

Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

Supplementary Method 1 Population-based cohorts, KLOSHA and KLOSCAD.

In the KLoSHA, 714 community-dwelling Koreans aged 65 years were randomly selected from the residents of Seongnam, South Korea, in 2005, and were first followed up in 2010 and every 2 years thereafter until 2020 at SNUBH. In the KLOSCAD, 6,818 community-dwelling Koreans aged 60 years were randomly selected from the residents of 13 districts across South Korea in 2010 and followed up every 2 years at 12 university hospitals, including SNUBH, until 2020. The current SNUBH Eye Study included 500 participants who agreed to receive ophthalmic evaluations, specifically 180 participants from the KLOSHA and 320 from the KLOSCAD who were living in the city of Seongnam and Yongin.

Supplementary Method 2 Cognitive performance scores, CERAD-K and MMSE.

Neuropsychological Assessment Battery (CERAD-K-N), Digit Span Test, and Frontal Assessment Battery. The CERAD-K-N consists of the Verbal Fluency Test (VFT), 15-item Boston Naming Test (BNT), Mini-Mental Status Examination (MMSE), Word List Memory Test (WLMT), Constructional Praxis Test (CPT), Word List Recall Test (WLRT), Word List Recognition Test (WLRcT), Constructional Recall Test, and Trail Making Test A/B. We calculated the CERAD-K total score (CERAD-TS) by summing the scores of the VFT, BNT, WLMT, WLRT, WLRcT, CPT and the CERAD memory score (CERAD-MS) by summing the WLMT/3, WLRT, and WLRcT scores. Geriatric neuropsychiatrists with expertise in dementia research performed face-to-face standardized diagnostic interviews as well as physical and neurological examinations using the CERAD-K Clinical Assessment Battery to diagnose cognitive disorders.

Supplementary Table 1. Baseline retinal layer thickness data of the participants.

	Baseline (N = 430)	Drop-out group (N = 215) ^a	Follow-up group (N = 215) ^b
Subfoveal choroid	180.2±67.1	184.0±69.2	176.6±64.7
Retinal nerve fiber layer			
Average peripapillary	96.7±11.4	97.6±12.6	95.8±10.1
Macular			
Outer	151.5±24.7	149.7±24.9	152.4±23.4
Inner	92.7±13.6	90.4±12.4	94.7±14.0
Total	253.6±34.9	250.2±34.9	257.2±34.7
Ganglion cell layer			
Outer	133.5±19.2	135.6±19.8	131.3±18.3
Inner	186.5±24.9	185.0±24.1	187.8±25.6
Total	334.9±37.1	335.6±37.1	334.2±37.1
Inner plexiform layer			
Outer	111.4±13.5	112.6±14.3	110.1±12.6
Inner	152.9±15.2	152.3±15.2	153.6±15.2
Total	279.3±24.9	279.9±25.7	278.7±24.1
Inner nuclear layer			
Outer	127.2±11.9	127.7±11.9	126.7±11.9
Inner	158.5±15.7	156.9±15.7	160.1±15.6

Total	305.7±24.2	304.7±24.0	306.8±24.5
Outer plexiform layer			
Outer	109.6±9.0	109.1±9.2	109.9±8.8
Inner	137.8±20.5	136.1±20.4	139.5±20.4
Total	267.3±26.5	265.3±26.4	269.4±26.5
Outer nuclear layer			
Outer	205.7±26.8	206.7±28.0	204.7±25.6
Inner	262.6±36.1	263.1±38.2	262.0±33.8
Total	498.3±59.7	499.8±63.4	496.7±55.8

*Student t test for continuous variables and chi square test for categorical variables

†paired t test for continuous variables

Supplementary Table 2. Differences in cognitive performance between the below-lowest-quartile and the above-lowest-quartile groups

