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ORIGINAL RESEARCH

Chronic Central Serous Chorioretinopathy in Elderly Subjects: Structure and Blood Flow Characteristics of Retina and Choroid

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ABSTRACT

Introduction: With advancements in imaging technology, researchers have been able to identify more distinctive imaging features of central serous chorioretinopathy (CSC). However, existing research primarily concentrates on young patients aged 50 years and below, leaving a dearth of studies on elderly CSC patients. Previous studies indicate that elderly CSC patients may exhibit unique imaging characteristics and have a clinical prognosis that significantly differs from younger patients. This study aimed to evaluate the characteristics of retina, choroid structure, and blood flow in elderly patients with chronic CSC (cCSC) examined multimode imaging and try to find new pathogenesis information of it.

Methods: Using a cut-off age of 50 years, patients with chronic central serous chorioretinopathy were divided into two groups: older and younger. The control group consisted of 40 healthy individuals, with their right eyes assigned. Various clinical features were recorded, including the incidence of ellipsoid zone rupture (EZ-), fibrin in the subretinal fluid (SRF), pachydrusen, subretinal drusenoid deposits (SDD), pigment epithelial detachment (PED), double-layer sign (DLS), and choroidal lipid globule cavern. Measurements were taken for the thickness of the outer nuclear layer (ONL), the length of the extended outer photoreceptor segment (POS), the height and width of SRF, the vascular density of each layer of the retinal capillary plexus, the central macular thickness (CMT), and the subfoveal choroidal thickness (SFCT).

Results: The proportion of females in the elderly group (43.75%) was significantly higher than that in the youth group (22.41%) ($p = 0.034$). The degree of hyperopia in the elderly group (1.03 ± 0.73) was higher than that in the youth group (0.26 ± 1.06), with a significant difference in BCVA ($p = 0.05$). The thickness of SFCT, CMT, ONL in the elderly group, and the length of photoreceptor outer segment in the elderly group were thinner than those in the youth group ($p < 0.05$). Choroidal

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capillary perfusion area (CCPA), macular area, and paramacular area were lower in the elderly group than those in the youth group in the full scan range ($p < 0.05$). The blood flow densities of deep capillary plexus (DCP), intermediate capillary plexus (ICP), and superficial capillary plexus (SCP) in the whole scan range, macular area, and paramacular area were lower in the elderly group than in the youth group, but the differences were not statistically significant.
Conclusions: In conclusion, our data suggest that elderly patients with cCSC may experience different disease outcomes. Elderly cCSC patients exhibit less gender bias, poorer vision, more severe structural damage and ischemia in the choroid and retina, and have a higher risk of developing choroidal neovascularization.

Keywords: Chronic central serous chorioretinopathy; Vascular density; Subfoveal choroidal thickness; Ellipsoid zone rupture; Pachydrusen; Outer nuclear layer; Outer photoreceptor segment; SS-OCT

Key Summary Points

Why carry out this study?

Limited research has been conducted on geriatric chronic central serous chorioretinopathy, resulting in a lack of understanding regarding its clinical characteristics and disease progression.

This study aims to explore the potential differences in imaging features and prognosis between older and younger patients with chronic chorioretinopathy (cCSC).

What was learned from the study?

Elderly patients with central chronic serous chorioretinopathy may experience different disease outcomes.

Elderly cCSC patients exhibit less gender bias, poorer vision, more severe structural damage and ischemia in the choroid and retina and have a higher risk of developing choroidal neovascularization.

INTRODUCTION

Central serous chorioretinopathy (CSC) is a disease characterized by the detachment of the retina, with or without detachment of the retinal pigment epithelium (PED). This condition is associated with increased permeability in the choroid and dysfunction of the retinal pigment epithelium [1, 2]. CSC typically presents with varying degrees of visual loss or blurred vision, distortion, diminution of vision, and changes in color vision [3]. The diagnosis of CSC usually involves the use of fluorescein angiography (FFA) and indocyanine green angiography (ICGA), which are considered the gold standard. FFA reveals one or more leakage points at the level of the retinal pigment epithelium, while ICGA shows increased volume, permeability, and delayed filling of choroidal capillaries in multiple regions [4–6]. However, the invasive nature of FFA and ICGA limits their widespread use. Non-invasive imaging techniques such as SD-OCT and subsequent SS-OCT have made it possible to observe the retina, choroid, and even the sclera [7]. Previous studies have demonstrated that CSC patients exhibit significantly increased choroidal thickness, expanded large and middle choroidal vessels, attenuated choroidal capillaries, and abnormal retinal perfusion compared to normal controls [8–10].

CSC affects predominantly middle-aged people (30 to 50 years old) with a mean age of onset around 40 years old (39 to 41 years) and has a significant male preference [11–13]. The incidence rate of senile CSC is low, and it is easy to be complicated with choroidal neovascularization. Its clinical manifestations are very different from those of young CSC patients, and it is easy to confuse age-related macular degeneration (AMD) and polypoid choroidal vasculopathy (PCV), which makes the diagnosis of elderly CSC patients difficult [14, 15]. The number of elderly CSC patients seems to be increasing due to the aging population and the development of multimodal imaging. However, we know little about the unique pathological changes and clinical manifestations of elderly CSC patients.

Our purpose is to investigate the characteristic changes of retina, choroid structure, and blood flow in elderly patients with cCSC using scanning laser fundus color photography, FFA, ICGA, SS-OCT, SS-OCTA, and other imaging technologies, explore the unique clinical characteristics them and reveal new information about its pathogenesis.

METHODS

This retrospective study was approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University, and all research and data collection complied with the Declaration of Helsinki. Patients were informed of the risks of invasive examinations and signed informed consent forms.

