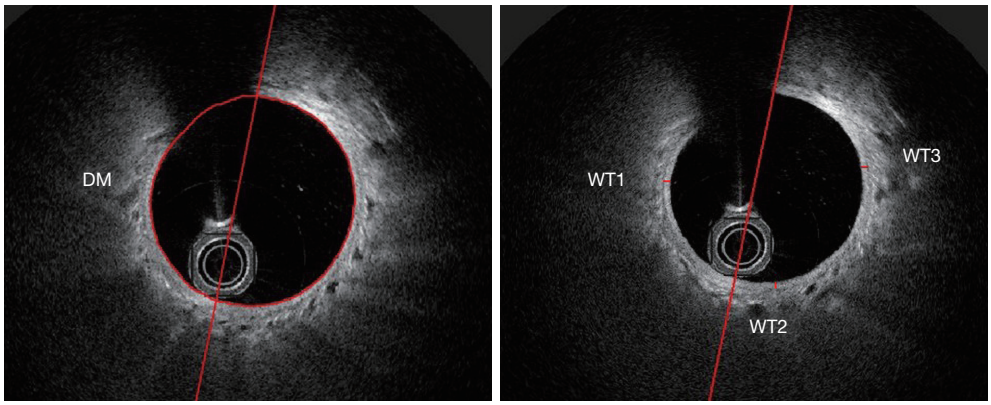

Figure 2 Analysis of the OCT records. Analysis of the OCT records was a standardised procedure. Per patient, three cross-sections were analysed. In each analysed cross-section, DM was analysed semiautomatically once (left picture), and WT was analysed at three different locations in the pulmonary arterial wall (WT1, WT2, WT3) (right picture). DM, diameter; WT, wall thickness; OCT, optical coherence tomography.

Table 1 Baseline characteristics

Variable	n	Values
Demographic data		
Age (years)	28	14.0 [60.0, 2.0–62.0]
Height (cm)	28	152.0 [111.0, 81.0–192.0]
Weight (kg)	28	42.7 [82.4, 8.6–91.0]
BSA (m^2)	28	1.4 [1.7, 0.4–2.1]
Haemodynamic data		
mPAP (mmHg)	28	19.5 [81.0, 7.0–88.0]
sPAP (mmHg)	28	25.0 [114.0, 10.0–124.0]
mSAP (mmHg)	28	74.4±10.3
Risk parameters		
mPAP/mSAP	28	0.3 [1.1, 0.1–1.2]
PVRI (WU × m^2)	14	7.9 [31.4, 1.6–33.0]
CI (L/min/m^2)	17	3.8 [3.2, 2.3–5.5]

Data are presented as med [R, Min-Max] or mean ± standard deviation. BSA, body surface area; mPAP, mean pulmonary arterial pressure; sPAP, systolic pulmonary arterial pressure; mSAP, mean systemic arterial pressure; mPAP/mSAP, quotient of mPAP and mSAP; PVRI, pulmonary vascular resistance index; WU, Wood units; CI, cardiac index; med, median; R, range; Min, minimum; Max, maximum.

(non-parametric variables). For ICC and Bland-Altman Plot the 95% confidence interval (95% CI) is presented. A value of P<0.05 was considered statistically significant.

Results

Patient's characteristics

Study population

There were 15 females (53.6%) and 13 males (46.4%). Thirteen patients were in the PH group (46.4%) and 15 patients (53.6%) were in the control group. Baseline characteristics are summarized in *Table 1*.

Patients with PH

Diagnostic classification of patients with PH

According to the current haemodynamic definitions in Nizza 2018 (30), 10 patients (76.9%) had pre-capillary PH [mPAP <20 mmHg, PVR ≥3 WU, pulmonary capillary wedge pressure (PCWP) ≤15 mmHg] and 3 patients (23.1%) had combined pre- and post-capillary PH (mPAP <20 mmHg, PVR ≥3 WU, PCWP >15 mmHg).

