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Choroidal Thickness in Children with Congenital Heart Disease Measured by Spectral Domain Optical Coherence Tomography[§]

Özgün Araştırma
Research Article

Doğuştan Kalp Hastalıklı Çocuklarda Optik Koherens Tomografi ile Koroid Kalınlığının Değerlendirilmesi

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ABSTRACT

Objective: *The main reason for complications in congenital heart diseases (CHD) is decreased blood oxygen saturation and polycythemia which are typical for cyanosis. These parameters may promote the damage of the retina because haemodynamic regulation is essential for the structural and functional integrity of the macular subfields. The aim of this study was to evaluate choroidal thickness (CT) measurements in children with CHD using spectral domain optical coherence tomography (OCT).*
Methods: *This prospective study compared 30 CHD and 30 healthy control children. CT was examined with spectralis spectral-domain OCT (Retinascan RS-3000; Nidek). CT was obtained at the subfovea, 500 µm and 1000 µm nasal to the fovea (N500, N1000) and 500 µm and 1000 µm temporal to the fovea (T500, T1000). Only the right eye values were used for statistical comparisons between the groups. The domain cardiac lesions were divided physiologically into two categories: volume overload and cyanotic.*
Results: *Mean age was 11.0±3.5 years in CHD childrens and 10.9±3.6 years in the control group (p=0.971). Children with CHD had no statistically significant CT measurements compared with healthy controls (p>0.05).*
Conclusion: *Although in high haematocrit, low oxygen saturation or the presence of the volume overload in the history of CHD patients, our data suggests that patients with CHD show normal CT. The reason may be medical and surgical treatment of hypoxia, erythrocytosis and volume overload in CHD patients.*

Keywords: *Congenital heart disease, choroidal thickness, optical coherence tomography, polycythemia, cyanosis*

ÖZ

Amaç: *Spektral-domain optik koherens tomografi (SDOKT) kullanarak doğuştan kalp hastalıklı (DKH) çocuklarda koroid kalınlığının değerlendirilmesi amaçlanmıştır. Doğuştan kalp hastalığında komplikasyonların başlıca nedeni, siyanoz için tipik olan düşük arteriyel oksijen saturasyonu ve polisitemidir. Bu parametreler retinal hasarı artırabilir, çünkü hemodinamik regülasyon makuler alt alanların yapısal ve işlevsel bütünlüğü için gereklidir.*
Yöntem: *Bu prospektif çalışmada 30 DKH'lı ve 30 sağlıklı çocuk karşılaştırıldı. Koroid kalınlığı SDOKT ile incelendi (Retinascan RS-3000; Nidek). Koroidal kalınlık; subfovea, 500 µm ve 1000 µm nazal fovea (N500, N1000) ve 500 µm ve 1000 µm temporal foveal alan (T500, T1000) ölçülerek elde edildi. Gruplar arasındaki istatistiksel karşılaştırmalar için sadece sağ göz değerleri kullanıldı. Kardiyak patolojiler fizyolojik olarak volüm yükü yapan ve siyanotik olarak iki kategoriye ayrıldı.*
Bulgular: *DKH'li çocuklarda yaş ortalaması 11.0±3.5 yıl, kontrol grubunda 10.9±3.6 yıl idi (p = 0.971). DKH'li çocuklar, sağlıklı kontrollerle karşılaştırıldığında istatistiksel olarak anlamlı koroidal kalınlık ölçümleri saptanmadı (p>0.05).*
Sonuç: *DKH çocuklar da yüksek hematokrit, düşük arteriyel oksijen saturasyonu veya aşırı volüm yükü nedeniyle olası retinal vasküler değişikler beklenmesine karşın, çalışmamızda DKH'lı hastaların normal koroidal kalınlık gösterdiklerini saptadık. Bu durum hastalarımızın çoğunda uygulanmış medikal yada cerrahi tedavi ile retinal vasküler değişiklerin iyileştirilmesine bağlı olabilir.*

Anahtar kelimeler: *Doğuştan kalp hastalığı, koroid kalınlığı, optik koherens tomografi, polisitemi, siyanoz*

