

## ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

# The effect of hemodialysis on macular thickness

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**Introduction/Objective** During hemodialysis (HD) treatment great fluctuations were recorded in the systemic hemodynamic parameters and in the volume and composition of ocular fluid. There are only a few studies that analyzed the effect of HD on retinal and macular thickness with conflicting results. Objective of this study was to determine macular thickness, marked as central foveal thickness, average macular thickness and macular volume, shortly before and after HD.

**Methods** This prospective study included 30 chronic renal failure (CRF) patients of HD treatment. Thorough ophthalmologic examinations were performed including evaluation of best corrected visual acuity, intraocular pressure and slit-lamp examination of all eye segments. Macular thickness was determined by optical coherence tomography shortly before and after HD. The next parameters were evaluated: central foveal thickness, average macular thickness and macular volume. The correlation between systemic parameters and macular thickness changes during HD was tested.

**Results** There were significant changes in body weight and blood pressure pre- and post-HD. Results showed macular thickness (central foveal thickness, average macular thickness and macular volume) decreased, but the change was not significant. There was no significant correlation between systemic hemodynamic parameters and macular thickness changes.

**Conclusion** Results of this study showed there was no statistically significant changes in macular thickness CRF patient undergoing HD. Further research on a larger group of patients and a longer follow-up time are required to confirm these findings.

**Keywords:** macular thickness; hemodialysis; optical coherence tomography

**INTRODUCTION**

Most patients with chronic renal failure (CRF) undergo hemodialysis treatment. Although hemodialysis is effective, in the long term it can lead to numerous changes in many patients. The most common eye problems that occur in patients treated with hemodialysis are changes in visual acuity and refraction, dry eye, calcium deposits on the conjunctiva, “band” keratopathy, corneal endothelial damage, and lens clouding [1, 2]. Furthermore, it has been shown that these patients have morphologic and physiologic changes in the retina [3, 4].

During one hemodialysis (HD) session, there are substantial changes in electrolyte concentrations and the volume and distribution of body fluids, which can affect many systemic parameters, as well as the composition and volume of fluid in the eye.

Previous studies have shown that HD has an effect on central corneal thickness and intraocular pressure (IOP), axial length and ocular surface [5, 6, 7]. A very small number of researchers investigated retinal and macular thickness changes during HD. The results of these studies are contradictory. A few studies have shown that HD has an effect on retinal thickness (RT) [8, 9, 10], while in others this effect was not significant [11, 12].

The aim of this study was to determine macular thickness expressed as central foveal thickness (CFT), volume, and average macular thickness immediately before and after hemodialysis.

**METHODS**

The prospective study enrolled 30 patients who are on a chronic hemodialysis program at the Department of Nephrology of the Clinic for Internal Medicine, Zvezdara Medical Center in Belgrade. The research was conducted from December 2014 to March 2015 at the Prof. Dr. Ivan Stanković Clinic for Eye Diseases, Zvezdara Medical Center. Informed consent was obtained from all patients and the Ethics Committee of the Zvezdara Medical Center approved the study. The patients were enrolled in the study according to the following criteria: patients with CRF treated with hemodialysis and visual acuity greater than 0.1. The exclusion criteria from the study were the presence of opaque optical media and refractive anomalies greater than  $\pm 10$  Dsph.

Patients underwent hemodialysis three times a week for three to four hours. It was used standardized dialysate flow rate of 500 ml / min at blood flow rate 250–300 ml / min.

