• Clinical Research •

Long-term retinal microvascular alterations after endoscopic endonasal surgery in patients with sellar region tumors

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Abstract

● **AIM:** To evaluate retinal microcirculation changes at the 3rd and 12th months following endoscopic endonasal surgery in patients with sellar region tumors using optical coherence tomography angiography (OCT-A).

● **METHODS:** This prospective longitudinal observational study included 78 eyes of 39 patients with sellar tumors and 78 eyes of 39 age- and gender-matched healthy controls. Standard automated perimetry and OCT-A were performed preoperatively and at 3- and 12-month follow-ups. Visual field (VF) recovery was assessed using mean deviation (MD) values, and correlations between preoperative structural parameters and postoperative visual outcomes were analyzed.

● **RESULTS:** Baseline OCT-A values revealed significantly reduced papillary and foveal vessel densities in almost all quadrants in sellar tumor patients compared to controls (P<0.05, respectively). While VF MD values improved significantly postoperatively (P<0.001), no significant improvement was observed in microvascular vessel density or retinal nerve fiber layer (RNFL) thickness (P>0.05, respectively); instead, a tendency toward reduction was noted over 12mo. Correlation analysis between postoperative MD values and preoperative parameters showed a strong positive correlation with the superior quadrant of papillary vessel density (r=0.703, P<0.001) and RNFL thickness (r=0.518, P<0.001).

● **CONCLUSION:** Although decompressive surgery improves visual function, retinal microvascular alterations appear to deteriorate over time. These findings suggest that irreversible neurovascular damage occurs despite surgical intervention, emphasizing the importance of early diagnosis and treatment in patients with chiasmal compression. OCT-A may serve as a valuable prognostic tool for assessing structural and functional recovery in these patients.

● **KEYWORDS:** chiasmal compression; optical coherence tomography angiography; optical coherence tomography angiography; retinal microcirculation; sellar region tumors
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INTRODUCTION

Lesions in the sellar region, such as pituitary neuroendocrine tumours (PitNETs), craniopharyngiomas, aneurysms, astrocytomas and meningiomas, can lead to a variety of neuroophthalmic symptoms such as compressive optic neuropathy and ophthalmoplegia due to their proximity to critical optic pathways and structures[1]. Chiasmal compression due to these masses can lead to retrograde axonal degeneration in the anterior visual pathway, resulting in a reduction in both the retinal nerve fiber layer (RNFL) thickness and the ganglion cell layer, accompanied by visual field (VF) defects. These changes can be clinically detected using optical coherence tomography (OCT) and VF tests[2-4].

Optical coherence tomography angiography (OCT-A) is an imaging technique that provides high-resolution visualization of the retinal and choroidal vasculature[5]. The non-invasive nature, high reproducibility, and capability to evaluate retinal microvascular changes make the OCT-A technique

a potentially valuable tool for ophthalmological assessment in cases of intracranial masses interacting with the optic chiasm[6]. Previous studies have evaluated the changes in retinal microvascular structures in patients with sellar region masses using OCT-A[7-10]. However, few studies reported the microvascular changes after decompressive surgery, and the mechanisms underlying these changes remain unclear. While some studies suggest that vessel density (VD) may improve in the postoperative period[11], others report a decline in VD following surgery[12].

Remyelination and restoration of axonal flow following decompressive surgery for sellar region tumors can take months or even years to complete[13-14]. Therefore, this study evaluated long-term data with a detailed perspective on structural and functional outcomes in patients with sellar tumors undergoing endoscopic endosnasal surgery. In this context, this research seeks to expand upon previous findings by evaluating the diagnostic utility of OCT-A in patients with sellar region tumors, assessing its prognostic role in visual outcomes, and examining its correlation with functional tests. Notably, with a follow-up period of one year, this study stands out as one of the longest-term studies published in the literature.

PARTICIPANTS AND METHODS

Ethical Approval The study adhered to the ethical standards outlined in the Declaration of Helsinki and received approval from the local ethics committee of the Kocaeli University Faculty of Medicine, Kocaeli, Türkiye (approval No.GOKAEK-2022/8.12). Written informed consent was obtained from all participants.