Newly diagnosed treatment-naïve chronic CSC patients were included in this study from June 2021 to January 2023 at the First Affiliated Hospital of Zhengzhou University. They were divided into two groups according to age: the young group (aged between 20 and 50 years old), 45 men with 47 eyes and 13 women with 15 eyes; the elderly group (age $\geq$ 50 years old), 18 males with 20 eyes and 14 females with 17 eyes. Among the young group, no complications were observed. However, in the elderly group, seven patients had comorbidities of hypertension, three patients had comorbidities of diabetes, and two patients had comorbidities of lower limb varicose veins. At the same time, we recruited 40 age- and sex-matched normal controls (40 eyes), all of whom were included in the right eye data for statistical analysis.

Chronic central serous chorioretinopathy was diagnosed as a neurosensory detachment resulting from one or more sites of leakage at the level of the retinal pigment epithelium (RPE) during the initial clinical examination. Additionally, there was evidence of persistent subretinal fluid (SRF) lasting for a duration of 3 months or longer. PCV can be ruled out by the presence of polypoidal lesions on SS-OCT B-scan images or ICGA. AMD can be ruled out by evaluating choroidal thickness and leakage pattern on FFA. Exclusion criteria include: (1) other retinal or choroidal diseases those can cause SRF; (2) the patient has a history of laser photocoagulation or other eye surgery; (3) choroidal neovascularization (CNV) was detected by OCT angiography (OCTA) or FFA; (4) poor image quality cannot be accurately analyzed; (5) high myopia, equivalent spherical lens > — 6D or eye axis > 26 mm.

All CSC patients received complete ophthalmic examination, including optometry, intraocular pressure measurement, slit lamp biomicroscope, scanning laser fundus color photography, FFA, SS-OCT, SS-OCTA (SS-OCTA, VG200D, micro-image, Luoyang, China), and some patients received ICGA examination. The OCT instrument VG-200 used in this study is equipped with a scanning laser with a central wavelength of 1050 nm, with a scanning speed of 200000A-Scans/s, axial resolution of 1.8 μm, and scanning depth of 6 mm. All the eyes examined were centered on the fovea of the macula, and the images were obtained by using Angio 6 mm × 6 mm 512 × 512 R4 and Star 18Line R16 scanning modes. The choroid is defined as the area from the base boundary of RPE-Bruch membrane complex to the junction of choroid and sclera. Except FFA and ICGA, healthy subjects received the same ophthalmic examination as CSC patients.

In this study, we recorded the demographic and basic clinical characteristics of cCSC patients at the time of treatment, such as age, sex, eye type, equivalent spherical lens degree, BCVA (expressed in logarithm of the equivalent value of the minimum resolution angle (logMAR). According to SS-OCT b-scan images, determine whether there are ruptured ellipsoid zone (EZ-), subfoveal fibrin in SRF, pachydrusen, subretinal drusenoid deposits (SDD), pigment epithelial detachment (PED, defined as dome-shaped detachment of the pigment epithelium from Bruchx's membrane), double layer sign (DLS, defined as the detachment of RPE from the shallow irregular elevation of irregularly pigmented epithelium on Bruch's membrane), choroidal lipid globule cavern (choroidal lipid globule cavern is defined as the appearance of choroidal void, focal ellipsoid low reflection area in the Sattler and Haller layers, with a high penetration imaging trail behind, and no blood flow signal in OCTA [16, 17]). We used the SS-

OCT built-in caliper to measure the thickness of the outer nuclear layer (ONL) (the distance between the inner boundary film of the concave and the outer film), the length of the extended photoreceptor outer section (POS) (the distance between the outer film of the concave and the tip of the extended photoreceptor), and the height and width of the SRF; SS-OCT built-in artificial intelligence quantitative software was used to measure the vascular density of superficial capillary plexus (SCP), intermediate capillary plexus (ICP) and deep capillary plexus (DCP). Meanwhile, the choroidal capillary perfusion area (CCPA), the central macular thickness (CMT), and subfoveal choroidal thickness (SFCT) were measured using the artificial intelligence quantitative software.

SPSS 25 statistical software was used for statistical analysis. Shapiro–Wilk test was used for the normality of statistical variables before analysis: for continuous variables with normal distribution, independent sample *t* test was used, on the contrary, Mann–Whitney *U* test was used, and chi-square test was used for categorical variables; single factor analysis of variance is used in the comparison of multiple groups. Welch test is selected if the variance between groups is unequal, and nonparametric test is selected if the statistical variable is not normal; The difference was statistically significant ($p < 0.05$). The statistical value is expressed as mean ± standard deviation.

RESULTS

The typical clinical characteristics of normal controls, elderly cCSC and young cCSC are shown in Figs. 1, 2, and 3, respectively. The average age of the elderly group is 55.91 ± 5.10, and the average age of the young group is 40.09 ± 6.20. The proportion of women in the elderly group (43.75%) is significantly higher than that of the young group (22.41%) ($p = 0.034$), and the proportion of both eyes in the elderly group (18.5%) is higher than that of the young group (5.13%), with no statistically significant difference ($p = 0.095$). The basic characteristics of the elderly group and the young group are shown in Table 1. The degree of hyperopia in the elderly group (1.03 ± 0.73) was higher than that in the young group (0.26 ± 1.06), the BCVA was poor.

The length of the outer segment of the photoreceptor was thinner than that of the young group (464.69 ± 109.57 vs. 539.32 ± 111.18; 300.56 ± 105.66 vs. 371.17 ± 168.97; 77.11 ± 26.44 vs. 94.38 ± 26.35; 58.64 ± 25.03 vs. 66.85 ± 20.58, $p < 0.05$). The incidence of pachydrusen, double layer sign, rupture of the ellipsoid zone, and subretinal fibrin in the old group was significantly higher than that in the young group (70.27 vs. 39.34%; 59.46 vs. 27.87%; 70.27 vs. 26.23%; 32.43 vs. 14.75; $p < 0.05$). The incidence of PED and choroidal lipid globule cavern in the elderly group was higher than that in the young group, but there was no statistical difference (72.97 vs. 67.21%; 56.76 vs. 50.82%, $p > 0.05$). Only two cases (5.41%) of SDD were found in the elderly group. Table 2 shows clinical characteristics of the two groups. Figure 4 illustrates the SS-OCT characteristics of elderly patients (Fig. 4).