	Below lowest quartile(<231 μm) (n = 55)		Above lowest quartile(\geq 231 μm) (n = 160)	
Age (years)	75.9 \pm 6.7		76.5 \pm 6.5	
Women (%)	52.4		47.2	
Education (years)	9.2 \pm 5.7		9.1 \pm 5.6	
	CERAD-TS	MMSE	CERAD-TS	MMSE
Annual cognitive decline Scores (Points)	3.79 \pm 0.28	0.89 \pm 0.07	2.42 \pm 0.34	0.58 \pm 0.08
Baseline	65.4 \pm 3.6	23.6 \pm 1.5	68.5 \pm 3.8	25.2 \pm 1.6
Follow-up	46.9 \pm 2.5	20.1 \pm 1.1	56.7 \pm 2.7	22.9 \pm 1.2
Prevalence of cognitive disorders (%)	Baseline	Follow-up	Baseline	Follow-up
Mild cognitive impairment	49.1	69.1	6.3	9.4
Alzheimer's dementia	10.9	16.4	1.3	1.9

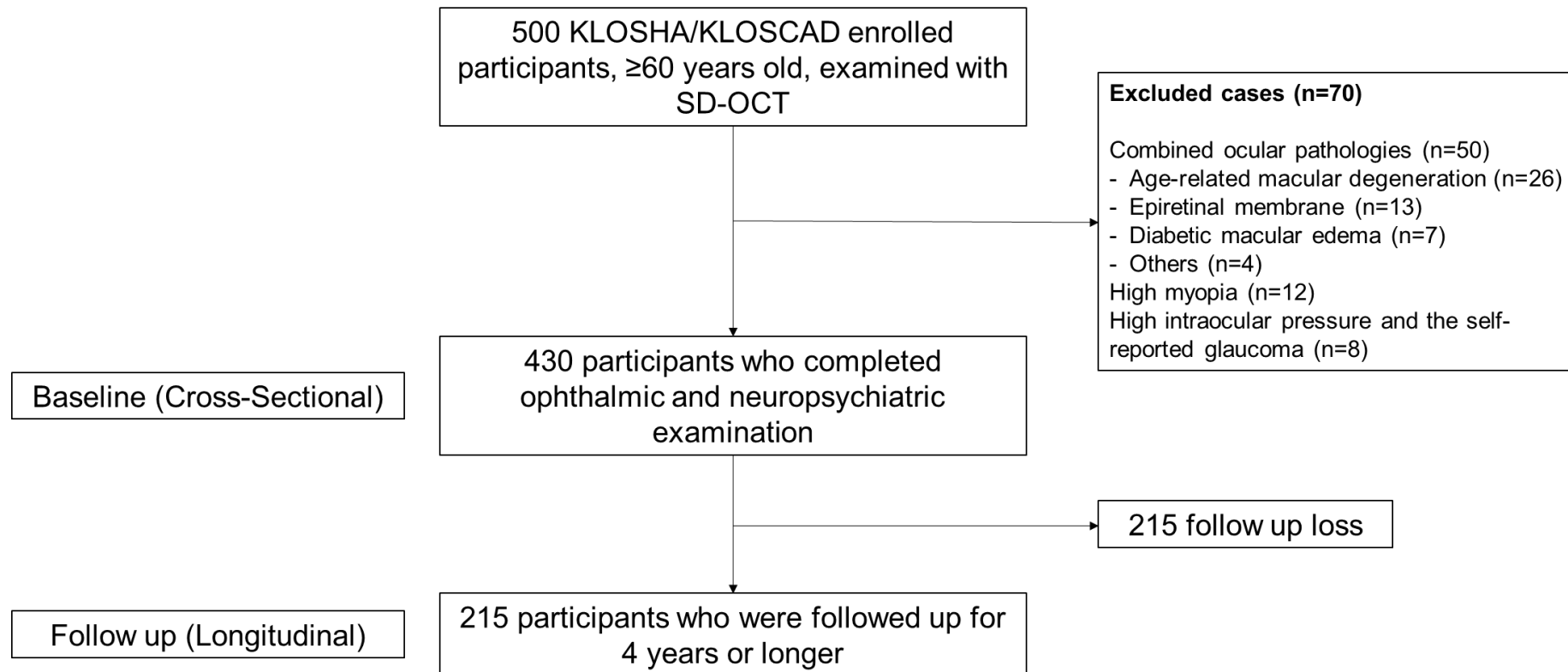
CERAD-TS, Consortium to Establish a Registry for Alzheimer's Disease Neuropsychological Battery total score; MMSE, Mini-Mental State Examination.