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INTRODUCTION

Congenital heart disease (CHD), especially cyanotic heart diseases, is a complex group with high morbidity and mortality. Advances in invasive and surgical procedures and clinical treatment applied and the life expectancy of these patients have improved significantly. There are anecdotal reports of an increased frequency of ocular pathologies in congenital heart diseases [1]. The vascular system of the eye is exposed to the same internal and environmental effects, except for some features, and many features of the heart with the vascular system are similar [2]. The CHD patients may have vascular abnormalities such as arterial and venous occlusive disease, increased retinal vascular tortuosity, retinal arteriolar aneurysm, and embolic events. This may be due to chronic hypoxia, polycythemia and vascular changes especially in cyanotic CHD patients. This situation is parallel with the improvement of retinal vascular patterns with the improvement of hypoxia and erythrocytosis after surgery. Spectral-domain OCT enables noninvasive visualization and measurement of retinal and choroidal layers. We aimed to evaluate the CT in children with CHD measured by OCT.

MATERIALS and METHODS

A cohort study among 30 CHD (22 male, 8 female) and 30 healthy children (22 male, 8 female) was conducted in Celal Bayar University, Department of Pediatric Cardiology, Turkey between January 2016 and January 2017. Ethics committee approval was obtained by the local ethics committee (14.10.2015, 20478486-362), and written consent was obtained from parents.

The participants were devided into two groups: patients with CHD and the control group with healthy children. Congenital heart disorders are classified into two categories, cyanotic and acyanotic. In the acyanotic category included lesions that cause volume load with increased pulmonary blood flow (ventricular septum defect, atrial septal defect, patent ductus arteriosus, atrio-ventricular septal defect). In the cyanotic category, there were lesions with decreased pulmonary blood flow (tetralogy of fallot, pulmonary atresia, tricuspid atresia, ebstein anomaly) or increased pulmonary blood flow (large artery transposition, truncus arteriosus, double outlet right ventricle, total pulmonary venous return anomaly). The CHD patients were compared with 30 healthy children (control group) who were admitted to the pediatric cardiology department with nonspecific symptoms such as murmur, chest pain and dizziness, who were matched in terms of age and gender and whose cardiac evaluations were found to be negative. Systolic and diastolic blood pressures were measured. The CHD group was evaluated for hematocrit and hypoxia.

Participants with a history of ocular disorders, such as any type of glaucoma, previous ocular surgery or injury, and participants with a history of any systemic disease that could affect the choroidal circulation, such as hypertension, diabetes, vasculitis or kidney failure, were excluded from the study. Each participant underwent a complete ocular examination. CT was examined with spectral domain OCT (Retinascan RS-3000; NIDEK, Gamagori, Japan).

Spectral domain OCT is a new radiation-free imaging technique that can provide cross-sectional views of retinal anatomy. With the aid of near infrared 840 nm diode laser light, OCT uses the optically reflective properties of tissues to provide detailed information about inner retinal structures. CT of the right eyes were examined. Macula Line Raster scan protocol was used to evaluate the subfoveal CT, which enables good-quality depth penetration with 120 averaged B-scans [3,4]. CT was measured perpendicularly from Bruch's membrane equivalent to the choroid-sclera interface at the fovea and at 4 more points located at 500 µm nasal to the fovea, 1000 µm nasal to the fovea, 500 µm temporal to the fovea and 1000 µm temporal to the fovea drawn by one experienced examiner who was blinded to the diagnosis of the participants [3,4]. SD-OCT measurements of all patients were taken between 10:00 and 11:00 AM and three

images were taken from each participant, and the one with the highest signal strength was used for analysis.

Statistical Analysis

All data was documented into Statistical Package for Social Sciences (SPSS) on Windows 15.0. Data was expressed as mean and standard deviation. Independent T test was performed in independent groups for normal distribution parameters. Mann Whitney U test was performed not showing normal distribution in independent group. A p value <0.05 was considered statistically significant.