The CCPA in the whole scanning range, macular area, and paramacular area of the elderly group were lower than those in the young group (11.56 ± 2.17 vs. 13.11 ± 2.14; 2.62 ± 0.69 vs. 3.01 ± 0.66; 8.99 ± 1.70 vs. 10.17 ± 1.67; $p < 0.05$). The blood flow density of DCP, ICP, and SCP in the whole scanning range, macular area, and paramacular area of the elderly group were lower than those in the young group, however, the difference was not statistically significant (7.98 ± 4.50 vs. 8.62 ± 3.97; 2.16 ± 2.82 vs. 2.49 ± 2.28; 9.95 ± 5.48 vs. 10.69 ± 4.75; 14.85 ± 5.62 vs. 15.95 ± 5.39; 8.92 ± 4.61 vs. 9.61 ± 4.74; 16.84 ± 6.54 vs. 17.95 ± 5.92; 30.06 ± 5.39 vs. 30.67 ± 5.59; 23.70 ± vs. 5.93 vs. 24.13 ± 6.48; 32.21 ± 5.46 vs. 32.70 ± 5.63, $p > 0.05$). Compared with the control group, CCPA, DCP, ICP, and SCP in the elderly group and the young group was decreased. The characteristics of chorioretinal blood flow perfusion in the two groups are detailed in Table 3.

DISCUSSION

Previous studies have shown that CSC has obvious male tendency, and the proportion of

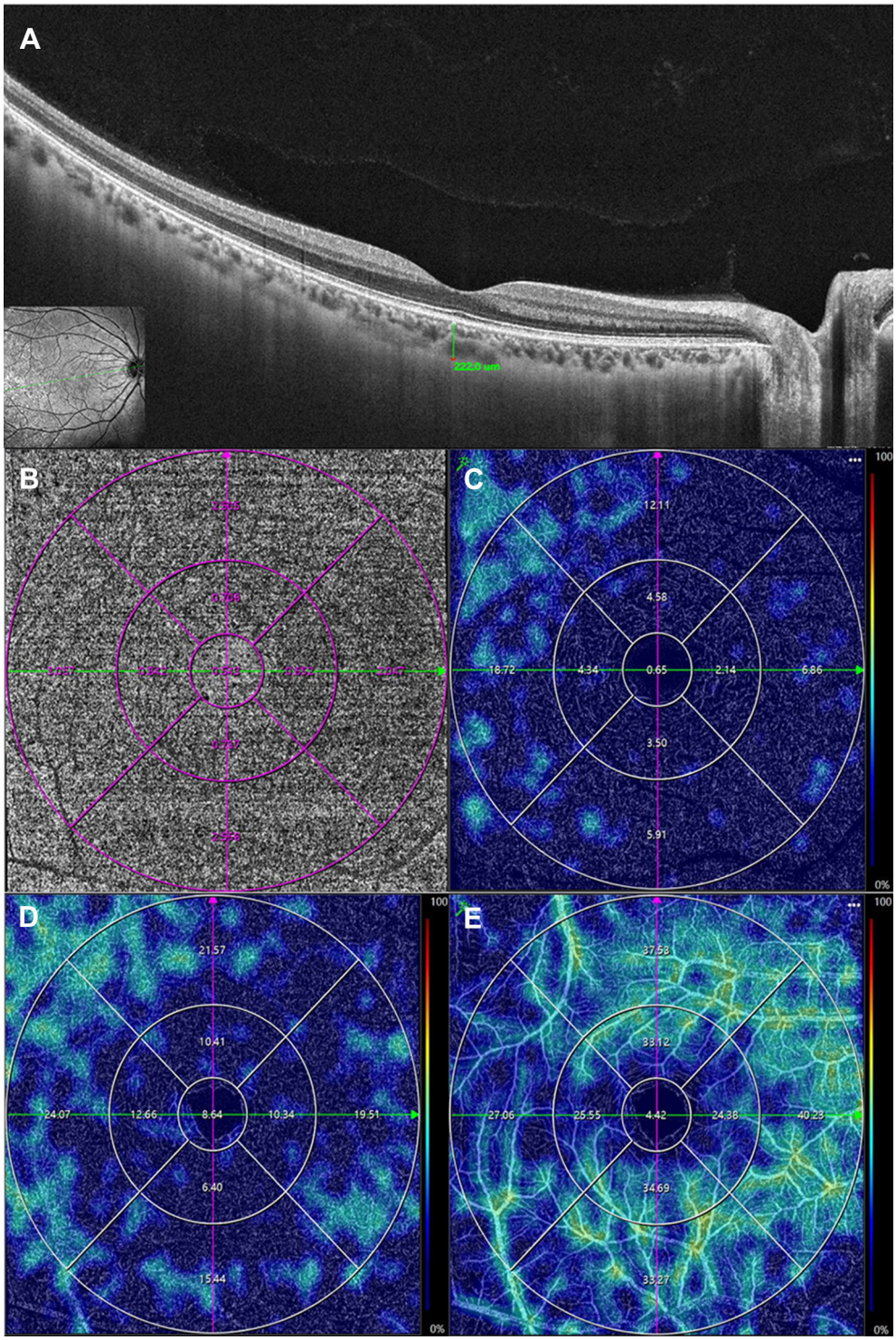

Fig. 1 Images of the healthy right eye of a 33-year-old man. The refraction was – 1.0 diopters. **A** 12-mm B-mode OCT image through the fovea showing normal appearance of the retina and choroid. The central choroidal thickness is 222.0 µm. **B** Perfusion area of choroidal capillary layer in normal human. **C** Deep capillary plexus in normal human. **D** Intermediate capillary plexus in normal human. **E** Superficial capillary plexus in normal human