Seven patients (53.8%) had pulmonary arterial hypertension (PAH) (Nizza Group 1): 5 patients with IPAH (Nizza Group 1.1) and 2 patients with PH associated with congenital heart disease (CHD-PAH) (Nizza Group 1.4.4). Two patients (15.4%) had PH due to left heart disease (Nizza Group 2), 1 patient (7.7%) had PH due to lung diseases and/or hypoxia (Nizza Group 3), 1 patient (7.7%) had PH due to PA obstructions (Nizza Group 4) and 2 patients

Table 2 Risk factors of patients with PH

Risk factors in PH group	n	Med [R, Min-Max]	Mean ± SD	95% CI
mPAP/mSAP	13	0.5 [0.9, R: 0.3–1.2]	0.6±0.3	0.4–0.8
PVRI (WU × m²)	11	9.0 [29.1, R: 3.9–33.1]	10.1±8.9	4.9–15.2
CI (L/min/m²)	11	3.6 [2.2, R: 2.3–4.5]	3.7±0.8	3.3–4.1
mRAP (mmHg)	8	4.5 [22.0, R: 1.0–23.0]	7.8±8.2	0.9–14.6
NT-pro-BNP (pg/mL)	12	658.0 [8,772.3, R: 28.7–8,801.0]	1,283.9±2,429.5	259.8–2,827.5
TAPSE	11	1.7 [3.2, R: 0.8–4.0]	1.7±0.5	1.4–2.1

PH, pulmonary hypertension; med, median; R, range; Min, minimum; Max, maximum; SD, standard deviation; 95% CI, 95% confidence interval; mPAP/mSAP, quotient of mean pulmonary arterial pressure and mean systemic arterial pressure; PVRI, pulmonary vascular resistance index; WU, Wood units; CI, cardiac index; mRAP, mean right atrial pressure; NT-pro-BNP, N-terminal prohormone of brain natriuretic peptide; TAPSE, tricuspid annular plane systolic excursion.

Table 3 Diagnosis of patients in the PH group and the control group

Groups	Diagnosis	n (%)
PH group		13 (100.0)
	PAH	7 (53.8)
	With idiopathic PAH	5
	With CHD-PAH	2
	PH due to left-heart disease	2 (15.4)
	PH due to lung-disease	1 (7.7)
	PH due to pulmonary artery obstructions	1 (7.7)
	PH with multifactorial mechanisms	2 (15.4)
Control group		15 (100.0)
	Congenital heart defect	6 (40.0)
	Post heart transplantation	3 (20.0)
	Pulmonary stenosis	2 (13.3)
	Myocarditis	2 (13.3)
	Interstitial lung diseases	1 (6.7)
	Hypertrophic cardiomyopathy	1 (6.7)

PH, pulmonary hypertension; PAH, pulmonary arterial hypertension; CHD-PAH, PAH with congenital heart disease.

(15.4%) had a PH with unclear and/or multifactorial mechanism (Nizza Group 5).

Medication of patients with PH

Common medication in the PH group included diuretics [6 patients (46.2%) were treated with Spironolactone, 4 patients (30.7%) were treated with Furosemide], phosphodiesterase type 5 inhibitors [6 patients (46.2%) were treated with Tadalafil, 2 patients (15.4%) were treated with Sildenafil], endothelin receptor antagonists [4 patients (30.7%) were treated with Macitentan, 1 patient (0.7%) was treated with Bosentan] and calcium channel blockers [3 patients (23.1%) were treated with Amlodipine].

Risk factors of patients with PH

Assessed risk factors for patients with PH are summarized in *Table 2*.

Diagnosis in the control group

Six patients (40.0%) had congenital heart defects (2 patients with tetralogy of Fallot, 1 patient with atrial septal defect, 1 patient with aortic atresia, 1 patient with open ductus arteriosus and 1 patient with truncus arteriosus communis), 3 patients (20.0%) were examined after heart transplantation, 2 patients (13.3%) had pulmonary valve stenosis, 2 patients (13.3%) had myocarditis, 1 patient (6.7%) had an interstitial lung disease and 1 patient (6.7%) had hypertrophic cardiomyopathy.

Diagnosis of PH group and control group are summarized in *Table 3*.

