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Characteristics and pathologies of the vitreo-macular interface—results from the Gutenberg Health Study

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ABSTRACT.

Purpose: **We aimed to determine the prevalence of characteristics and pathologies of the vitreo-macular interface within the general population.**

Methods: **The Gutenberg Health Study is a population-based study in Germany, including an ophthalmological examination with refraction, biometry and optical coherence tomography (OCT) imaging. Characteristics of the vitreo-macular interface were graded on volume scans including visibility of an epiretinal membrane, full-thickness macular hole, lamellar hole and pseudohole. Overall and age-specific prevalences including 95% confidence intervals [95%-CI] were calculated. Association analyses were conducted to determine systemic and ocular factors that are associated with epiretinal membranes (the most common pathology) using multivariable logistic regression.**

Results: **A total of 1890 people aged 40–80 years were included in the study. Of these, 4.7% (95%-CI: 3.8%–5.8%) had an epiretinal membrane in at least one eye, 0.1% a full-thickness macular hole, 0.6% a lamellar hole and 0.6% a pseudohole. The presence of an epiretinal membrane was associated with higher age, myopic refractive error and prior retinal laser therapy, but not with gender, body height, body weight, smoking, prior cataract surgery or intraocular pressure.**

Conclusions: **Epiretinal membranes are more frequent in older and myopic subjects and in those with prior retinal laser therapy.**

Key words: epidemiology – epiretinal membrane – optical coherence tomography – vitreous detachment – vitreous interface

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Introduction

Diseases of the vitreo-macular interface are a common cause of impaired vision at a higher age. Recent studies showed a prevalence of up to 34% for epiretinal membranes and 4% for a macular hole in a cohort of old to very old persons (63–102 years) in the USA (Meuer et al. 2015). In China, the prevalence for an epiretinal membrane is reported to be 8.4% in subjects 50 years and older (Ye et al. 2015).

New technologies, such as spectral-domain optical coherence tomography (SD-OCT), allow to detect pathologies of the vitreo-macular interface with high sensitivity and specificity and to differentiate different subtypes (Wilkins et al. 1996; Mori et al. 2004; Kawasaki et al. 2009; Hwang et al. 2012; Konidaris et al. 2015; Stevenson et al. 2016). Previous studies using ophthalmoscopy or fundus photography in general showed a lower prevalence of epiretinal membranes (ERMs) (Mitchell et al. 1997; McCarty et al. 2005; You et al. 2008; Duan et al. 2009; Aung et al. 2013; Kim et al. 2017) and of other pathologies of the vitreo-macular interface. In addition, since the introduction of the OCT technology, specific classification of vitreo-macular adhesion (VMA) into a focal and a broad type has been introduced (Duker et al. 2013). While previous studies used ophthalmoscopy and sonography to report the prevalence of vitreo-macular pathologies, recent population-based studies have used OCT technology to differentiate between different characteristics and pathologies (Meuer et al. 2015; Ye et al. 2015; Liesenborghs et al. 2018).

In this study, we determine the prevalence of characteristics and pathologies of the vitreo-macular interface in Germany using OCT imaging technology. In addition, we examine associations of systemic and ocular factors with ERM, the most common pathology of the vitreo-macular interface.

Materials and methods

The Gutenberg Health Study (GHS) is a prospective, population-based, observational cohort study conducted in the Rhine-Main region in Midwestern Germany. Out of all residents of the city of Mainz (n = 196 425) and the district of Mainz-Bingen (n = 201 371), those subjects aged 35–74 years at the time of inclusion were eligible (n = 210 867). A sample of 35 008 subjects stratified by decade of age, residence (Mainz/Mainz-Bingen) and gender was selected via residents' registration offices. The exclusion criteria for the GHS were insufficient knowledge of the German language and physical or mental inability to participate. The study sample was drawn in waves of equal stratification to allow defined subsample analyses after inclusion of each 5000 participants. Finally, a total study sample of 15 010 participants was enrolled and the overall response (recruitment efficacy proportion) was 61.2%. The baseline examination was conducted between the years 2007 and 2012, and the 5-year follow-up examination between 2012 and 2017. The presented data of this analysis is from the 5-year follow-up examination, where OCT imaging was included. Participating rate of the 5-year follow-up examination was 82.8%. More details of the study design were described by Hohn et al. (2015).