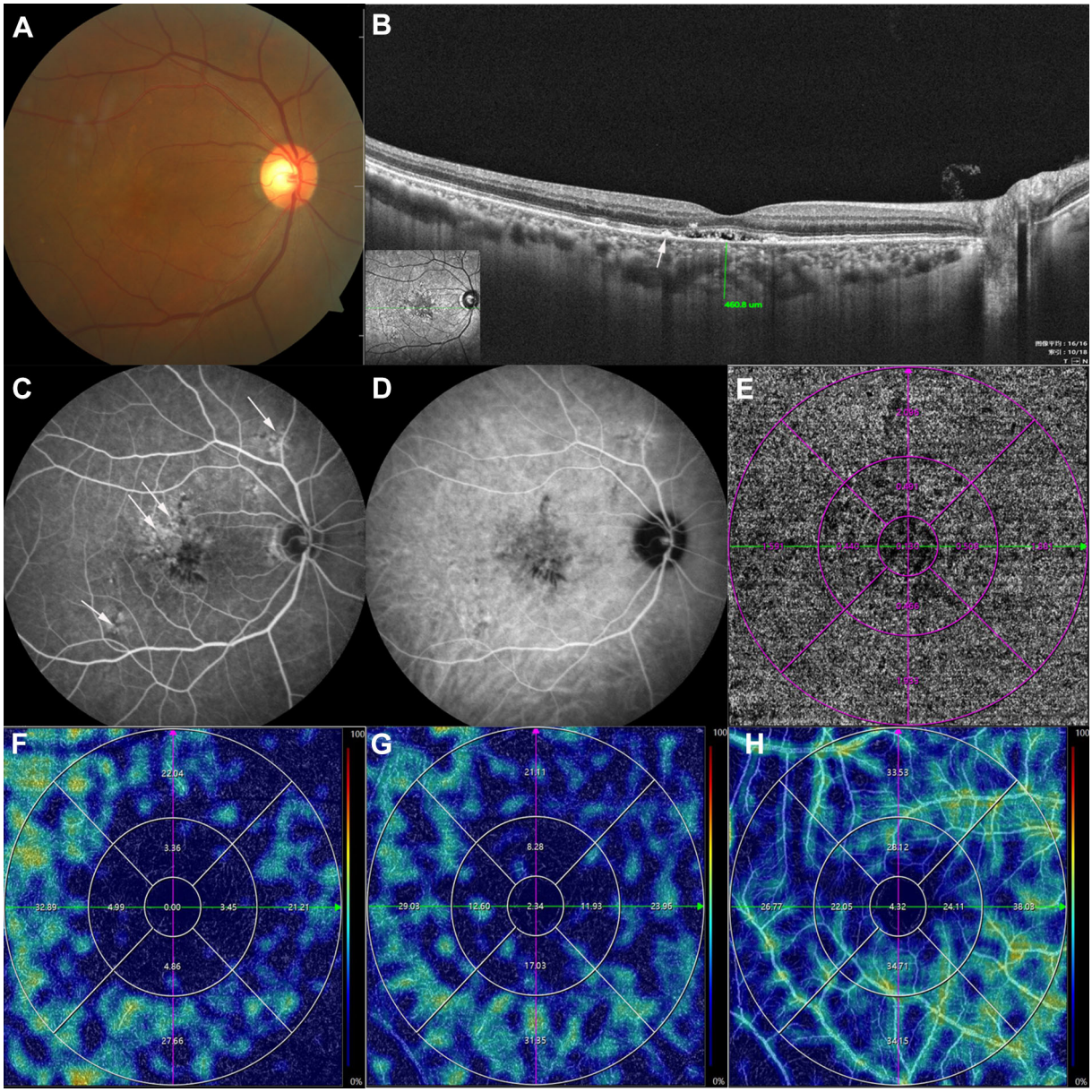

Fig. 2 Images of the right eye of a 62-year-old man with cCSC. The refraction was + 1.20 diopters. BCVA was 0.7 logarithm of the minimum angle of resolution units. **A** Color fundus photograph showing a serous retinal detachment (SRD) at the macular area. **B** 12-mm B-mode OCT image through the fovea showing EZ-, SRD and pachydrusen (*white arrow*). The central choroidal thickness is 460.8 µm. **C**, **D** FFA showed multifocal leakage in the macular area, and ICGA showed hypermeability of choroid(*white arrow*). **E** Perfusion area of choroidal capillary layer in elderly CSC patient. **F** Deep capillary plexus in elderly CSC patient. **G** Intermediate plexus in elderly CSC patient. **H** Superficial capillary plexus in elderly CSC patient

male and female is about 5/1. In this study, we found that the proportion of males in the elderly cCSC decreased significantly, which cannot be explained simply by the high proportion of females in the elderly population. Emine et al. [18] found that CSC is related to the increase of total testosterone level, which may play a role in making men vulnerable to CSC.