OCT records of the pulmonary arteries

OCT records in the study population

The WT of examined pulmonary arterial vessels in the whole study population was 0.110 [0.250, R: 0.0.080–0.330] mm and WT/DM was 0.04 [0.07, R: 0.02–0.09]. The DM

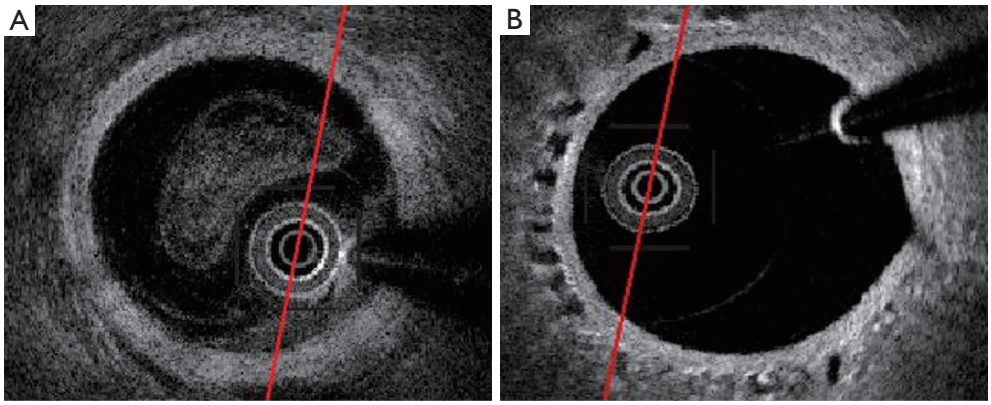

Figure 3 OCT cross-sections of the pulmonary arterial wall in a patient of PH group and control group. Figure 3 shows two OCT cross-sections of the PA in a patient with PH (A) and in a patient without PH (B). WT assessed with OCT in the PA of the patient with PH is higher compared to the patient without PH. (A) WT: 0.20 mm, DM: 2.17 mm, WT/DM: 0.09, mPAP: 79 mmHg, sPAP: 95 mmHg. (B) WT: 0.09 mm, DM: 2.24 mm, WT/DM: 0.04, mPAP: 11 mmHg, sPAP: 19 mmHg. OCT, optical coherence tomography; PA, pulmonary artery; PH, pulmonary hypertension; WT, wall thickness; DM, diameter; WT/DM, quotient of WT and DM; mPAP, mean pulmonary arterial pressure; sPAP, systolic pulmonary arterial pressure.

was 2.820 [3.270, R: 1.590–4.860] mm.

OCT records in patients with PH and comparison subjects

In PH patients, WT was significantly increased compared to control group {0.150 [0.230, R: 0.100–0.330] *vs.* 0.100 [0.050, R: 0.080–0.130] mm, P<0.001}. In addition, WT/DM in the PH group was significantly higher compared to control group {0.06 [0.06, R: 0.03–0.09] *vs.* 0.03 [0.04, R: 0.02–0.06], P=0.006}. There was no significant difference in DM between the groups {2.770 [3.060, R: 1.800–4.860] *vs.* 2.870 [2.580, R: 1.590–4.170] mm, P=0.85}.

Figure 3 shows two OCT cross sections of a patient from PH group and the control group.

In *Table 4*, comparison of PH group and control group in demographic data, haemodynamic data and OCT parameters is summarized.