For each participant, a comprehensive ophthalmological workup was conducted. Objective refraction (Humphrey Automated Refractor/Keratometer (HARK) 599, Carl Zeiss Meditec AG, Jena, Germany), biometry (Lenstar LS900, Haag-Streit Diagnostics, Koeniz, Switzerland) and SD-OCT imaging (Spectralis™, Heidelberg Engineering, Heidelberg, Germany) took place under mesopic light conditions. Every subject received a macular volume scan of 15 × 15° with 37 horizontal scans in each eye. Fifty scans were averaged in each horizontal scan, and focus of depth was enhanced depth imaging mode. As a consequence, we were not able to differentiate a complete posterior vitreous detachment from an attached posterior hyaloid membrane with a premacular bursa when there was no visible posterior hyaloid membrane due to the limited focus of depth. Non-contact tonometry (Nidek NT-2000, Nidek Co, Japan) was performed and repeated three times. Within a computer-assisted personal interview, it was surveyed whether ophthalmic surgery or retinal laser therapy had previously been conducted and whether subjects have been suffering from severe ocular inflammation. General anthropometric parameters including body height and body weight were determined, and smoking habits were recorded.

All examinations were performed by experienced study nurses in accordance with standardized operating procedures.

This study was approved by the ethics committee (Ethics Commission of the State Chamber of Physicians of Rhineland-Palatinate). According to the tenets of the Declaration of Helsinki, written informed consent was obtained from all participants prior to entering the study. The GHS is a joint project of internal medicine, ophthalmology, psychosomatic medicine and epidemiology at the Johannes Gutenberg-University Mainz, Germany.

Study sample

This study sample was recruited from the 5-year follow-up examination of the GHS cohort including subjects with an age of 40–80 years at the time of examination. Three subsamples (waves) of 5000 participants were initially drawn to be representative to the underlying study population. We included 4130 subjects from the second wave as there were a considerably high number of inaccurate or missing OCT images in the first wave. Inclusion criteria for this analysis were available OCT imaging data of at least one eye with sufficient quality for grading. There was no exclusion criterion.

Data and statistical analysis

Grading of SD-OCT images was performed by a trained medical doctor (AKK) according to a prespecified protocol and been masked to medical history and other ocular data. This protocol included the visibility of the posterior hyaloid membrane in the volume scan. Each of the 37 scans was reviewed for a hyper-reflective line above to or at least partially separated from the internal limiting membrane without distortion or corrugation (grooves and ridges) of the inner retina. When such a structure was recognized, partial and total posterior vitreous detachments were differentiated. At a visible posterior hyaloid membrane in the foveal scan, further classification according to the definitions of the International Vitreomacular Traction Study Group (IVTSG) into vitreomacular adhesion (VMA) and vitreomacular traction (VMT) was conducted (Duker et al. 2013). Vitreomacular traction was defined as inner retinal distortion with local adhesion of the posterior hyaloid membrane and additionally graded as grade 1: inner retinal distortion, grade 2: intraretinal cysts and grade 3: subretinal fluid (Wu et al. 2016). Full-thickness macular hole (FTMH), lamellar hole and pseudohole were defined according to the IVTSG and graded on all OCT scans irrespectively of a visible posterior hyaloid membrane. The presence of an ERM was differentiated from a folded internal limiting membrane (ILM) by defining ERM as a hyper-reflective membrane along the surface of the ILM including any distortion, corrugation (grooves and ridges) or flattening of the inner retina, comparable to other grading schemes (Gattoussi et al. 2018) on all OCT scans as well. In addition, involvement of the fovea was recorded.

Regular quality controls including masked intra- and inter-rater comparison and re-adjustment were performed. Kappa statistics were calculated to evaluate reliability. All gradings flagged 'questionable' by the grader were solved in discussions with the supervisors (AKS, CAK).

Calculation of intrarater reliability (n = 274 eyes) and inter-rater reliability (n = 204 eyes) showed a kappa coefficient of 0.94 (intrarater) and 0.83 (inter-rater) for the visibility of the posterior hyaloid membrane in the volume scan, kappa = 0.60 and 0.73 for differentiation between partial and complete posterior vitreous detachment and 0.69 and 0.87 for grading the ERM presence. On the foveal scan, the visibility of the posterior hyaloid membrane was graded with kappa = 0.88 and 0.68, for VMA presence 0.65 and 0.80 and for differentiation between focal and broad VMA 0.61 and 0.60.

