Reproducibility of Choroidal Thickness Measurements in Hemodialysis Patients. A Spectral Domain Optical Coherence Tomography Study

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Research Article

Keywords: Hemodialysis, SD-OCT, Subfoveal Choroidal Thickness, Reproducibility

Posted Date: June 15th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-522828/v1

Abstract

Purpose

To investigate the effects of hemodialysis (HD) on the reproducibility of subfoveal choroidal thickness (SFCT) as measured by spectral domain-optical coherence tomography (SD-OCT)

Methods

In this study, 26 HD (26 eyes) patients had their pre- and post-HD SFCT measured, and the results were compared for reproducibility. Following a thorough ophthalmic examination, SD-OCT was performed three times in a row during a single session. The same physician measured SFCT after automatically identifying choroid with a software caliper. The reproducibility parameters, including intra-class correlation coefficients (ICCs), coefficients of variation (COV), and test-retest variability (TRTV) were then calculated.

Results

Males made up 53.85% of the 26 HD patients. There was a significant IOP difference between pre-HD (16.42±3.14 mmHg) and post-HD (14.21±2.78 mmHg) (P<0.001). SFCT decreased significantly from pre-HD 243.50±10.23 μm to post-HD 234.29±9.41 μm (P<0.001). ICC value increased significantly after HD, rising from 0.948 to 0.989 (P<0.001, for all). Pre- and post-HD COV values were 1.6% and 0.65%, respectively. Also, pre- and post-HD TRTV values were 7.864±1.996 μm and 3.074±1.536 μm, respectively.

Conclusion

The reproducibility of SFCT as measured by OCT was lower during pre-HD compared to post-HD. Post-HD SD-OCT assessment appears to improve the reliability of clinical outcomes in the diagnosis and monitoring of HD patients.

Introduction

Hemodialysis (HD) is a life-saving treatment for patients with end-stage renal disease. Uremia, volume load, and serum osmolality in the body all decrease secondary to HD [1]. Changes in ocular fluid balance may also result from this procedure. Intraocular pressure (IOP), corneal thickness, retinal nerve fiber layer, as well as subfoveal choroidal thickness (SFCT) have been reported to change following HD [2–4].

Our understanding of ocular structures is growing in tandem with the rapid advancement of optical coherence tomography (OCT) technology. More precise choroidal measurements have been made possible thanks to enhanced depth imaging-OCT. Choroidal thickness has been shown to be affected by some diseases and to be an important predictor of treatment response in recent studies [5–9]. As a consequence, accurate SFCT measurements are critical in assessing and monitoring certain retinal diseases.

Reproducibility of SFCT has been a subject of several studies, which were performed in homogeneous groups of patients [10–14]. Further, Wong et al [11]., measured SFCT in patients with various types of retinal fluid and found that reproducibility was lower in patients with subretinal fluid.

We hypothesized that changes in body fluids would also influence SFCT measurements before and/or after HD for similar reasons. As a result, we intended to look into the effects of HD on SFCT reproducibility using spectral domain-OCT (SD-OCT).

Material And Methods

Study Design and Participants

Twenty-six eyes from 26 patients who received HD therapy secondary to diabetic nephropathy at Afyonkarahisar State Hospital were included in this comparative study. The study protocol complied with the ethical principles of the Declaration of Helsinki and received full approval from the institutional review boards of Afyonkarahisar Health Sciences University Ethics Committee (Approval Code: 2011-KAEK-2; 07 September, 2018). Prior to the study, all patients provided written consent. Our study included patients who underwent HD three days a week due to an end-stage renal failure, had an axial length (AL) of 22–26 mm, no retinal pathology, as well as no prior intra and/or extraocular surgery.

Ophthalmic Examination and OCT Imaging

A comprehensive ophthalmic examination was performed before HD, including measurement intraocular pressure by Goldmann applanation tonometer (Goldmann; Haag-Streit AG, Köniz, Switzerland), axial length by AL-Scan (Nidek CO., Gamagori, Japan) as well as anterior and posterior segment slit-lamp biomicroscopy before and after full pupil dilation.