RESULTS

This study included 30 eyes with 30 CHD and 30 healthy eyes. Mean age was 11±3.51 years (range, 5-17 years) in CHD children and 10.9±3.6 years (range, 5-18 years) in the control group. No significant difference was found between the groups in terms of gender or age. There was no statistically significant difference in the SBP and DBP values between the groups. The clinical characteristics of the CHD and control group participants are shown in (Table 1). Physiologic cardiac categories included two groups: volume overload in 18 (60%), cyanotic in 12 (40%). The most common anatomic cardiac anomalies were ventricular or atrial septal defects 15 (50%), followed by tetralogy of Fallot 8 (26,6%). Other lesions were transposition of the great arteries 1 (3,3%), double-outlet right ventricle 2 (6,6%), atrio-ventricular canal 3 (10%) and ebstein anomaly 1 (3,3%) (Table 2). Two participants with atrio-ventricular septal defect were Down syndrome. There was no correlation between the anatomic types of CHD and CT.

Table 1. Baseline characteristics of the congenital heart disease and control groups.

	CHD group	Control group	P
Number of patients	30	30	
Age, years Mean ± SD, range	11±3.51, (5-17)	10.9 ± 3.6, (5-18)	0.971[a]
Number of male/female	22/8	22/8	1.000[b]
CHD Cyanotic (%) Volume overload (%)	NA 40 60	NA	
SBP, mmHg Mean ± SD	104.6 ± 14.5	102.3 ± 11.8	0.499[a]
DBP, mmHg Mean ± SD	64.5 ± 11.3	65.6 ± 8.4	0.653[a]

CHD,congenital heart disease
SBP, systolic blood pressure; DBP, diastolic blood pressure; SD, standard deviation.
[a]Independent Student t test, [b]Chi-square test.
A p value of less than 0.05 was considered significant.

Table 2. Distribution of congenital heart lesions.

	N(30)		Htc range%
Tetralogy of Fallot	8	26.6	38.9-60.9%
Double-outlet right ventricle	2	6.6	41-61%
Ebstein's anomaly of the tricuspid valve	1	3.3	37%
Transposition of the great arteries	1	3.3	48.6%
Complete atrioventricular septal defect	3	10	39.2-40.2%
Ventricular septal defect	13	43.3	29-41%
Atrial septal defect	1	3.3	45.5%
Ventricular septal defect+ Atrial septal defect	1	3.3	35.8%

Table 3. Foveal thickness and choroidal thickness measurments.

Group	SFCT	N500	N1000	T500	T1000
CHD group	351.3±39.2	330.3±55.4	322.7±59.0	318.6±45.5	325.0±50.3
cyanotic (N:12)	354.9 ± 29.5	332.1±52.1	332.0±53.4	324.0±40.6	326.9±44.4
volume overload (N:18)	349.0 ± 45.2	329.1 ± 58.9	316.6 ± 63.2	315.0 ± 49.3	323.7 ± 55.1
Control group (N:30)	341.3± 69.2	319.0±67.6	322.4±80.2	317.9±75.0	323.4±75.7
P[a]	0.564	0.965	0.671	0.886	0.906

CHD,congenital heart disease SFCT: Subchoroidal thickness ; N500, choroidal thickness at 500 µm nasal to the fovea; N1000, choroidal thickness at 1000 µm nasal to the fovea; T500, choroidal thickness at 500 µm temporal to the fovea; T1000, choroidal thickness at 1000 µm temporal to the fovea.
[a]Kruskal Wallis Test
A p value of less than 0.05 was considered significant.

27% of patients with volume overload were operated (n=5) and 61% (n=11) of them were receiving medical treatment. 66% [8] of the patients in the cyanotic group were operated, and only 33% [4] of the patients in this group had continued cyanosis.

A total of 13 (43%) participants had undergone some type of surgical intervention prior to the eye examination. In cyanotic group, the hematocrit level of 2 patients was above 55% and only 4 patients in this group had continued cyanosis. There was no correlation between CT, level of haematocrit and low arterial oxygen saturation. There was no significant difference between CT with cyanotic, volume overload and control participants in the subfovea, N500 µm, N1000 µm nasal to the fovea and T500 µm, T1000 µm temporal to the fovea. Table III shows the results of the between-group comparison of SFCT, N500, N1000, T500, T1000.