Kappa statistics could not be performed for the pathologies VMT, FTMH, lamellar hole and pseudohole due to the small amount of these cases.

Central corneal thickness, corneal power, anterior chamber depth, lens thickness and axial length were measured with Lenstar LS900 (Haag-Streit Diagnostics, Koeniz, Switzerland). Non-cycloplegic refraction (Humphrey Automated Refractor/Keratometer (HARK) 599, Carl Zeiss Meditec AG, Jena, Germany) was included as spherical equivalent in the analysis.

Data were processed by statistical analysis software (R version 3.1.1 [2014-07-10]). Median, inter-quantile range, minimum and maximum were calculated for all variables. For variables found to be within normal distribution, mean and standard deviation were computed. Non-responder analysis was carried out to compare systemic and ocular characteristics between subjects with and those without SD-OCT imaging of the macular region.

First, prevalence of the characteristics and pathologies of the vitreo-macular interface was calculated for the presence in right eyes, left eyes and in at least one eye of a person.

Associated factors were evaluated using a generalized estimating equation model with consideration of the correlation structure between both eyes of the subjects.

We performed a two-step analysis: in the first model we examined associations with anthropometric and ocular parameters and evaluated general associations without specific consideration of ocular biometry. This model included gender, age, body height, body weight, smoking, spherical equivalent, intraocular pressure, prior severe ocular inflammation, prior retinal laser treatment as independent variables. The second model included biometric characteristics of phakic eyes. Phakic eyes were defined as those having lens thickness measurement over 2 mm.

This study was performed as an explorative study to analyse prevalence and associations of characteristics of the vitreo-macular interface. All p-values should be regarded as a continuous parameter that reflects the level of evidence and are therefore reported exactly.

Results

In this cross-sectional study, 1874 right and 1869 left eyes of 1890 subjects (48.4% female) were included, and others did not have SD-OCT imaging. The mean age of the study participants was 58.8 ± 10.5 years. The study sample is further characterized in Table 1. 0.6% (n = 12) of included subjects reported previous retinal surgery, and 3.0% (n = 57) previous retinal laser treatment. Non-responder analysis revealed that the included subjects were slightly younger with better visual acuity and lower intraocular pressure, while other factors showed a comparable distribution (Table S1).

81.8% (1546 of 1882) of the examined subjects had a visible posterior hyaloid membrane in at least one eye. In 0.4% of the subjects (n = 8), the volume scans were not gradable.

A complete posterior vitreous detachment (PVD) in at least one eye was present in 9.1%. 5.2% (95%-CI: 4.1%–6.5%) of right, 5.9% of left eyes (95%-CI: 4.7%–7.2%; p = 0.46 for the comparison between right and left eyes); 2.2% (95%-CI: 1.6%–3.2%) in both eyes had such a finding; distribution is given in Fig. 1. Further stratification on age decades showed that 0.5% (95%-CI: 0.1%–1.9%) at age 40–50 years had a complete PVD in at least one eye, 1.6% (95%-CI: 0.7%–3.2%) at age 50–60 years, 8.3% (95%-CI: 5.7%–11.8%) at age 60–70 years and 28.1% (95%-CI: 20.5%–37.1%) at age 70–80 years.

Visible posterior hyaloid membrane on the foveal scan was found in 55.3% of right (1027 of 1838 eyes; 95%-CI: 53.6%–58.2%) and 62.2% of left eyes (1149 of 1847; 95%-CI: 59.5%–64.4%). Vitreo-macular adhesion (VMA) on the foveal scan was found in 92.3% in right (95%-CI: 90.4%–93.8%) and 91.2% in left eyes (95%-CI: 89.4%–92.8%; p = 0.39 for comparison between right and left eyes) and 84.8% (95%-CI: 82.3%–87.1%) in both eyes. Of those with VMA, 7.9% of right and 10.4% of left eyes had focal VMA (≤1500 μm) seen, the rest showed a broad VMA (>1500 μm). Vitreo-macular adhesion (VMA) was detected in 1.0% of the right and 1.4% of the left eyes; 6 out of 10 had focal VMT (≤1500 μm) in the right and 8/16 in the left (Fig. 2). The average VMT length was 1423 ± 1259 μm in the right and 1403 ± 1383 μm in the left eyes, and the difference was not statistically significant. In the right eyes with VMT, 8 eyes showed inner retinal distortion (grade 1), 1 eye additional intraretinal cysts (grade 2), and 1 eye additional subretinal fluid (grade 3). In the left eyes with VMT, 14 eyes showed inner retinal distortion (grade 1), 1 eye additional intraretinal cysts (grade 2), and 1 eye additional subretinal fluid (grade 3).