Dataset and Study Design This prospective longitudinal study involving 39 patients with sellar region tumor and 39 age and gender matched healthy control was conducted at Kocaeli University Pituitary Research Center. The surgeries were performed by same neurosurgeons (Ceylan S, Anik I, Cabuk B, Caklili M), and total tumor resection was achieved in all cases. The procedure was carried out using the previously described endoscopic transsphenoidal technique[15].

This study included patients with chiasmal compression caused by sellar region masses, confirmed by magnetic resonance imaging (MRI); among these, 48 eyes had varying degrees of VF defects. All patients underwent comprehensive ophthalmic examinations, including best-corrected visual acuity converted to logMAR, slit-lamp biomicroscopy, intraocular pressure measurement, fundus examination, standard automated perimetry, and OCT-A. Detailed ophthalmic examinations were repeated at the 3rd and 12th months postoperatively.

The exclusion criteria of the study are identical to those used in our previous study[16], which evaluated postoperative third-month outcomes in a different patient cohort. Accordingly, the detection of any retinal or optic disc pathology during fundus examination or OCT imaging, a history of systemic diseases such as diabetes, hypertension, rheumatologic, or oncologic diseases, and non-compliance with ophthalmologic examinations were considered exclusion criteria. Additionally, patients with a history of intracranial surgery or defined intracranial lesions were excluded from the study. The patients who experienced postoperative complications such as sellar hematoma, tumor recurrence, or residual tumor were not included in the study.

Analysis of Visual Field Test VF testing was performed using the Humphrey 750I Field Analyzer (30-2 SITA-standard, Carl Zeiss Meditec, USA). Tests were considered reliable if fixation losses were <20% and false-positive/negative rates were <33%. Patients were classified based on VF improvement at the 12-month follow-up using mean deviation (MD) values: normal VF (baseline MD≥-2.00 dB, remained stable), full recovery (baseline MD<-2.00 dB, improved to>-2.00±0.2 dB), and non-recovered (baseline MD<-2.00 dB, partial improvement but not >-2.00±0.2 dB)[17].

Optical Coherence Tomography Angiography Measurements The foveal and papillary microvasculature, along with RNFL thickness, were assessed using the Optovue AngioVue system (RTVue XR Avanti, Optovue Inc., Fremont, CA, USA). Spectral-domain OCT and AngioVue software were utilized to measure retinal thickness and VD. A 4.5 mm×4.5 mm scan was performed for the peripapillary region, and a 6 mm×6 mm scan for the macular area. Only high-quality scans were included (scan quality index greater than 7/10). The software automatically quantified peripapillary vessel density (PpVD), papillary vessel density (PVD), and RNFL thickness. Superficial (SRCP) and deep (DRCP) retinal capillary plexuses were segmented, and VD was computed accordingly.

Statistical Analysis Statistical analyses were performed using IBM SPSS 26.0. Normality was assessed *via* skewness and kurtosis, and normally distributed data were reported as mean±standard deviation (SD). The Chi-Square test compared demographic and clinical characteristics, while the independent sample *t*-test assessed ocular parameters between healthy controls and sellar tumor patients. One-way ANOVA analyzed intra-group ocular changes over time, with post-hoc tests for intergroup differences. Pearson correlation examined associations between preoperative parameters and recovery, classifying correlations as low (0.00–0.30), moderate (0.30–0.70), or high (0.70–1.00). Receiver operating characteristic (ROC) analysis predicted recovery likelihood. Statistical significance was set at 0.05 and 0.01.

RESULTS

Participants Data The study included a total of 78 eyes from

Table 1 Comparison of the retinal vessel densities and RNFL thicknesses between the healthy control and the patients at preoperative, 3-month postoperative, and 12-month follow-up evaluations