DISCUSSION

In the past few decades, advancing surgical techniques and advances in cardiopulmonary bypass surgery, intensive care, cardiac catheterization, non-invasive imaging, and medical treatments have significantly reduced mortality rates for children and adolescents with complex CHD [5-7]. As a result of improved survival rates, the target of clinical research in pediatric cardiology has shifted from short-term surgical survival to assessment of long-term morbidity [7]. Children under the age of 15 years old with primary CHD have a high prevalence of ocular alterations, with external ocular and retinal manifestations, with higher occurrence rate among cyanotic cases [8]. K. Schuster et al. [9] found evidence of a correlation between subfoveal choroidal thickness and cardiovascular risk factors which was mediated by aging. These studies are often in adults and are associated with structural eye diseases [8,9]. There are very few studies evaluating direct choroid in congenital heart disease, especially in children. In cyanotic CHD, arterial hypoxemia occurs when unsaturated blood distribution into the systemic circulation due to intracardiac right-to-left shunt [10-12]. The cyanotic CHD patients had significant thinning of the central macula and macular subfields [12].These findings may be due to the effect of low oxygen levels due to hemodynamic irregularity, which affects the structural and functional integrity of the retina [13-15]. Therefore, there may be structural changes in the retina due to systemic hemodynamic changes in CHD patients [16]. Vascular changes caused by chronic hypoxia severely affect whole body and blood parameters, and cardiac effects of reoxygenation after chronic hypoxia may be more severe than in acute hypoxia [17]. Petersen et al. [18] found that hypoxia and polycythemia were associated with dilatation and tortuosity of retinal vessels in about half of patients with cyanotic CHD. Mansour et al. [19]

suggested that patients with high or low haematocrit develop retinal tortuosity. In patients with normal haematocrit, low oxygen saturation or velocardiofacial syndrome may be responsible for tortuosity. Retinal arteriolar tortuosity has been reported previously in approximately half of patients with aortic coarctation, and more recently these patients were found not to exhibit these findings due to early surgical correction of the cardiac lesion, suggesting the hemodynamic etiology of vascular tortuosity [16,19]. Similarly, previous studies have shown that retinal vascular dilatation and tortuosity in patients with cyanotic CHD are reduced after surgical correction and appear to be associated with a combination of polycythemia and hypoxia [19-21]. Chronic ischemia caused by hypoxia in particularly patients with cyanotic CHD occurring secondary to this may be the reason for low subfoveal choroidal thickness. Thin choroidal layer may lead to the development of retinal diseases such as maculopathy, macular degeneration [12].

Our patients also had early surgery and medical treatment to control hypoxia and polycythemia before the eye exam. Therefore, we didn't find any statistically significant difference in choroidal thickness of CHD and age- and gender-matched healthy controls. This may confirm other authors' hypothesis [15,20,21].

In conclusion, It has been reported that choroidal thickness decreases according to the degree of polycythemia and hypoxia, especially in cyanotic CHD [10]. Improvement of hypoxia and polycythemia in cardiac lesions with early surgical correction and medical treatment may make retinal changes reversible. For this reason, we didn't find any difference between choroidal thickness of CHD group compared to the control group in our study. In order to reach a more definitive conclusion, studies with larger groups and longer follow-up periods are needed, especially before and after the operation.

Ethics Committee Approval: Celal Bayar University Ethics Committee approval was received (14.10.2015, 20478486-362).