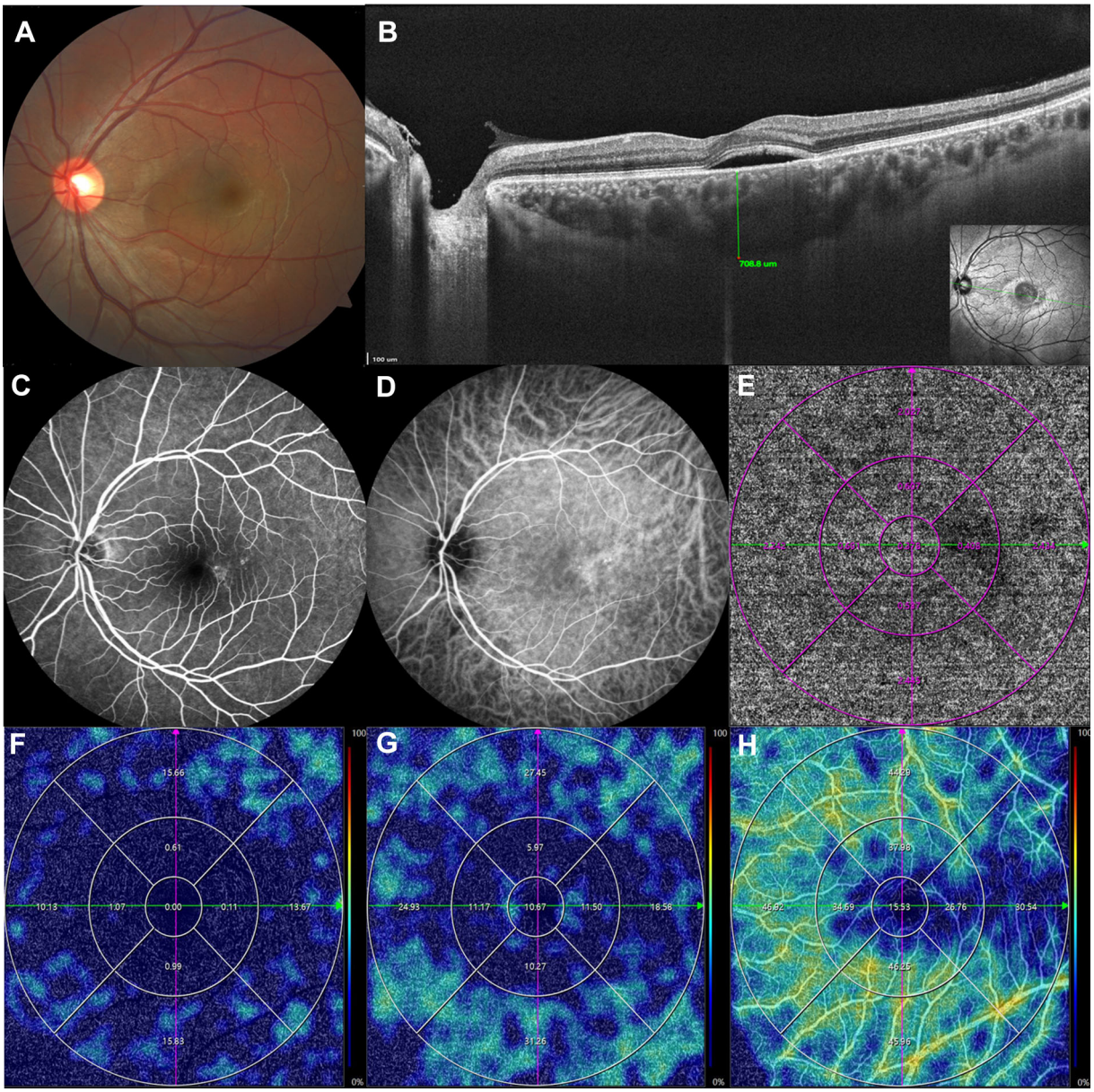

Fig. 3 Images of the right eye of a 34-year-old man with cCSC. The refraction was 0 diopters. Best-corrected visual acuity was 0.15 logarithm of the minimum angle of resolution units. **A** Color fundus photograph showing a serous retinal detachment (SRD) at the macular area. **B** 12-mm B-mode OCT image through the fovea showing SRD. The central choroidal thickness is 708.8 µm. **C**, **D** FFA shows cooking smoke exudation in macular area, and ICGA shows hypermeability of choroid. **E** Perfusion area of choroidal capillary layer in young CSC patient. **F** Deep capillary plexus in young CSC patient. **G** Intermediate capillary plexus in young CSC patient. **H** Superficial capillary plexus in young CSC patient

After the age of about 45, the testosterone level of men will decline significantly, and the gap between male and female in androgen level will gradually narrow, which may be one of the reasons for the decline in the proportion of men in the elderly CSC. Many studies have found that CSC may involve both eyes [19, 20], which seems to be more common in elderly CSC.

Table 1 Baseline characteristics of elderly and young cCSC

Parameters	Elderly (n = 32)	Young (n = 58)	p value
Age, year	55.91 ± 5.10	40.09 ± 6.20	< 0.001
Sex,(M/F), N	18/14	45/13	0.034
Bilaterality, N (%)	5(18.52%)	3(5.17%)	0.095

Tanaka et al. [21] found that the incidence of bilateral macular structure abnormalities in CSC patients over 70 years old is very high.