Parameters	Healthy control	Patients			P^a	P^b	P^c	P
		Baseline	3rd-month	12th-month				
SRCP whole	52.42±2.23	48.55±4.82	46.98±5.08	47.4±4.64	<0.001	<0.001	<0.001	0.308
SRCP fovea	19.5±7.08	18.72±7.39	18.03±6.97	17.92±7.96	0.509	0.218	0.242	0.506
SRCP parafovea	54.59±3.21	49.01±6.29	47.73±7.02	48.84±6.40	<0.001	<0.001	<0.001	0.642
SRCP perifovea	53.2±2.53	49.59±5.18	47.8±5.68	48.33±5.08	<0.001	<0.001	<0.001	0.366
DRCP whole	56.42±6.97	51.53±7.21	49.06±7.07	49.54±6.94	<0.001	<0.001	<0.001	0.086
DRCP fovea	37.57±8.52	35.97±8.73	34.43±8.83	34.46±9.72	0.260	0.054	0.059	0.531
DRCP parafovea	59.09±4.62	56.17±4.48	54.29±5.42	54.74±5.61	<0.001	<0.001	<0.001	0.051
DRCP perifovea	58.86±5.11	52.94±7.37	49.97±8.08	50.82±7.6	<0.001	<0.001	<0.001	<0.05[d,e]
PVD peripapillary	52.44±2.43	50.32±4.65	49.8±7.06	48.17±7.67	0.001	0.003	0.001	0.323
PVD N	49.69±3.04	46.68±5.94	45.29±8.8	43.59±9.78	<0.001	<0.001	<0.001	0.158
PVD I	53.74±3.92	52.08±5.55	52.48±7.83	51.81±7.71	0.048	0.224	0.133	0.444
PVD T	54.6±3.59	52.45±5.6	51.42±6.77	48.97±7.96	0.001	<0.001	<0.001	0.162
PVD S	52.26±3.23	50.22±6.17	51.09±7.05	49.1±8.36	0.019	0.025	0.024	0.583
RNFL peripapillary	116.06±8.48	110.84±22.08	107.78±22.02	102.64±21.36	0.078	0.011	<0.001	0.177
RNFL N	103.77±10.61	97.16±22.69	94±24.99	90.05±23.72	0.037	0.010	<0.001	0.259
RNFL I	147.85±14.74	143.06±34.36	137.83±31.37	134.43±30.77	0.306	0.032	0.010	0.121
RNFL T	137.24±13.73	133.42±31.85	128.72±27.8	122.49±30.88	0.374	0.042	0.005	0.212
RNFL S	76.49±9.06	72.98±14.3	70.96±14.79	64.50±13.50	0.105	0.020	<0.001	0.296
MD		-7.28±8.96	-4.7±6.96	-3.78±6.63				<0.001[d,e,f]
FAZ		270.06±115.65	277.66±106.42	285.28±97.82				0.673

Test statistics: Independent sample *t* test. [a]Comparison of preoperative parameters of patients and healthy controls; [b]Comparison of the parameters of healthy controls and patients at the 3rd month after surgery; [c]Comparison of the parameters of healthy controls and patients at the 12th month after surgery. [d]Comparison of the parameters of patients at preoperative and 3rd month after surgery; [e]Comparison of the parameters of patients at preoperative and 12th-month after surgery; [f]Comparison of the parameters of patients at 3rd-month and 12th-month. DRCP: Deep retinal capillary plexus; FAZ: Foveal avascular zone; I: Inferior; N: Nasal; PVD: Papillary vessel density; RNFL: Retinal nerve fiber layer; S: Superior; SRCP: Superficial retinal capillary plexus; T: Temporal.

39 patients diagnosed with sellar tumors and 78 eyes from 39 healthy control participants. The mean age was 37.31±8.03y in the sellar tumor patients, and 39.72±15y in controls (P=0.213). Five patients had prolactinoma, five patients had somatotrophic PitNET, three patients had corticotropic PitNET, four patients had craniopharyngioma and one patient had optic glioma. The remaining 21 patients had non-secreting PitNET. VF defect were detected in 48 of 78 eyes (61.5%).

Comparative Analysis of Preoperative, Postoperative 3-month, and 1-year Data of Sellar Tumor Patients and Healthy Controls The baseline PpVD and parafoveal VD parameters in sellar tumor patients were significantly lower compared to those in the control group (all P<0.05), except for the foveal sector in both the DRCP and SRCP. Statistically significant differences were shown to persist in all parameters except for the inferior quadrant of PpVD when comparing the postoperative 3-month and 1-year data of patients with the control group (all P<0.05). No statistically significant differences were observed in the inferior quadrant of PVD at 3mo (P=0.224) and 1y (P=0.133) when compared to the control group (Table 1).

In the preoperative RNFL assessment of the patients, a statistically significant difference was observed only in the nasal sector compared to healthy controls (P=0.037). However, at the 3-month and 1-year follow-up evaluations, statistically significant reductions were noted in all quadrants (all P<0.05).