**Received • Примљено:**

October 28, 2021

**Revised • Ревизија:**

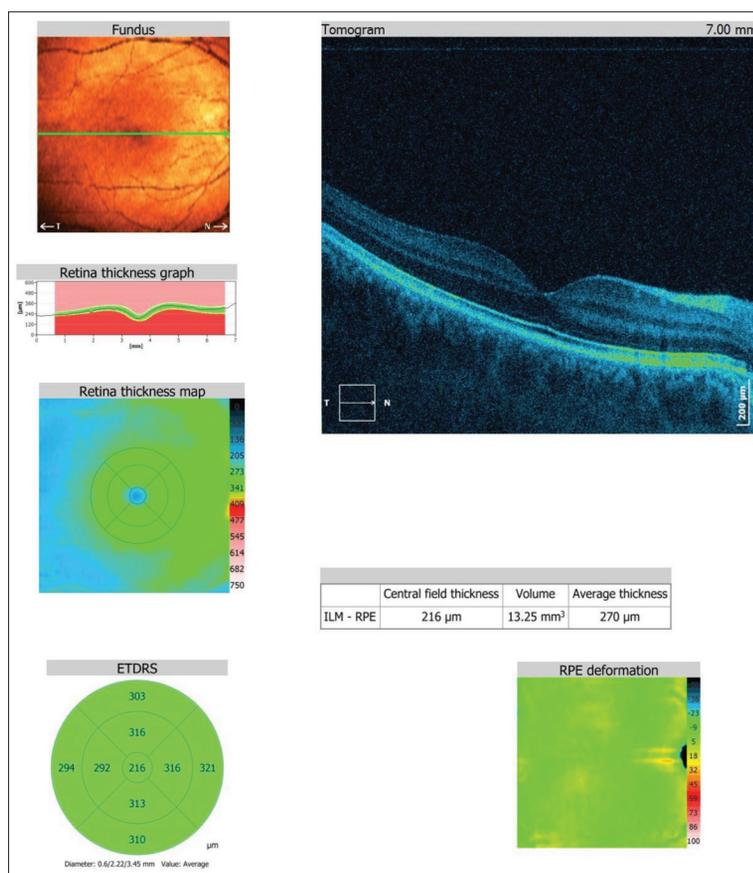
February 1, 2022

**Accepted • Прихваћено:**

February 7, 2022

**Online first:** February 14, 2022**Correspondence to:**

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**Figure 1.** Optical coherence tomography scan with early treatment diabetic retinopathy study retinal thickness map

**Table 1.** The effect of hemodialysis on blood pressure

Parameters	HD	$\bar{x}$	SD	med	min	max	p
Systolic blood pressure	before HD	140	26.9	140	80	190	< 0.001
	after HD	116.8	14.9	120	80	140	
Diastolic blood pressure	before HD	74.6	13.7	80	40	110	< 0.001
	after HD	64.7	9.8	65	40	80	
Mean blood pressure	before HD	90	29.2	98.3	0	126.7	< 0.001
	after HD	52	41	78.3	0	100	

HD – hemodialysis; mean blood pressure –  $(2 \times \text{diastolic blood pressure} + \text{systolic blood pressure}) / 3$

A thorough ophthalmological examination was performed, which consisted of the determination of the best corrected visual acuity, IOP, examination of the anterior and posterior segment of the eye. Snellen optotype was used to determine visual acuity, while IOP was measured using Goldmann's applanation tonometer. Macular thickness was determined by optical coherence tomography (Spectral Domain Optical Coherence Tomography, SD [OCT]; Copernicus HR, Optopol, Zawiercie, Poland) immediately before and after hemodialysis. OCT imaging was performed after the pupils were dilated using local mydriatics (2.5% Sol. Phenylephrin and 1% Sol. Tropicamid). RT was analyzed using data obtained by a map defined by the Early Treatment Diabetic Retinopathy Study [13]. The following were analyzed: inner, intermediate and outer ring of radius 0.6 vs. 2.2 vs. 3.45 µm. The average RT corresponding to the inner ring is marked as CFT, while the average macular thickness (MEAN) is the average thickness of all three rings. Volume is the volume of the macular region radius 3.45 µm (Figure 1).

Blood pressure and body weight were recorded before and after the HD session. Weight change represents the amount of fluid removed by hemodialysis. Standard monitoring parameters (serum concentrations: Ca, P, urea, creatinine, PTH, Fe, Er, ALP; eGFR and Kt / V) are taken from the patient's medical history. Based on the cause of CRF, patients were divided into three groups: hypertensive nephrosclerosis (HTA), diabetes mellitus (DM) and others.

In total, 30 eyes from 30 patients were used for statistical analysis. Which eye (right or left) will be included in the analysis was determined by randomization, except for six patients in whom only one eye met the inclusion criteria. Descriptive statistical methods and methods for testing statistical hypotheses were used for primary data analysis. The t-test for two dependent samples and analysis of variance (ANOVA) were used. Pearson's correlation coefficient was used to examine the correlation of age, HD length, and system parameters with changes of macular thickness. Value  $p < 0.05$  was considered statistically significant.