With respect to ERM, 4.7% (95%-CI: 3.8%–5.8%) had an ERM present in at least one eye (2.3% of the right (43 of 1877; 95%-CI: 1.7%–3.1%); 3.0% of left eyes (56 of 1867; 95%-CI: 2.3%–3.9%; p = 0.19 for comparison between right and left eyes) and 0.5% in both eyes (10 of 1860; 95%-CI: 0.3%–1.0%)). In 65% of the right (28 of 43; 95%-CI: 49%–79%) and 57% of the left eyes (32 of 56; 95%-CI: 43%–70%), this pathology was also seen in the foveal OCT scan. 45% of the eyes with ERM (n = 45 of 99 eyes) showed foveal involvement with embedding of the centre leading to a thicker central foveal thickness (363 ± 91.7 μm compared to 231 ± 30.6 μm). Epiretinal membrane (ERM) prevalence in at least one eye increased with age from 0% (95%-CI: 0.0%–1.1%) in those aged 40–49 years, 1.3% (95%-CI: 0.6%–2.7%) for the decade 50–59 years, 7.4% (95%-CI: 5.3%–10.0%) for the decade 60–69 years and 12.1% (95%-CI: 9.0%–16.0%) for the decade 70–80 years (Fig. 3). Visual acuity was descriptively lower in eyes with epiretinal membrane than in those without (median: logMAR 0.10 versus 0.00).

Full-thickness macular hole was rare (0.1%; 2 subjects, one right and one left eye). Lamellar hole was found in 0.6% (n = 12; 5 right and 7 left eyes), while a pseudohole was found present in 0.5% (n = 10; 6 right and 5 left eyes, one was bilateral).

Table 1. Characteristics of the study sample with OCT imaging from the Gutenberg Health Study.

Variable	All (1890)	Men (975)	Women (915)
Sex (women)	48.4% (915)	0% (0)	100.0% (915)
Age [y]	58.8 ± 10.5	59.0 ± 10.6	58.6 ± 10.4
Height [cm]	171 ± 10	177 ± 7	164 ± 7
Weight [kg]	80.8 ± 16.9	87.9 ± 14.5	73.2 ± 16.0
Body mass index [kg/m²]	26.9 (24.2/30.4)	27.4 (25.1/30.3)	26.1 (23.1/30.6)
Smoking (yes)	15.3% (289)	15.6% (152)	15.0% (137)
Obesity (BMI ≥ 30) (yes)	27.5% (519)	27.1% (264)	27.9% (255)
Diabetes (yes)	9.1% (171)	10.6% (103)	7.4% (68)
Hypertension (yes)	54.6% (1032)	60.3% (588)	48.5% (444)
Dyslipidaemia (yes)	34.1% (643)	41.9% (407)	25.8% (236)
Ophthalmic parameters			
Visual acuity [logMAR] OD	0.10 (0/0.20)	0.10 (0/0.20)	0.10 (0/0.20)
Visual acuity [logMAR] OS	0.10 (0/0.10)	0 (0/0.10)	0.10 (0/0.10)
Intraocular pressure [mmHg] OD	14.56 ± 2.84	14.62 ± 2.98	14.49 ± 2.70
Intraocular pressure [mmHg] OS	14.66 ± 2.86	14.77 ± 2.93	14.54 ± 2.78
Spherical equivalent [dpt] OD	−0.37 ± 2.21	−0.37 ± 2.10	−0.37 ± 2.31
Spherical equivalent [dpt] OS	−0.40 ± 2.28	−0.41 ± 2.23	−0.39 ± 2.33
Available biometric measurement OD	65.5% (N = 1238)	65.9% (N = 643)	65.0% (N = 595)
Available biometric measurement OS	64.7% (N = 1222)	64.9% (N = 633)	64.4% (N = 589)
Central corneal thickness [µm] OD	549 ± 34	553 ± 34	545 ± 34
Central corneal thickness [µm] OS	549 ± 34	553 ± 34	545 ± 35
Axial length [mm] OD	23.7 ± 1.2	24.0 ± 1.1	23.5 ± 1.1
Axial length [mm] OS	23.7 ± 1.2	24.0 ± 1.2	23.5 ± 1.2
Lens thickness [mm] OD (N describes the subjects with lens thickness over 2 mm)	4.35 (4.10/4.60) (N = 1147)	4.38 (4.10/4.66) (N = 598)	4.31 (4.09/4.54) (N = 549)
Lens thickness [mm] OS (N describes the subjects with lens thickness over 2 mm)	4.40 (4.16/4.65) (N = 1130)	4.43 (4.18/4.70) (N = 592)	4.37 (4.15/4.58) (N = 538)
Anterior chamber depth [mm] OD	3.26 (3.02/3.53)	3.31 (3.04/3.56)	3.21 (3.00/3.46)
Anterior chamber depth [mm] OS	3.26 (3.02/3.51)	3.29 (3.05/3.54)	3.22 (3.01/3.49)
Mean corneal power [dpt] OD	43.2 ± 1.5	42.9 ± 1.4	43.6 ± 1.5
Mean corneal power [dpt] OS	43.3 ± 1.5	42.9 ± 1.5	43.6 ± 1.5