Relationship between OCT parameters and haemodynamic parameters and risk factors

Correlations between the OCT parameters WT and WT/DM and the haemodynamic parameters mPAP (r_s=0.702, P<0.001; r_s=0.621, P<0.001) and sPAP (r_s=0.668, P<0.001; r_s=0.658, P<0.001) were highly significant. Additionally, WT correlated significantly with the haemodynamic parameter PVR (n=14) (r_s=0.590, P=0.02). Also, the OCT parameters correlated significantly with two risk factors for patients with PH: WT and WT/DM and mPAP/mSAP (r_s=0.686, P<0.001; r_s=0.644, P<0.001) and WT and WT/DM and PVRI (n=14) (r_s=0.758, P=0.002; r_s=0.594, P=0.02). Correlation between the OCT parameters WT and WT/DM and demographic variables and other haemodynamic parameters and risk factors were not significant: age (r_s=0.018, P=0.92; r_s=–0.012, P=0.95), body height (r_s=–0.163, P=0.40; r_s=–0.096, P=0.62), body weight (r_s=–0.230, P=0.23; r_s=–0.095, P=0.63), body surface area (BSA) (r_s=–0.213, P=0.27; r_s=–0.113, P=0.56), mSAP (r_p=–0.181, P=0.35; r_p=–0.113, P=0.56), PCWP (r_p=–0.143, P=0.53; r_p=0.126, P=0.58), cardiac output (CO) (r_s=–0.315, P=0.21; r_s=–0.455, P=0.06), CI (r_s=–0.124, P=0.635; r_s=–0.211, P=0.41), mRAP (r_s=–0.542, P=0.165; r_s=–0.327, P=0.42), NT-pro-BNP (r_s=0.375, P=0.22; r_s=0.457, P=0.135), tricuspid annular plane systolic excursion (TAPSE) (r_s=0.149, P=0.66; r_s=–0.113, P=0.74) (also, correlation between WT and DM was not significant (r_s=0.085, P=0.66).

Table 5 summarizes significant correlations between OCT parameters and haemodynamic and risk parameters.

Significant correlations between the OCT parameters and the haemodynamic parameters and risk factors are presented in *Figures 4,5*.

Table 4 Comparison of PH group and control group in demographic data, haemodynamic data and OCT parameters

Variable	Total (n=28)	PH (n=13)	CG (n=15)	P
Demographic data				
Age (years)	14.0 [60.0, 2.0–62.0]	10.0 [60.0, 2.0–62.0]	15.0 [18.0, 3.0–21.0]	>0.99
Height (cm)	152.0 [111.0, 81.0–192.0]	152.0 [94.5, 81.0–175.5]	160.0 [90.0, 102.0–192.0]	0.33
Weight (kg)	42.7 [82.4, 8.6–91.0]	43.6 [66.4, 8.6–75.0]	41.7 [77.0, 14.0–91.0]	0.18
BSA (m^2)	1.4 [1.7, 0.4–2.1]	1.4 [1.5, 0.4–1.9]	1.4 [1.5, 0.6–2.1]	0.18
Haemodynamic data				
mPAP (mmHg)	19.5 [81.0, 7.0–88.0]	40.0 [67.0, 21.0–88.0]	14.0 [14.0, 7.0–21.0]	<0.001*
sPAP (mmHg)	25.0 [114.0, 10.0–124.0]	69.7±28.5	19.6±4.5	<0.001*
mSAP (mmHg)	74.4±10.3	73.2±8.5	75.4±11.8	0.58
mPAP/mSAP	0.3 [1.1, 0.1–1.2]	0.5 [0.9, 0.3–1.2]	0.2 [0.2, 0.1–0.3]	<0.001*
OCT parameters				
WT (mm)	0.110 [0.250, 0.080–0.330]	0.150 [0.230, 0.100–0.330]	0.100 [0.050, 0.080–0.130]	<0.001*
DM (mm)	2.820 [3.270, 1.590–4.860]	2.770 [3.060,1.800–4.860]	2.870 [2.580, 1.590–4.170]	0.85
WT/DM	0.04 [0.07, 0.02–0.09]	0.06 [0.06, 0.03–0.09]	0.03 [0.04, 0.02–0.06]	0.006*

Data are presented as med [R, Min-Max]; mean ± standard deviation. *, P value <0.05 is considered as statistically significant. Statistical tests: age, height, weight, BSA, mPAP, mPAP/mSAP, WT, DM. WT/DM: Mann-Whitney-U-test. sPAP and mSAP: *t*-test. PH, pulmonary hypertension; BSA, body surface area; mPAP, mean pulmonary arterial pressure; mPAP/mSAP, quotient of mPAP and mSAP; mSAP, mean systemic arterial pressure; WT, wall thickness; DM, diameter; WT/DM, quotient of WT and DM; sPAP, systolic pulmonary arterial pressure; M, mean; SD, standard deviation; CG, control group; OCT, optical coherence tomography; med, median; R, range; Min, minimum; Max, maximum.