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REFERENCES

1. Vilela MA, Sbruzzi G, Pellanda LC. Prevalence of ophthalmological abnormalities in children and adolescents with CHD: Systematic review and meta-analysis of observational studies. Cardiol Young 2016;26:477-84. [CrossRef]
2. Flammer J, Konieczka K, Bruno RM, Virdis A, Flammer AJ, Taddei S. The eye and the heart. Eur Heart J 2013;34:1270-8. [CrossRef]
3. Spaide RF, Koizumi H, Pozzoni MC. Enhanced depth imaging spectral-domain optical coherence tomography. Am J opthalmol 2008;146:496-500. [CrossRef]
4. Margolis R, Spaide RF. A pilot study of enhanced depth imaging optical coherence tomography of the choroid in normal eyes. Am J Ophthalmol. 2009;147(5):811-5. [CrossRef]
5. Mahle WT, Spray TL, Wernovsky G, Gaynor JW, Clark BJ 3rd. Survival after reconstructive surgery for hypoplastic left heart syndrome: a 15-year experience from a single institution. Circulation 2000;102:136-41. [CrossRef]
6. Jacobs JP, Quintessenza JA, Burke RP, et al. Analysis of regional congenital cardiac surgical outcomes in Florida using the Society of Thoracic Surgeons Congenital Heart Surgery Database. Cardiol Young 2009;19:360-9. [CrossRef]
7. Marino BS, Lipkin PH, Newburger JW, et al; American Heart Association Congenital Heart Defects Committee, Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, and Stroke Council. Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management: a scientific statement from the American Heart Association. Circulation 2012;126:1143-72. [CrossRef]
8. Vilela MA, Colossi CG, Freitas HP, Valle GD, Pellanda LC. Ocular Alterations Associated with Primary Congenital Heart Disease - A Cross-sectional Study. Middle East Afr J Ophthalmol. 2020;27(1):28-33. [CrossRef]
9. Schuster AK, Leuschner A, Feretos C, et al. Choroidal thickness is associated with cardiovascular risk factors and cardiac health: the Gutenberg Health Study. Clin Res Cardiol. 2020;109(2):172-182. [CrossRef]
10. Friedman AH, Fahey JT. The transition from fetal to neonatal circulation: normal responses and implications for infants with heart disease. Semin Perinatol 1993;17:106-21.
11. Rudolph AM. The changes in the circulation after birth. Their importance in congenital heart disease. Circulation 1970; 41: 343-359. [CrossRef]
12. De Aguiar Remigio MC, Brandt CT, Santos CCL, Arantes TE, de Aguiar MIR. Macular and peripapillary retinal nerve fibre layer thickness in patients with cyanotic congenital heart disease. Eye 2015; 29:465-468. [CrossRef]
13. Flammer J, Mozaffarieh M. Autoregulation, a balancing act between supply and demand. Can J Ophthalmol 2008;43:317-21. [CrossRef]
14. Neufeld AH, Kawai SI, Das S, et al. Loss of retinal ganglion cells following retinal ischemia: the role of inducible nitric oxide synthase. Exp Eye Res 2002;75:521-528. [CrossRef]
15. Caprara C, Grimm C. From oxygen to erythropoietin:

relevance of hypoxia for retinal development, health and disease. Prog Retin Eye Res 2012; 31: 89-119. [CrossRef]
16. Johns KJ, Johns JA, Feman SS. Retinal vascular abnormalities in patients with coarctation of the aorta. Arch Ophthalmol 1991;109:1266-8. [CrossRef]
17. Corno AF, Milano G, Samaja M, Tozzi P, von Segesser LK. Chronic hypoxia: A model for cyanotic congenital heart defects, The Journal of Thoracic and Cardiovascular Surgery 2002;124:105-12. [CrossRef]
18. Petersen RA, Rosenthal A. Retinopathy and papilledema in cyanotic heart disease. Pediatrics 1972;49:243-9.
19. Mansour AM, Bitar FF, Traboulsi EI, et al. Ocular pathology in congenital heart disease. Eye (Lond) 2005; 19:29-34. [CrossRef]
20. Crowe RJ, Kohner EM, Owen SJ, Robinson DM. The retinal vessels in congenital heart disease. Med Biol 1969;19: 95-9.
21. Kohner EM, Allen EM, Saunders KB, Emery VM, Pallis C. Electroencephalogram and retinal vessels in congenital cyanotic heart disease before and after surgery. Br Med J 1967; 4:207-10. [CrossRef]