Analysis of Retinal Vessel Density and Retinal Nerve Fiber Layer Thickness Change of Patients with Sellar Tumors Statistically significant improvement was observed in the VF MD value at 3mo and 1y compared to baseline values (P<0.001, respectively). There was no statistically significant difference in PpVD and RNFL thickness in all

quadrants both preoperatively and postoperatively at both the 3-month and 12-month follow-ups (all $P>0.05$). While no significant difference was found in SRCP density in all zones between follow-ups, a significant decrease was observed in the perifoveal area of the DRCP at both the 3-month and 12-month follow-ups compared to baseline ($P<0.05$; Table 1).

Correlation Between the Postoperative 1-Year MD Values and Preoperative Structural Parameters Among the PVD parameters, the superior quadrant demonstrated a strong positive correlation with postoperative MD values ($r=0.703$, $P<0.001$), while moderate positive correlations were observed in the nasal ($r=0.465$, $P<0.001$), inferior ($r=0.483$, $P<0.001$), and temporal quadrants ($r=0.435$, $P=0.001$). Regarding the SRCP, a moderate positive correlation was identified in the perifoveal region ($r=0.390$, $P<0.001$). In contrast, the DRCP parameters did not show any statistically significant relationships with postoperative MD values ($P>0.05$ for all). Additionally, the RNFL parameters exhibited strong positive correlations with MD values in the superior quadrant ($r=0.518$, $P<0.001$) and moderate correlations in the nasal ($r=0.481$, $P<0.001$), inferior ($r=0.458$, $P<0.001$), and temporal quadrants ($r=0.278$, $P=0.034$; Table 2).

Analysis of Preoperative Structural Values in Relation to Visual Field Recovery in Patients No statistically significant differences were observed in the SRCP and DRCP across all quadrants. Similarly, no significant differences were noted in the RNFL for the nasal and temporal quadrants, and in the PVD for the nasal, inferior, and temporal quadrants ($P>0.05$).

The preoperative PVD in the superior quadrant was found to be significantly higher in the VF recovery group compared to the non-recovery group ($P=0.013$). Similarly, RNFL thickness was significantly greater in the superior ($P=0.003$), inferior ($P=0.044$), and peripapillary regions ($P=0.028$) in the VF recovery group (Table 3).

ROC analysis was performed to assess the predictive value of preoperative retinal parameters for VF recovery. The area under the curve (AUC) values for different test variables are presented in Table 4. Among the analyzed parameters, PVD superior demonstrated a significant predictive value with an AUC of 0.734 [$P=0.017$, 95% confidence interval (CI): 0.566–0.902], indicating a moderate predictive ability. Similarly, RNFL peripapillary showed a statistically significant association with VF recovery (AUC=0.700, $P=0.041$, 95%CI: 0.529–0.871). Also, RNFL superior exhibited the highest predictive ability among all parameters, with an AUC of 0.802 ($P=0.002$, 95%CI: 0.651–0.953).

Table 2 Correlation analysis between preoperative structural parameters and postoperative 12th-month VF MD values in sellar tumor patients

Preoperative parameters	Coefficient	12th month MD value
SRCP whole	*r*	0.385
	P	0.001
SRCP fovea	*r*	0.289
	P	0.014
SRCP parafovea	*r*	0.19
	P	0.11
SRCP perifovea	*r*	0.390
	P	0.001
DRCP whole	*r*	-0.059
	P	0.624
DRCP fovea	*r*	0.072
	P	0.547
DRCP parafovea	*r*	-0.048
	P	0.69
DRCP perifovea	*r*	-0.038
	P	0.759
PVD peripapillary	*r*	0.448
	P	0.000
PVD N	*r*	0.465
	P	0.000
PVD I	*r*	0.483
	P	0.000
PVD T	*r*	0.435
	P	0.001
PVD S	*r*	0.703
	P	0.000
Faz	*r*	-0.002
	P	0.986
RNFL peripapillary	*r*	0.523
	P	0.000
RNFL N	*r*	0.481
	P	0.000
RNFL I	*r*	0.458
	P	0.000
RNFL S	*r*	0.518
	P	0.000
RNFL T	*r*	0.278
	P	0.034

r: Correlations coefficient; VF: Visual field; DRCP: Deep retinal capillary plexus; I: Inferior; N: Nasal; PVD: Papillary vessel density; RNFL: Retinal nerve fiber layer; S: Superior; SRCP: Superficial retinal capillary plexus; T: Temporal; MD: Mean deviation; Faz: Foveal avascular zone.