Table 5 Correlation between OCT parameters and haemodynamic and risk parameters

Variable	N	n (PH)	n (CG)	C	WT (mm)	WT/DM
mPAP (mmHg)	28	13	15	r_s	0.702	0.621
				P	<0.001*	<0.001*
sPAP (mmHg)	28	13	15	r_s	0.668	0.658
				P	<0.001*	<0.001*
mPAP/mSAP	28	13	15	r_s	0.686	0.644
				P	<0.001*	<0.001*
PVR (WU)	14	11	3	r_s	0.590	0.460
				P	0.02*	0.09
PVRI (WU × m^2)	14	11	3	r_s	0.758	0.594
				P	0.002*	0.02*

*, P value <0.05 is considered as statistically significant. Statistical test: Spearman correlation analysis. r_s: Spearman correlation coefficient. OCT, optical coherence tomography; PH, pulmonary hypertension; CG, control group; WT, wall thickness; WT/DM, quotient of WT and DM; DM, diameter; mPAP, mean pulmonary arterial pressure; sPAP, systolic pulmonary arterial pressure; mPAP/mSAP, quotient of mPAP and mSAP; mSAP, mean systemic arterial pressure; PVR, pulmonary vascular resistance; WU, Wood units; PVRI, pulmonary vascular resistance index.