Supplementary Table 3. Baseline and follow-up cognitive scores and RNFL thickness according to the ApoE4 status

	Baseline			Follow-up		
	ApoE4 negative (N=360)	ApoE4 positive (N=70)	<i>p</i> -value	ApoE4 negative (N=185)	ApoE4 positive (N=30)	<i>p</i> -value
CERAD-TS	66.9±15.3	66.9±15.3	.661	54.1±14.5	52.9±14.4	.780
MMSE	24.7±4.5	24.5±4.7	.478	22.0±4.1	21.4±3.5	.529
RNFL thickness						
Outer	151.1±24.9	150.9±20.2	.169	155.0±25.8	147.8±19.0	.315
Inner	92.5±13.2	92.8±14.2	.832	90.6±12.8	89.3±9.7	.221
Total	249.6±35.6	249.7±31.4	.552	252.6±37.2	249.2±28.1	.370

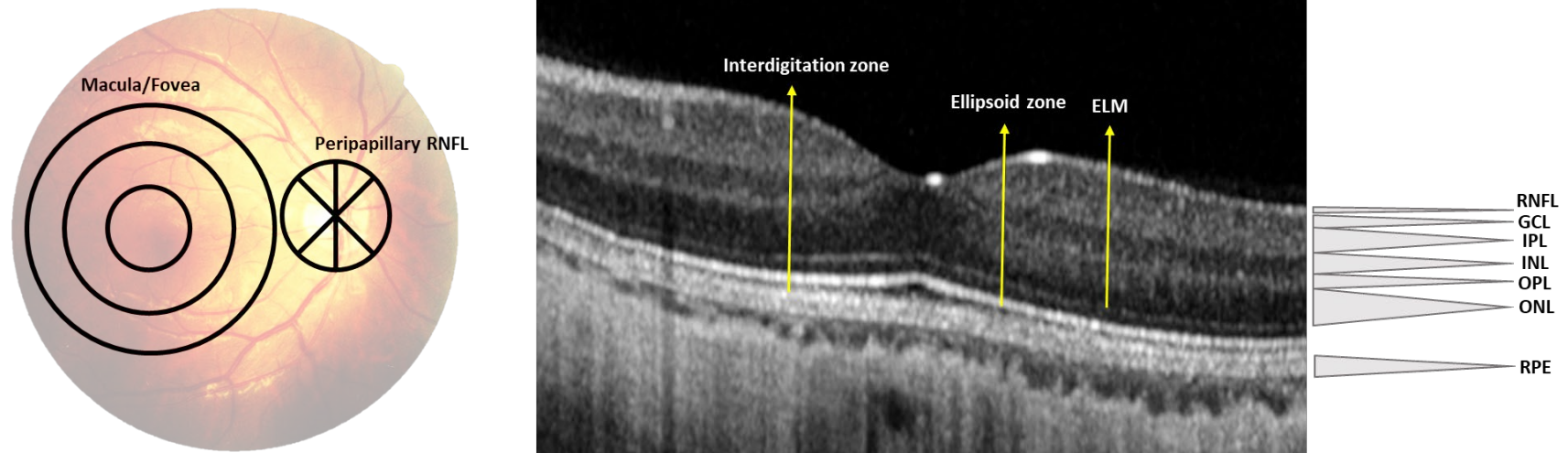
Student t test for continuous variables

Supplementary Figure 1 (eFigure 1)



Supplementary Figure 1. Flow chart of patient enrollment in the KLOSHA/KLOSCAD longitudinal cohort study. After identifying 500 participants who underwent ophthalmic evaluation including SD-OCT, 70 participants were excluded for combined ocular pathologies (n=50), high myopia (n=12), and high intraocular pressure and self-reported glaucoma history (n=8). Consequently, the cross-sectional analysis included 430 participants. Among these, 215 who were followed up at 5- to 6-year intervals were analyzed in the longitudinal study.

Supplementary Figure 2 (eFigure 2)



Supplementary Figure 2. (Left) Peripapillary RNFL fields and macula/fovea outer, inner, and center ETDRS fields. We measured each layer thickness and integrated them as the average peripapillary RNFL thickness and outer ring, inner ring, and total macular area macular thickness. (Right) Automated retinal layer calculation in the built-in analysis program.