The structural changes of retina and choroid in cCSC patients have been extensively studied. Plenty of studies have shown that the pathological changes of CSC can occur simultaneously at the vitreoretinal level, retinal level, RPE level, choroid level, and even sclera level [22–24]. CSC has always been considered as one of the pachychoroid disease spectrum. Thicker choroidal thickness and macular thickness are closely related to poor vision [22, 25]. However, in our study cohort, compared with the younger group, the elderly cCSC patients had significantly decreased SFCT and CMT compared to the younger group, yet they had worse visual acuity. Apparently, the cause of low visual function in the elderly cCSC is different from the younger group. We found that the elderly cCSC patients had significantly thinner outer nuclear layer (ONL), shorter photoreceptor outer segment (POS) length, and higher incidence of ellipsoid zone rupture (EZ-) is significantly. Also, the retinal pigment epithelial layer (RPE) damage is more serious in the elderly group. Recent studies have shown that the thickness of ONL is positively correlated with the best corrected visual acuity (BCVA) in cCSC patients. The thinner the ONL and the lower the BCVA, the higher the incidence of EZ- [26]. Mingwei Zhao et al. [27] believed that the thinning of foveal ONL was positively correlated with the course of CSC, and the longer duration of disease limited the recovery of foveal ONL. ONL is composed of pyramidal cell bodies, so the decrease of ONL thickness indicates that the number of pyramidal cells decreases. POS length is the distance between the outer membrane and the extended POS tip, which can indicate the integrity of the foveal photoreceptor [28]. Some studies have shown that POS length is positively correlated with BCVA and is a good predictor of the visual outcome after SRF absorption [29]. We found that POS length in the elderly group is significantly lower than that in the young group, which indicates that the damage of photoreceptors in the elderly group is more serious. Previous studies have shown that there is a strong correlation between the integrity of EZ and visual function [28]. EZ is the expression of the mitochondria of photoreceptors on OCT. The occurrence of EZ-will inevitably affect the physiological and metabolic activities of photoreceptors, and may also affect RPE cells, which will eventually reduce their pumping capacity and lead to the decline of vision. We analyzed the FFA results of elderly cCSC patients and found that the proportion of diffuse punctate exudation on RPE was significantly higher than that of the younger group, which means more extensive RPE damage in elderly group. RPE uptakes and digests the exfoliated photoreceptor extracellular segments and participates in the renewal of photoreceptor extracellular segments. RPE damage will lead to a decrease in its phagocytic degradation function and affect the renewal and metabolism of photoreceptor cells. The proportion of DLS is significantly higher in elderly cCSC patients than that in young patients. The existence of DLS is often associated with asymptomatic type 1 CNV, which is more common in PCV and is associated with worse visual outcomes [22, 30, 31]. Some studies have shown that the presence of fibrin in subretinal fluid is related to the serious damage of RPE and poor visual acuity [32]. The incidence of fibrin in our cohort is significantly higher in the elderly group.

Drusen are deposits of yellow-white extracellular debris composed of complement protein, esterified and non-esterified cholesterol, apolipoprotein, carbohydrate and trace elements, which are located above the retinal pigment epithelium (RPE) or between RPE and Bruch membrane. Soft glass verruca and

Table 2 Clinical characteristics of elderly and young cCSC

Parameters	Elderly (n = 37)	Young (n = 62)	p value
SER, D	1.03 ± 0.73	0.26 ± 1.06	< 0.001
BCVA, logMAR	0.38 ± 0.23	0.21 ± 0.27	< 0.001
SRF height (μm)	297.10 ± 836.69	246.67 ± 333.19	0.129
SRF width (μm)	2567.16 ± 1521.24	2891.63 ± 1931.43	0.720
SFCT (μm)	464.69 ± 109.57	539.32 ± 111.18	0.002
CMT (μm)	300.56 ± 105.66	371.17 ± 168.97	0.019
ONL thickness (μm)	77.11 ± 26.44	94.38 ± 26.35	0.002
Elongated POS length (μm)	58.64 ± 25.03	66.85 ± 20.58	0.048
PED, *N* (%)	27 (72.97%)	41 (67.21%)	0.549
Pachydrusen, *N* (%)	26 (70.27%)	24 (39.34)	0.003
Double layer sign, *N* (%)	22 (59.46%)	17 (27.87%)	0.002
SDD, *N* (%)	2 (5.41%)	0.00	NA
EZ-, *N* (%)	26 (70.27%)	16 (26.23%)	< 0.001
Choroidal lipid globule cavern, *N* (%)	21 (56.76%)	31 (50.82%)	0.568
SRF fibrin, *N* (%)	12 (32.43%)	9 (14.75%)	0.039

SER spherical equivalent refraction, *BCVA* best-corrected visual acuity, *NA* not applicable, *logMAR* logarithm of the minimum angle of resolution, *SRF* subretinal fluid, *CMT* central macular thickness, *ONL* outer nuclear layer, *PED* pigment epithelial detachment, *SDD* subretinal drusenoid deposits, *EZ-* ellipsoid zone disrupt

reticular pseudovitreous verruca (also known as verruciform sediment SDD) are considered as typical pathological changes of age-related age degeneration (AMD) [33, 34]. Rick Spaide reported in 2018 that pachydrusen, a special entity, was isolated, with a diameter greater than 125 μm. It is related to choroidal thickening in non-exudative macular degeneration [35]. Hidetaka et al. [36] studied 302 eyes with CSC and found that the incidence of pachydrusen in CSC was 27.2%, and often located in the delayed area of choroidal capillary filling and above the dilated choroidal vessels. Kihwang et al. [37] concluded that the attenuation of choroidal capillaries was the main reason for the occurrence of pachydrusen and found that the incidence of pachydrusen in cCSC was closely related to age. In this study, we found that the probability of pachydrusen and SDD was significantly higher in the elderly group than in the younger group, but no soft drusen was found in either group. Also, the choroidal capillary perfusion area was markedly lower in the elderly group than that in the young group, supporting the above view. Jay et al. [38] believed that pachydrusen might be a potential risk factor for the development of PCD. When the eyes with pachydrusen developed macular neovascularization (MNV), the main manifestation was PCV [39]. The incidence of SDD in our cohort is very low and only found in the elderly group. It is reported that the incidence of SDD in PCV is 4.1%, which is considered as an independent risk factor for neovascularization [40], while the incidence of pachydrusen in PCV is 70% [41]. We believe that elderly cCSC patients with hyaline warts are more likely to develop PCV. In the next study, we will perform a longitudinal observation of elderly cCSC patients with hyaline to validate our view.