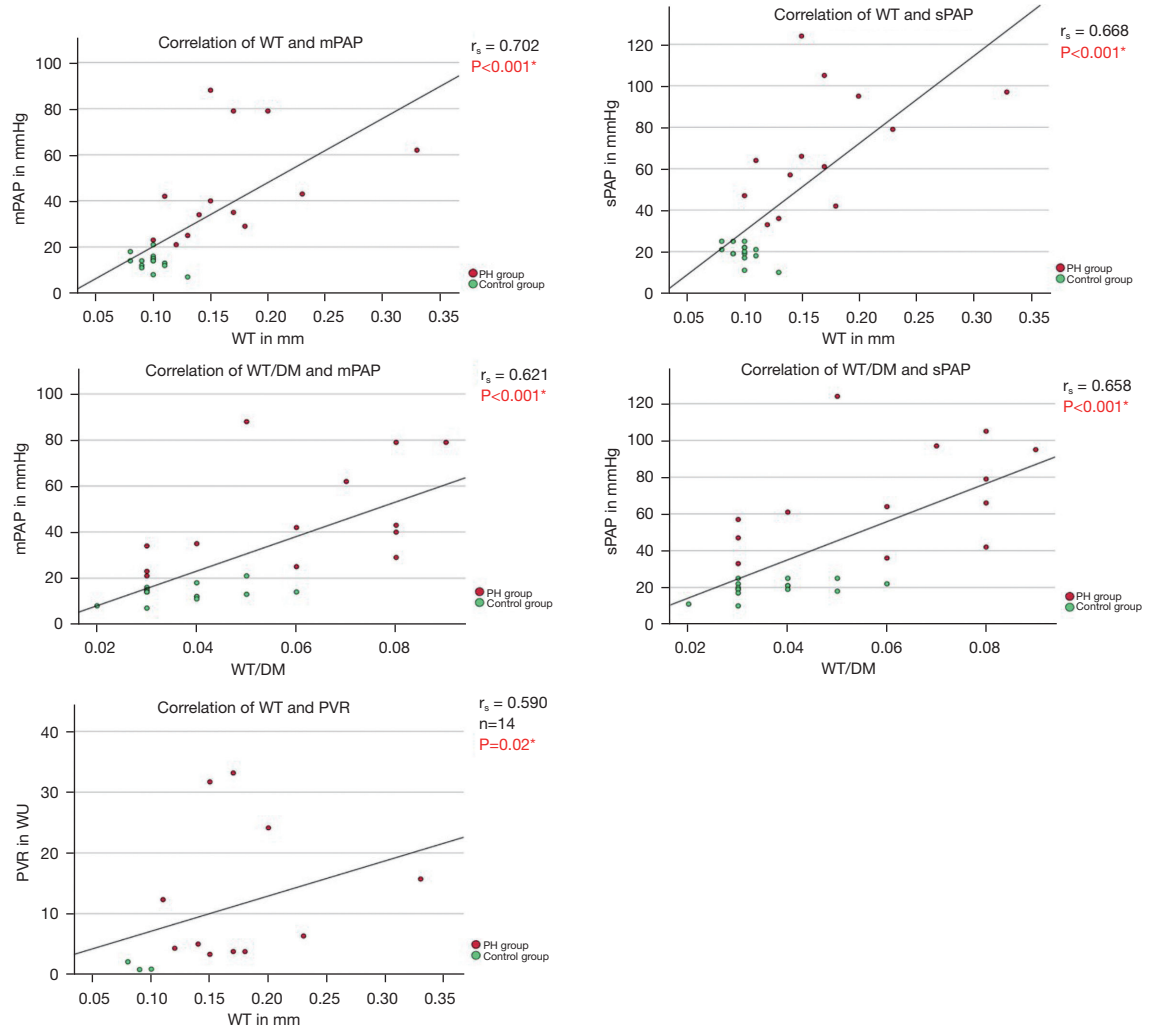

Figure 4 Correlation of OCT parameters and haemodynamic parameters. Statistical test: Spearman correlation analysis. *, P value <0.05 is considered as statistically significant. In a group of 28 patients (PH: n=13, CG: n=15), the OCT parameters WT and WT/DM showed significant correlation with the haemodynamic parameters mPAP (r_s=0.702, P<0.001; r_s=0.621, P<0.001) and sPAP (r_s=0.668, P<0.001; r_s=0.658, P<0.001, also, correlation between WT and the haemodynamic parameter PVR was significant (r_s=0.590, P=0.02). r_s: Spearman correlation coefficient. WT, wall thickness; mPAP, mean pulmonary arterial pressure; PH, pulmonary hypertension; sPAP, systolic pulmonary arterial pressure; WT/DM, quotient of WT and DM; DM, diameter; PVR, pulmonary vascular resistance; WU, Wood units; OCT, optical coherence tomography; CG, control group.

Intraobserver-variability of OCT in pulmonary arteries

The comparison of two independent analyses of 23 of the 28 OCT records showed good reproducibility of OCT in the PA. ICC was 0.953 with a 95% CI of 0.893 to 0.980 (P<0.001). Bland-Altman plot showed only a mean difference in both independent OCT analyses of −0.0004 with a 95% CI of −0.036 to 0.035 mm. Apart from one value, the differences of both analyses were within the 95% CI.

Technical data

In total, 73 OCT images of 28 patients were recorded. Forty-six out of 73 (63.0%) had sufficient quality to perform the OCT analysis procedure. In 24 analysed OCT records (85.7%), pullback speed during OCT examination was 20.0 mm/s and in 4 OCT records (14.3%) it was 40.0 mm/s. The image rate per OCT record was 158.0 images/s. Image number per OCT record was 320.0 [626.0] images/record.