DISCUSSION

This study aims to investigate the differences in structural parameters between patients with and without VF defects among those with chiasmal compression due to sellar tumors, while also evaluating these parameters in comparison with healthy controls. Additionally, we sought to investigate the changes in structural and functional test results after 3 and 12mo of follow-up and to analyze the relationship between postoperative VF data and preoperative parameters. The

Table 3 Comparison of preoperative parameters based on visual field recovery status in patients with sellar tumors

Preoperative parameters	VF non-recovery group	VF recovery group	*P*
SRCP whole	46.61±5.37	47.77±4.3	0.428
SRCP fovea	15.57±5.32	18.24±8.35	0.209
SRCP parafovea	48.48±5.2	47.29±6.99	0.522
SRCP perifovea	47.6±6.09	48.8±4.53	0.484
DRCP whole	52.3±6.91	50.38±7.64	0.385
DRCP fovea	34.57±6.89	34.00±11.20	0.840
DRCP parafovea	56.70±4.61	54.05±7.39	0.157
DRCP perifovea	53.45±7.39	50.40±11.50	0.325
Faz	299.26±131.87	275.05±110.07	0.514
PVD peripapillary	45.79±8.26	49±4.28	0.150
PVD N	41.11±10.27	44.39±5	0.232
PVD I	47.58±8.21	50.88±5.29	0.166
PVD T	50.35±7.41	51.69±6.37	0.584
PVD S	45.58±7.87	51.17±4.5	0.013[a]
RNFL peripapillary	95.37±22.34	113.44±25.71	0.028[a]
RNFL N	83.5±25.16	94.56±20.51	0.158
RNFL I	123.79±31.5	151±45.9	0.044[a]
RNFL S	109.89±30.52	145.11±37.62	0.003[a]
RNFL T	64.00±13.23	72.38±16.35	0.115

[a]*P*<0.05. DRCP: Deep retinal capillary plexus; I: Inferior; N: Nasal; PVD: Papillary vessel density; RNFL: Retinal nerve fiber layer; S: Superior; SRCP: Superficial retinal capillary plexus; T: Temporal; Faz: Foveal avascular zone; VF: Visual field.

Table 4 Results of the ROC analysis for predicting the likelihood of VF recovery based on preoperative data

Test variables	AUC	Std. error	*P*	95%CI
PVD S	0.734	0.086	0.017	0.566-0.902
RNFL peripapillary	0.700	0.087	0.041	0.529-0.871
RNFL I	0.670	0.091	0.081	0.492-0.848
RNFL S	0.802	0.077	0.002	0.651-0.953

ROC: Receiver operating characteristic; AUC: Area Under the ROC curve; DRCP: Deep retinal capillary plexus; I: Inferior; PVD: Papillary vessel density; RNFL: Retinal nerve fiber layer; S: Superior; CI: Confidence interval.

findings of this research address a significant gap in the current literature by providing long-term data on retinal microvascular alterations in patients with sellar tumors, offering a more comprehensive understanding of the disease's progression and postoperative outcomes.

In our study, a significant reduction in PVD and foveal VD values in almost all quadrants was demonstrated in patients with sellar tumors compared to healthy controls, which is supported by previous studies[7-9,12,18]. Upon sectoral analysis of PVD, nasal and temporal quadrants demonstrated highly significant reductions in VD (P<0.001 for both). This pattern closely resembled the characteristic changes in peripapillary RNFL thickness reported in previous studies[19]. Among the proposed causes of changes in retinal microvascular density in masses adjacent to the chiasm are retrograde degeneration leading to retinal ganglion cell loss and decreased metabolic activity causing a reduction in microcirculation[9,18]. Additionally, there is a theory suggesting that compression may directly impair ophthalmic artery blood flow, thereby affecting retinal function[20]. In our study, the finding that the difference in retinal microvascular density is more pronounced in specific regions rather than representing a generalized equal decrease is more consistent with the theory attributing these changes to regional metabolic adaptations caused by optic nerve compression, rather than a systemic disruption in ophthalmic artery blood flow.