## RESULTS

The study included 30 patients (17 men and 13 women). The average age of all subjects in the study was  $61.2 \pm 11.1$  years. The youngest participant had 27 and the oldest 77 years. The causes of CRF in the subjects were hypertensive nephrosclerosis ( $n = 17$ ), diabetes mellitus ( $n = 4$ ), while in nine patients the causes were other (chronic pyelonephritis ( $n = 3$ ), primary glomerulopathies ( $n = 3$ ), obstructive uropathy ( $n = 2$ ) and polycystic kidney disease ( $n = 1$ ).

Changes in arterial blood pressure (systolic, diastolic and mean) before and after hemodialysis was statistically significant. Average values of differences between systolic blood pressure, diastolic blood pressure and mean blood pressure before and after HD were  $33.16 \pm 19.09$  vs.  $10.53 \pm 9.85$  vs.  $38 \pm 36.59$  mmHg ( $p < 0.001$ ). (Table 1).

The average value of body weight in subjects before HD was  $72.1 \pm 15.9$  kg, while after HD  $67.3 \pm 20$  kg, which is a statistically significant difference ( $t = 8.999$ ;  $p < 0.001$ ). (Table 2). There was no statistically significant correlation

**Table 2.** The effect of hemodialysis on body weight

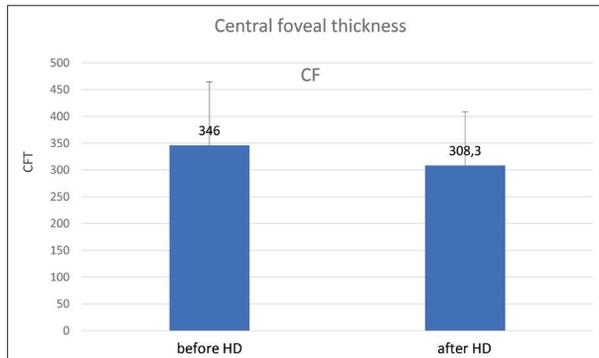
Parameters	n	$\bar{x}$	SD	med	min	max	p
BW before HD	22	72.1	15.9	67.9	53.5	110	
BW after HD	29	67.3	20	66	0	107	
$\Delta$ BW	21	2.6	1.2	2.5	0.5	5	< 0.001

BW – body weight; HD – hemodialysis;  $\Delta$ BW – difference in body weight before and after HD

**Table 3.** The effect of hemodialysis macular thickness

Parameter	HD	SD	med	min	max	p	
CFT	before HD	346	118.4	329.5	175	583	0.142
	after HD	308.3	100.1	300.5	128	545	
MEAN	before HD	280.1	52.1	263.5	199	448	0.734
	after HD	275.1	52.6	269.5	185	398	
Volume	before HD	13.44	2.69	263.5	7.01	21.96	0.347
	after HD	13.17	2.59	269.5	9.06	18.96	

HD – hemodialysis; CFT – central foveal thickness; MEAN – average macular thickness; Volume – macular volume



**Figure 2.** The effect of hemodialysis on central foveal thickness

**Table 4.** Changes of macular thickness after hemodialysis in groups of patients formed based on CRF causes

Parameter	Group	$\bar{x}$	SD	min	max	p
$\Delta$ CFT	HTA	73.3	131.20	-46	455	0.432
	DM	-7.5	139.82	-216	80	
	Other	7.33	161.17	-272	294	
$\Delta$ MEAN	HTA	-1	48.25	-75	88	0.862
	DM	17.25	98.02	-106	131	
	Other	5.89	62.41	-91	93	
$\Delta$ Volume	HTA	-0.46	2.56	-5.20	4.31	0.060
	DM	3.44	2.88	0.19	6.44	
	Other	-0.15	3.17	-3.91	4.55	

HTA – hypertensive nephrosclerosis; DM – diabetes mellitus;  $\Delta$ CFT – difference of central foveal thickness before and after hemodialysis;  $\Delta$ MEAN – difference of average macular thickness before and after hemodialysis;  $\Delta$ Volume – difference in macular volume before and after hemodialysis