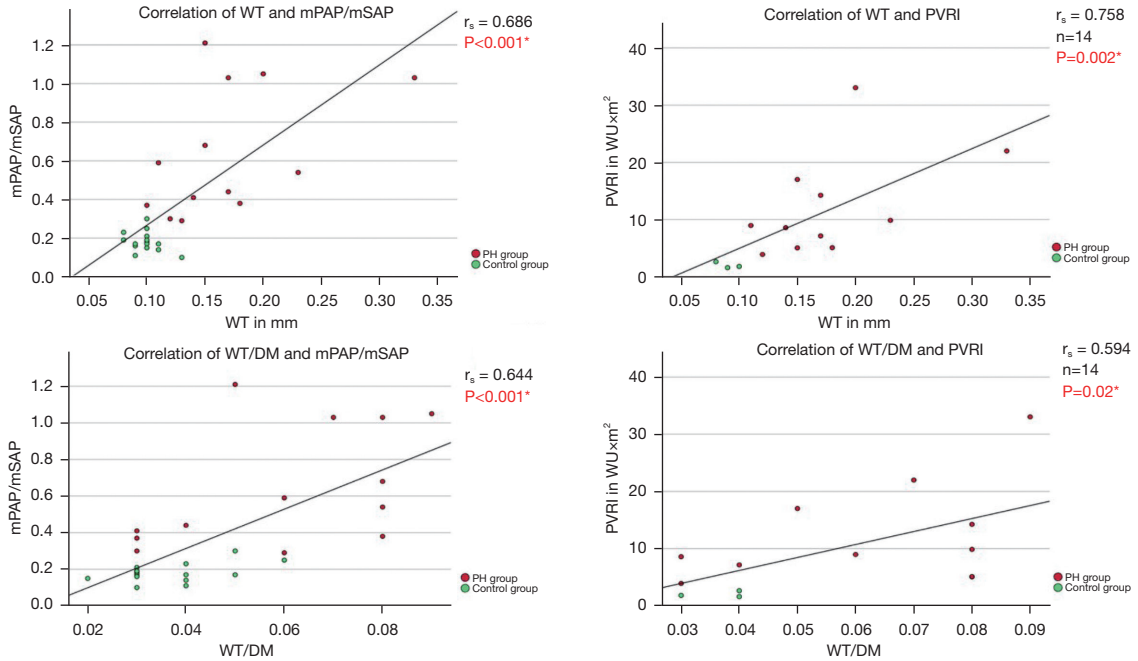

Figure 5 Correlation of OCT parameters and risk factors. Statistical test: Spearman correlation analysis. *, P value <0.05 is considered as statistically significant. In a group of 28 patients (PH: n=13, CG: n=15), the OCT parameters WT and WT/DM showed significant correlation with the risk factors mPAP/mSAP (r_s=0.686, P<0.001; r_s=0.644, P<0.001) and PVRI (r_s=0.758, P=0.002; r_s=0.594, P=0.02). r_s: Spearman correlation coefficient. WT, wall thickness; mPAP/mSAP, quotient of mPAP and mSAP; mPAP, mean pulmonary arterial pressure; mSAP, mean systemic arterial pressure; PH, pulmonary hypertension; PVRI, pulmonary vascular resistance index; WU, Wood units; WT/DM, quotient of WT and DM; DM, diameter; OCT, optical coherence tomography; CG, control group.

In 25 OCT records (89.3%) cross-sectional slice-thickness of the OCT records was 0.13 mm and in 3 OCT records (10.7%) it was 0.25 mm. In all OCT records, the length of the recorded segment was 52.8 [80.5] mm.

Discussion

This is one of the rare studies using OCT of the PA in children. It demonstrates that pulmonary OCT shows significant differences in the pulmonary arterial WT between the PH group and the control group. Furthermore, in a group of 28 with pulmonary OCT examined patients, OCT shows a significant correlation with haemodynamic factors and risk factors. Even though we performed OCT image analysis in a small group of patients because PH in paediatric patients is a rare disease this study revealed a very good reproducibility.

Stereotyped progressive structural changes of the intima and media of the pulmonary arterial wall in patients with PH typically appear in the PA as a sign of progressive hypertensive pulmonary vascular disease (31). However, the thickening of the pulmonary arterial vessel wall can also be related to other factors such as vessel DM and patient age (22,32-35). In the current study, the tested correlation between WT and vessel DM, as well as WT and patient age was not significant. Wall thickening in our investigation might represent pulmonary vascular remodelling related to the evaluated haemodynamic changes in the PA.