Friedman and Smith [42] first described the existence of choroidal lipid globule cavern in

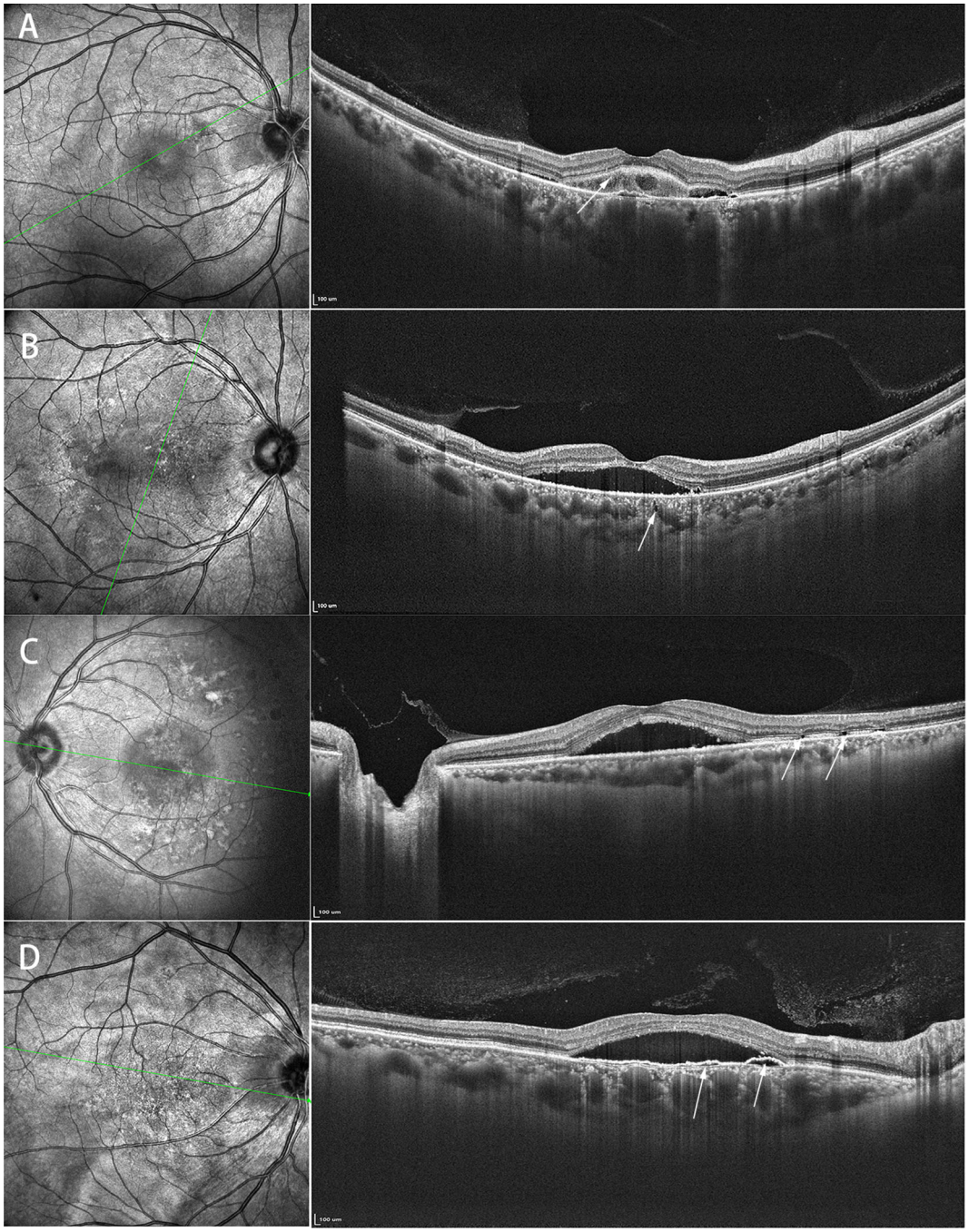

Fig. 4 Characteristic SS-OCT changes in elderly patients. **A** Image of the right eye of a 51-year-old male patient showing subretinal fibrinoid exudation (*white arrow*). **B** Image of the right eye of a 66-year-old female patient showing choroidal lipid globule cavern (*white arrow*). **C** Image of the left eye of a 52-year-old male patient with visible EZ- (*white arrow*). **D** Image of the right eye of a 57-year-old female patient with visible DLS (*white arrow*)

human eyes after death. Rosa et al. [43] used OCT to observe the focal ellipsoid low reflection area at the choroidal level in patients with AMD map-like atrophy, followed by a high

Table 3 Choroid and retinal blood perfusion of elderly and young cCSC

Parameters	Elderly (n = 37)	Young (n = 62)	Controls (n = 40)	p value	p value between groups		
					Elderly vs. young	Elderly vs. controls	Young vs. controls
CCPA (mm^2)							
Whole retina	11.56 ± 2.17	13.11 ± 2.14	13.36 ± 1.46	< 0.001	< 0.001	< 0.001	1.000
Macula	2.62 ± 0.69	3.01 ± 0.66	3.43 ± 0.48	< 0.001	0.006	< 0.001	0.005
Paramacula	8.99 ± 1.70	10.17 ± 1.67	9.93 ± 1.06	< 0.001	0.004	< 0.001	1.000
DCP (%)							
Whole retina	7.98 ± 4.50	8.62 ± 3.97	10.10 ± 3.20	0.034	0.86	0.196	0.058
Macula	2.16 ± 2.82	2.49 ± 2.28	3.70 ± 1.81	< 0.001	0.499	< 0.001	0.003
Paramacula	9.95 ± 5.48	10.69 ± 4.75	12.25 ± 3.81	0.065	0.873	0.108	0.198
ICP (%)							
Whole retina	14.85 ± 5.62	15.95 ± 5.39	20.01 ± 3.25	< 0.001	1.000	< 0.001	< 0.001
Macula	8.92 ± 4.61	9.61 ± 4.74	15.21 ± 4.19	< 0.001	0.863	< 0.001	< 0.001
Paramacula	16.84 ± 6.54	17.95 ± 5.92	21.62 ± 3.57	< 0.001	0.787	0.001	0.001
SCP (%)							
Whole retina	30.06 ± 5.39	30.67 ± 5.59	32.49 ± 3.11	0.047	1.000	0.048	0.236
Macula	23.70 ± 5.93	24.13 ± 6.48	26.71 ± 3.56	0.021	1.000	0.027	0.079
Paramacula	32.21 ± 5.46	32.70 ± 5.63	34.36 ± 3.24	0.127	NA	NA	NA