**Table 5.** Values of serum concentrations of the examined system parameters

Parameters	n		SD	med	min	max
Ca	30	2.3	0.2	2.2	1.9	2.9
P	30	1.3	0.5	1.4	0	2.4
Urea	30	21.4	4.9	21.5	13.4	31.7
Creatinine	30	835.4	128	809	623	1211
eGFR	30	5.2	1.1	5	3	8
PTH	30	244	265.1	153.8	15.7	1213
Fe	29	10.2	3.8	9.6	3.2	22.6
Er	27	3.2	0.5	3.4	1.8	4.4
ALP	30	83.6	57.6	64.5	28	310
Kt/V	20	1.4	0.3	1.4	0.8	2.2

between patient age and changes in body weight and blood pressure, as well as between length of HD and the above parameters ( $p > 0.5$ ).

**The effect of hemodialysis on macular thickness**

The mean value of CFT before HD was  $346 \pm 118.4 \mu\text{m}$ , while after HD  $308.3 \pm 100.1 \mu\text{m}$ . Difference in CFT before and after HD was not statistically significant ( $t = 1.514$ ;  $p > 0.05$ ). Average value of average macular thickness (MEAN) before HD was  $280.1 \pm 52.1 \mu\text{m}$ , while after HD  $275.1 \pm 52.6 \mu\text{m}$ . The difference in average macular thickness before and after HD was not statistically significant ( $t = 0.343$ ;  $p > 0.05$ ). Average macular volume before HD was  $13.44 \pm 2.69 \text{ mm}^3$ , while after HD was  $13.17 \pm 2.59 \text{ mm}^3$ . The difference in macular volume before and after HD was not statistically significant ( $t = 1,347$ ;  $p > 0.05$ ). (Table 3, Figure 2)

There was no statistically significant correlation between age and macular thickness ( $r = 0.079$ ;  $p = 0.689$ ), HD length and macular thickness ( $r = 0.180$ ;  $p = 0.359$ ), as well as between hemodynamic parameters ( $\Delta$ BW,  $\Delta$ BP) and macular thickness ( $p > 0.5$ ).

**Change in macular thickness in the examined groups**

Mean values of macular thickness changes after HD in groups of patients formed based on CRF causes are listed in Table 4. There were not statistically significant differences in macular thickness before and after HD between groups ( $p > 0.05$ ).

**Correlation of system parameters with macular thickness**

The average values of serum concentrations of the examined system parameters are given in Table 5. There was no statistically significant correlation between the parameters listed in Table and macular thickness ( $p > 0.05$ ).

**DISCUSSION**

There was a statistically significant difference between body weight and blood pressure (systolic, diastolic and mean) before and after hemodialysis. The principal goal of hemodialysis is to regulate metabolic disbalance and to remove excessively accumulated fluid. Volume overload is one of the main mechanisms of blood pressure elevation in patients undergoing HD [14]. Therefore, the change in body weight and blood pressure during HD is expected because the difference between body weight before and after HD represents the amount of removed liquids.

The results of this research showed that there was a decrease in the macular thickness, expressed as CFT and average macular thickness, after HD, however this difference was not statistically significant. Furthermore, findings of our study showed there was no statistically significant

correlation between examined systemic parameters and changes in macular thickness. Possible explanation for this result is the mechanisms responsible for maintaining the balance between plasma volume and dynamic changes in fluid volume during HD. Bauer and Brooks [15] showed that, although there is a decrease in the total volume of extracellular fluid during HD, this decrease is present only in the interstitial compartment, while the plasma volume remains unchanged. One of the possible pathophysiological mechanisms that explains this effect represents an increase in colloidal osmotic pressure. Namely, during HD due to fluid loss there is an increase in colloidal osmotic pressure and the creation of a pressure gradient between plasma and interstitial fluids. The pressure gradient causes movement of interstitial fluid to plasma, which maintains the balance between plasma volume and dynamic changes in total fluid volume in patients with HD [16]. It is possible that because of these mechanisms, HD has a low effect on retinal circulation.