Baseline retinal capillary plexus analysis demonstrated a significant reduction in both SRCP and DRCP, except in the foveal zone, compared to healthy controls. Similarly, Dallarto *et al*[7], in their study on 17 patients with pituitary adenomas, reported a significant decrease in SRCP but did not observe a corresponding difference in DRCP when compared to healthy individuals. This discrepancy may be attributed to the fact that the deep retinal plexus, which is vascularized by the anastomoses of the superficial vessels, can be secondarily affected[21]. Given that retrograde axonal degeneration originates from the chiasmal region, these differing results may be associated with the evaluation of patients at different disease stages, ranging from relatively early to advanced phases[22]. Indeed, in our study, when comparing patients with and without VF loss, a significant difference was observed in the superficial plexus, whereas such a distinction had not yet emerged in the deep plexus.

When the preoperative data of the patients were evaluated, a significant difference was observed in the nasal quadrant of the RNFL compared to healthy controls, while a marked reduction in PVD was evident in all four quadrants. Previous studies have demonstrated that thinning of the RNFL can provide insight into the presence of compression, even in patients without any VF defects[23]. At this point, it is suggested that there may be sensitivity differences between devices, and the discrepancy in the predictive power of OCT and OCT-A parameters may stem from the inherent sensitivity differences in the measurements rather than the temporal sequence of the injury[18].

One of the key aspects we particularly focused on in our study was whether there is a potential recovery in VD loss following decompressive surgery in patients with optic chiasm distortion due to tumor compression. Despite significant improvements in VF MD values at the 3rd month and 1st year postoperatively, we observed no significant increase in microvascular VD. In fact, there was a tendency for VD to decrease in nearly all quadrants. A similar decreasing trend was also observed in postoperative RNFL thickness. The fact that

nerve loss may not recover even if the VF improves has been demonstrated in previous studies[24-25]. Ben Ghezala *et al*[12] reported a significant reduction in microvascular VD at 6mo postoperatively in patients undergoing decompressive surgery for chiasmal compression. Conversely, a study by Cennamo *et al*[11] with a one-year follow-up observed significant increases in RNFL thickness and VD, indicating progressive structural and vascular recovery. In our earlier study, we demonstrated that retinal microvascular density, as measured by OCT-A, can be reduced even in patients without evident chiasmal distortion on MRI[16]. Furthermore, we observed potential improvements in vascular parameters in these patients as early as 3mo postoperatively[16]. In this study, our findings suggest that while decompression surgery can alleviate functional deficits in patients with chiasmal compression, the structural impact on the retinal microvasculature may not be entirely reversible. These contrasting outcomes may be attributed to several critical factors in the baseline characteristics of the patient populations, including the presence or absence of compression, the duration of compression, tumor size, and the severity of pressure exerted on the optic chiasm. This highlights the importance of early surgical intervention to minimize irreversible damage. Additionally, the lack of significant increases in VD and RNFL thickness despite VF improvements after decompression surgery further supports the hypothesis that ganglion cell loss has a lasting effect on reducing metabolic activity and microcirculation.

VF testing and RNFL thickness assessment are effective methods for localizing intracranial lesions and predicting visual outcomes[17,26-27]. The role and significance of OCT-A in these patients will become more evident with future studies**.** Previous studies using OCT have demonstrated that RNFL thickness has a strong correlation with baseline MD[17,23]. In our study, when evaluating the correlation between baseline RNFL and PVD parameters and postoperative VF MD, we found that the strongest correlation was observed in the superior quadrant, where superior quadrant PVD and RNFL values also demonstrated significant predictive power in estimating the likelihood of recovery in eyes with initial VF loss. Considering the characteristic pattern of band atrophy, this finding suggests that the reduction observed in a relatively later-affected quadrant may provide a more reliable prediction regarding disease progression following surgery. Overall, these findings indicate that OCT-A, in addition to conventional OCT, may provide complementary and sensitive information for predicting visual function in the postoperative period.

In conclusion, this study highlights the importance of OCT-A in assessing structural and microvascular changes in patients with chiasmal compression. While decompressive surgery effectively improves VF outcomes, our findings suggest that retinal microvascular alterations may not fully recover postoperatively. These results underscore the need for early intervention and further longitudinal studies to better understand the long-term implications of microvascular changes in these patients.

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