CCPA choroidal capillary perfusion area, *DCP* deep capillary plexus, *ICP* intermediate capillary plexus, *SCP* superficial capillary plexus, *NA* not applicable

penetration imaging trail. There was no blood flow signal in OCTA, and it was proved from the histology that the low reflection area was lipid droplets. Subsequently, some studies showed that in about 52% of eyes with thick choroidal membranes there are lipid granular cavities. Compared with the normal control and AMD patients, cCSC patients had a greater size and number of lipid grain-like cavities patients, and more cavities appeared in the area of increased choroidal vascular permeability, which was associated with increased choroidal thickness and the loss of choroidal stroma [17]. The incidence of choroidal lipid globule cavern in both groups was 56.76 and 50.82%, respectively, suggesting that choroidal matrix loss and lipidation in cCSC patients also explain, to some extent the decrease in choroidal thickness in the elderly group. The increase in lipid-like cavities means the increase in extracellular lipid deposition, which is involved in the process of choroidal oxidative stress. However, histology shows no evidence of inflammatory cells in the vicinity of the lipid droplets [43]. The prognostic significance of lipid-like cavities on cCSC still needs further study.

The nutrients of outer layer of retina (outer nuclear layer, photoreceptor layers and retinal

pigment epithelial layer) is mainly supplied by choroidal capillary [44], and nutrients of the middle layer of retina (inner core layer and inner subordinate layer) and inner layer (nerve fiber layer and ganglion cell layer) are supplied by retinal capillary [45]. Vascular dilation and attenuation of choroidal capillaries in CSC patients have been widely recognized. However, there are few studies on their retinal capillary system, and little is known about the blood supply of the inner and middle retina of CSC among the elderly and young groups. Compared with the control group, CCPA, DCP, ICP and SCP were significantly reduced in the cCSC group. It proved that cCSC affects not only affected the choroidal vascular system, but also affected the retinal capillary system, and the whole retina was in a state of hypoperfusion. The CCPA reduction in the elderly group is particularly significant compared with the young group, suggesting that the blood supply of the outer retina in the elderly group is seriously insufficient, which corresponds to the more serious destruction of RPE [44]. At the same time, the hypoperfusion of choroidal capillaries is a trigger for increased VEGF secretion, and the risk of neovascularization is significantly increased in the elderly group. [46]The retinal capillary system provides a powerful supply for the inner and middle retinal membranes with active metabolism [45]. The decrease in blood perfusion of DCP, ICP and SCP will definitely lead to the disorder of metabolism in the corresponding retinal regions. Although there were no statistical difference in DCP, ICP, and SCP perfusion between the elderly group and the young group, the elderly group was lower in all measured ranges, which corresponded to the shorter ONL thickness and POS length in the elderly group. At present, little is known about the role of decreased retinal capillary perfusion in the pathogenesis of CSC. We believe that it may be caused by the compression of the retina by SRF. However, some patients with little SRF may also have serious severe middle and inner retinal perfusion deficits, which depends on further research.

There are limitations in this study: (1) The subjects included in the study are all Han Chinese, and the results may not be applicable to cCSC patients of other races; (2) It is a challenge to accurately identify the integrity of EZ when there are many SRFs, especially in the young group, which is expected to be solved with the further increases of OCT scanning depth; (3) This study is a cross-sectional study based on clinical data. The hypothesis proposed in this paper depends on the further confirmation from large, multicenter, and prospective studies; (4) In this study, the age cut-off value was set at 50 years old, which was determined according to the age of previous CSC and the reference age of AMD. Due to the limited number of cases, we did not further study the changes of clinical characteristics of cCSC with age in a smaller age scale, which will be the direction of our further studies.

CONCLUSIONS

In conclusion, we have described in detail the unique clinical features of elderly cCSC from the aspects of retina, choroid anatomy, and blood perfusion, and we realize that elderly cCSC patients may have different disease outcomes than young cCSC patients. Elderly cCSC patients have less gender tendency, poorer vision, more serious choroidal and retinal structural damage and ischemia, and have a higher risk of choroidal neovascularization.

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Author Contribution. Pei Liu and Xuemin Jin designed the study. Guangqi An and Chenyu Lu performed the photodynamic therapy. Shu Li, Pei Liu, Bo Jin, and Guangqi An collected the data. Fan Yang, Haixin Fang, and

Chenyu Lu analyzed and interpreted the data. Pei Liu was a major contributor in writing the manuscript. Pei Liu and Guangqi An participated in drafting the manuscript. Xuemin Jin and Liping Du revised the manuscript. All authors read and approved the final manuscript.

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Data Availability. The datasets during collected and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. The authors declare that they have no conflicts of interest.

Ethical Approval. This study was approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University [2022-KY-0547-002], and the procedure was in accordance with the principles of the Declaration of Helsinki. Patients were informed of the risks of invasive examinations and signed informed consent forms.

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