Spectral domain-OCT (Spectralis, Heidelberg Engineering, Inc., Heidelberg, Germany) scanning was performed 30 minutes before and after HD using the Macula Line Raster scanning protocol. The measurements were taken three times, with two-minute rest periods in between. Subfoveal CT was measured by a physician who was blinded to the patients as a vertical distance between the outer boundary of the retinal pigment epithelium-Bruch membrane layer and the manually drawn sclera-choroidal interface automatically determined by SD-OCT from the subfoveal region.

Statistical Analysis

Statistical analysis was performed using SPSS v. 21.0 for Windows (SPSS, Inc., Chicago, IL, USA). The Shapiro-Wilk test was used to determine the normality of the data distribution. Since variables were normally distributed, the paired-t test was used to compare them before and after HD. Reproducibility was analyzed using the intra-class correlation coefficient (ICC), coefficient of variation (COV), as well as test-retest variability (TRTV). For choroidal measurement comparison, the mean of the three scans was used. Data significance level was set at $P < 0.05$.

Results

Twenty-six HD patients (female-to-male: 14:12) who met the predetermined inclusion criteria were investigated. These patients were 46.23 ± 9.54 years old on average. Table 1 displays demographic characteristics of the study patients. There was a statistically significantly decreased IOP following HD **(P < 0.001).** When compared to pre-HD measurements, there was also a statistically significantly decreased post-HD SFCT measurements **(P < 0.001).**

Table 1
Demographic characteristics and other findings of HD patients

Parameter	**($\bar{x}$±s)**		
HD duration (months)	56.54 ± 7.76		
AL (mm)	23.76 ± 1.45		
	Pre-HD ($\bar{x}$±s)	**Post-HD ($\bar{x}$±s)**	**P-value**
IOP (mmHg)	16.42 ± 3.14	14.21 ± 2.78	**0.001**
SCT (μm)	243.50 ± 10.23	234.29 ± 9.41	**0.001**
$\bar{x}$: Mean; s; Standard deviation; HD: Hemodialysis; AL: Axial length; IOP: Intraocular pressure; SCT: Subfoveal choroidal thickness; P < 0.05 was accepted as statistically significant.			

Post-HD ICC increased statistically significantly when compared to pre-HD ICC (P < 0.001, for all). Pre- and post-HD COVs were 1.6% and 0.6%, respectively. The pre-HD TRTV measured 7.864 ± 1.996 μm, while the post-HD TRTV measured 3.074 ± 1.536 μm (Table 2).

Table 2
Intra-session reproducibility of consecutive SFCT measurements based on changes in pre- and post-HD ICC, COV, and TRTV values.

Parameter	**Pre-HD**	**Post-HD**	**P value**
ICC (95% CI)	0.948 (0.895–0.976)	0.989 (0.977–0.995)	0.001
COV ($\bar{x}$±s) (%)	0.016 ± 0.004	0.006 ± 0.003	
TRTV ($\bar{x}$±s) (μm	7.864 ± 1.996	3.074 ± 1.536	
$\bar{x}$: Mean; s; Standard deviation; HD: Hemodialysis; SFCT: Subfoveal choroidal thickness; ICC: Intra-class correlation coefficient; COV: Coefficient of variation; TRTV: Test- retest variability. P < 0.05 was accepted as statistically significant.			

Discussion

Pre- and post-HD reproducibility of SFCT measurements in diabetic nephropathy patients were investigated in this study. Overall, pre-HD SFCT measurements were associated with significantly lower

intra-session reproducibility values, including ICC, COV, and TRTV, compared to post-HD SFCT measurements.

The relationship between SFCT and various retinal diseases is becoming more understandable as OCT technology advances. Several studies have focused on the role of SFCT in especially diabetic retinopathy and its treatment. Farias et al [15]., reported choroidal thinning prior to diabetic retinopathy, as well as the association of thin choroid with microalbuminuria. By describing the short-term anatomic and functional responses to anti-VEGF therapy in patients with thicker SFCT, Rayes et al [16]., highlighted the significance of SFCT as a prognostic marker in the treatment of diabetic macular edema. Moreover, several factors, including AL, age, body mass index, diurnal variation, and systolic blood pressure, have been reported to affect choroidal thickness in healthy individuals [17–20].