Diagnostic value of OCT in PH patients

In this study, the OCT parameters WT and WT/DM were significantly higher in patients with PH. Other pulmonary OCT studies support these findings (18,20,22). In patients with PH, Jiang *et al.* even showed a positive predictive value of 91% for a WT of ≥0.176 mm, underlining the potential of OCT as an additional diagnostic parameter in PH patients (20). However, to our best knowledge, no standardised settings for the operational procedure (21) and image analysis procedure of pulmonary arterial OCT

have been determined. Comparison of absolute values for measured WT of the PA deviates (18,20,22). Further studies with a standardised approach for OCT operational procedure and image analysis are needed to assess the diagnostic value of OCT for patients with PH.

Prognostic value of OCT in PH patients

In PH patients, certain risk factors are established for prognostic evaluation (6). Nevertheless, the disease often takes an unpredictable course. Additional risk parameters could be valuable to improve prognostic accuracy. In our group of 28 patients, the OCT parameters WT and WT/DM correlated significantly with the haemodynamic parameters mPAP and sPAP and the risk factors mPAP/mSAP and PVRI. WT also correlated significantly with the haemodynamic parameter PVR. Other reports have previously identified significant correlations of WT with CI and BNP in plasma (18,22). In our study, the correlation between OCT parameters and CI, mRAP, NT-pro-BNP and TAPSE was not significant, challenging the idea of OCT as an additional risk parameter in PH patients. However, as in our study, the extent of pulmonary arterial wall thickening in OCT conformed to the haemodynamic changes, it underlines the prognostic value of OCT in the PA of patients with PH. As already mentioned by others (19), in future, pulmonary arterial OCT might be a useful tool to support risk evaluation and therapeutic decision-making in patients with PH.

Technical challenges specific to the paediatric population

The DM of the OCT catheter itself was 2.6 Fr (=0.87 mm) and so the target region in our study seem to be located as far peripheral as technically possible in the muscular and elastic section of the PA branch (36) and, therefore may be located in the middle of the pulmonary arterial tree. In patients with PH, the first proven pathologic alteration in the PA wall is the intima proliferation, which only appears in the small muscular arteries and arterioles and then extends to the larger PA arteries in later stages (31). Although—with a mean DM of 2.917 mm—the examined vessels in our study might be located in the middle between the pulmonary hilus and the periphery, significant wall thickening in PH patients with a median mPAP of 40.0 mmHg could be found. These aspects might encourage the use of OCT for diagnostic matters not only in patients with advanced disease.

As contrast medium is injected during the OCT of the PA with a flow of about 3.7 mL/min, the DM of the PA might be influenced and widened. However, OCT in that study was performed according to the international standards of OCT in the coronary arteries where OCT is a well-established analysis method. Therefore, we think that our results are not influenced by that physical process.

Study limitations

Due to the rarity of PH in paediatric patients, our monocentric study is limited to 28 subjects. Multicentric studies would enable to extend the number of analysed OCT records and therefore widen the informative value of OCT in the PA of patients with PH. Additionally, prospective studies with follow-up examinations are preferable to evaluate the diagnostic and prognostic value of OCT in the clinical care of patients with PH.

Also, the penetration depth of OCT in the PA is 2–3 mm which limits a detailed presentation of the strongly thickened pulmonary arterial walls (11,37). However, in this study, a minimum of one OCT record per patient had sufficient quality, although insufficient image quality is a limiting factor.

Conclusions

The OCT reveals significant differences in WT of the PA and can be assessed in patients with PH. OCT parameters correlate significantly with haemodynamic parameters and risk factors such as mPAP/mSAP and PVRI. Although our findings support tremendous diagnostic and prognostic potential of OCT in patients with PH, prospective clinical-pathological studies with a standardised OCT analysis procedure are needed to evaluate to what extent the impact of OCT can contribute to the clinical care of patients with PH.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://cdt.amegroups.com/article/view/10.21037/cdt-22-421/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cdt.amegroups.com/article/view/10.21037/cdt-22-421/coif). ISN recently passed away and thus was unable to provide the form. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the local Ethics Committee at the Medical Faculty of the Ludwig-Maximilians-University of Munich (No. 18-516) and conformed to the ethical guidelines of the Declaration of Helsinki (as revised in 2013). For all subjects, written informed consent was obtained. For minor patients, the consent of the legal guardian was obtained.

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