The results of research conducted by Sun et al. [11] and Azem et al. [12] are in accordance with the results in this paper. Namely, Sun et al. [11] examined the change in macular thickness, among other parameters, before and after one HD session on 202 patients using OCT. In their research there were no statistically significant changes in macular thickness, although there was a decrease of subfoveal choroidal thickness. Furthermore, in a study conducted by Azem et al. [12] changes in macular thickness were not statistically significant. In both of these studies' methodology was very similar to ours. In contrast to the research above, there are also studies which showed statistically significant reduction in macular thickness after hemodialysis [8, 9]. Studies by Jung et al. [8] and Theodossiadis et al. [9], although methodologically very similar to ours, showed that there was a statistically significant reduction in macular thickness after HD. Based on the obtained results, Theodossiadis et al. [9] concluded that the reduction in macular thickness was more pronounced in patients with clinically significant macular edema. In none of these studies, there was no statistically significant correlation between changes in macular thickness

and changes in monitored systemic parameters (body weight and blood pressure), which is complementary to the results presented in this study.

A lot of CRF patients undergoing HD have severe ocular problems involving retina. Proper diagnosing and treating these conditions can be particularly challenging. Knowing how systemic changes influence retinal changes, could help ophthalmologists in clinical practice to correctly interpret diagnostic tests and adequately treat patients. Results of this study showed that there was no significant change of macular thickness during HD, which is valuable information for planning OCT examination which can be done independently of time interval from a HD session.

It is important to note that there were limitations in this research. Total number of 30 patients examined represent an insufficiently large sample and therefore obtained results could not be generalized to all patients with CRF who are on hemodialysis. Moreover, this study examined only the short-term effects of hemodialysis. It is possible the results would be different if patients were examined before and after multiple hemodialysis sessions. Diabetic macular edema is one of the most important causes of vision impairment and it develops mainly due to disruption of blood-retinal barrier and capillary leakage. It is possible that systemic hemodynamic changes during HD have greater influence on macular thickness in diabetic patients. Considering that our study enrolled only four DM patients, further research with more diabetic patients in the study cohort could give us more useful information.

## CONCLUSION

The results of this study showed that there was no significant reduction in macular thickness after HD in CRF patients. However, further research with more patients is needed and a longer follow-up period to confirm these results.

**Conflict of interest:** None declared.

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## Утицај хемодијализе на дебљину макуле

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### САЖЕТАК

**Увод/Циљ** У току једне сесије хемодијализе (ХД) долази до великих промена системских хемодинамских параметара, као и састава и волумена течности која се налази у оку. Постоји мали број студија, са опречним резултатима, које су испитивале утицај ХД на дебљину ретине и макуле. Циљ ове студије је био одређивање дебљине макуле, исказане као централна фовеална дебљина, просечна дебљина макуле и укупан волумен макуларне регије, непосредно пре и после ХД.

**Метод** У проспективну студију укључено је 30 болесника са хроничном бубрежном инсуфицијенцијом који су на лечењу ХД. Обављен је детаљан офталмолошки преглед укључујући одређивање најбоље кориговане видне оштрине, интраокуларног притиска, преглед предњег сегмента ока и очног дна. Дебљина макуле је одређивана оптичком кохерентном томографијом непосредно пре и после ХД. Параметри праћења су били централна фовеална дебљина, просечна дебљина макуле и укупан волумен макуларне регије.

**Резултати** Постојала је статистички значајна разлика између телесне тежине и крвног притиска пре и после ХД, тј. дошло је до значајног смањења наведених параметара после ХД. Резултати овог рада су показали да је након ХД дошло до смањења дебљине макуле, исказане као централна фовеална дебљина, просечна дебљина макуле и укупан волумен макуларне регије, међутим та разлика није била статистички значајна. Није било статистички значајне корелације између испитиваних системских параметара и промене дебљине макуле.

**Закључак** Резултати овог рада су показали да нема значајног смањења дебљине макуле након ХД код болесника са хроничном бубрежном инсуфицијенцијом. Међутим, неопходна су даља истраживања са већим бројем болесника и дужим периодом праћења која би потврдила ове резултате.

**Кључне речи:** дебљина макуле; хемодијализа; оптичка кохерентна томографија