Subfoveal CT has also been measured before and after HD in previous studies, with the majority of them reporting lower post-HD SFCT values [21–25]. This could be ascribed to a decreased osmotic gradient in serum and choroidal interstitium as a result of post-HD decreased serum osmolality. A study published by Chang et al [23]., reported a correlation between decreased serum osmolality, body weight and a low systolic blood pressure, and lower SFCT. In addition to a significantly lower post-HD IOP ($P < 0.001$), our study's findings of a significantly lower post-HD SFCT compared to pre-HD SFCT ($P < 0.001$) in diabetic nephropathy patients who had HD for nearly five years were in line with previous reports. An increase in post-HD SFCT, on the other hand, has been observed in another study [26]. This finding, which is inconsistent with our study, could have resulted from misleading measurements caused by the low reproducibility of pre-HD SFCT.

Various studies have addressed SFCT reproducibility, and it has been noted that SFCT reproducibility ranges between 0.89 and 0.99, especially in healthy individuals [27, 28]. A study of neovascular age-related macular degeneration patients conducted by Hanumunthadu et al [14]., revealed that swept-source OCT could detect SFCT changes ≥ 57.2 μm. They also noted that SFCT changes > 35 μm in SD-OCT could be detected in the same group of patients. Further, Puigdollers et al [13]., reported that swept-source OCT can be used to measure SFCT with high reproducibility in patients with diabetic macular edema. Furthermore, SFCT measurements taken from the edge of choroidal stroma have been reported to be more reproducible [29]. Contrastingly, another study found no difference in SFCT reproducibility between healthy subjects and patients with diabetic retinopathy [10]. And, the presence of subretinal fluid has been shown to decrease CT reproducibility, which has been attributed to fluid signal attenuation and shadowing caused by the subretinal fluid [11]. Besides, several studies have found that as choroid thickness increases, reproducibility decreases [11, 12]. Pre-HD SFCT measurements had lower reproducibility in our study. Several hypotheses have been advanced to explain the lower pre-HD SFCT measurements. As previously stated, it is possible that increasing SFCT has a negative impact on reproducibility. Another possibility is that chronic renal failure may cause an increase in extracellular fluid volume, resulting in hemodynamic instability.

We acknowledge the limitations of this study. Importantly, the size of the study population was just not high enough to improve the efficacy of our study. The measurements were carried out only horizontally. Moreover, we evaluated only the reproducibility of SFCT, which was the goal of our study. Again, residual influencing factors might have led to an unexplained analytical preference. Thus, long-term prospective studies with a larger sample size may yield clinically useful results in determining relatively accurate reproducibility of SFCT and other ocular microstructures not only before but also after HD in diabetic patients with and/or without diabetic nephropathy

Conclusion

We found significant changes in post-HD SFCT as well as reproducibility in HD patients with diabetic nephropathy. Assessment of post-HD OCT during diagnosis and monitoring of HD patients may well be associated with relatively more consistent outcomes. Regardless, determining the consistent and accurate consequences of HD on SFCT measurements, as well as its reproducibility, necessitates large-scale randomized OCT studies.

Declarations

Funding

Authors declare no public or private financial support or involvement whatsoever in the products, methods or materials referred to in this manuscript.

Conflicts of interest/Competing Interests

The authors claim no conflict of interest.

Financial Interest

Both authors certify that they have no association or participation with any organization or individual with any financial interest or non-financial interest in the subject matter or materials discussed in this article.

Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Authors' contributions

Study design and recruitment of participants: MMU, ÖE, LEE, AGTU; Data analysis: MMU, ÖE, LEE, AGTU; Reviewing, editing and verifying the accuracy of the manuscript: MMU,ÖE,LEE,AGTU, HHG, Aİ; Complete access to all study data and accountability for data integrity and accuracy of data analysis: MMU,ÖE,LEE,AGTU, HHG, and Aİ;

Consent for publication

The authors note that human study participants have given informed consent to the release of the images.

Availability of data and material

Not applicable.

Code availability

Not applicable.

Clinical Trials Registration

Not applicable.

Gels and Blots/ Image Manipulation

Not applicable.

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