Logistic regression analysis revealed that ERM's presence is associated with higher age (OR = 1.12 (95%-CI: 1.09–1.14) per year; $p < 0.0001$) and with prior retinal laser therapy (OR = 3.09 (95%-CI: 1.56–6.13); $p = 0.0012$), as well as inversely associated with spherical equivalent (OR = 0.84 (95%-CI: 0.78–0.91) per diopter; $p < 0.0001$). There was no association with gender, body height, body weight, smoking, prior cataract surgery, intraocular pressure or prior severe ocular inflammation (Table 2). In those who had biometric measurement and were phakic, ERM was associated with longer axial length (OR = 2.58 (95%-CI: 2.01–3.32) per millimetre; $p < 0.0001$) and with a shallower anterior chamber depth (OR = 0.21 (95%-CI: 0.07–0.67) per millimetre; $p = 0.008$). There was no association with central corneal thickness, lens thickness, intraocular pressure and mean corneal power (Table 3).

Discussion

In our study, the prevalence of characteristic vitreo-macular interface pathologies in a population-based study is reported. Those 4.7% with ERM were older and more likely to have myopic refractive error and prior retinal laser therapy. Other pathologies of the vitreo-macular interface, such as VMT, FTMH, lamellar hole and pseudohole, are uncommon in the population.

The prevalence of a complete PVD increases with age up to 28.1% at age 70–80 years; while prevalence estimates in the literature vary, primarily due to different examination methods, similar age relationships are reported (Weber-Krause & Eckardt 1997; Shen et al. 2013). The population-based Handan Eye Study found a prevalence of 2.7% in Chinese subjects at age 30–70 years using funduscopy (Shen et al. 2013). Weber-Krause & Eckardt (1997) reported an 11% complete PVD prevalence in 65–69-year-old subjects using kinetic sonography in a German cohort, increasing to over 45% in those over the age of 80 years. The Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study, a population-based cohort study in South India, examined PVD incidence with sonography and indirect ophthalmoscopy and found that 33% converted from incomplete to complete posterior vitreous detachment (Gella et al. 2017).

In contrast, the Beijing Eye Study (Shao et al. 2013) used OCT to examine the presence of an incomplete PVD and found an association with younger age, while the advanced stage of incomplete PVD was associated with higher age.

In our study, the prevalence of the ERM (4.7%) was lower than in two other studies using OCT technology. While the Beaver Dam Eye Study reported a prevalence of 34% (Meuer et al. 2015), the Jiangning Eye Study estimated a much lower prevalence of 7.3% (Ye et al. 2015). These differences might be due to different age ranges of the study population; our study investigated 40- to 80-year-old subjects, Ye et al. (2015) examined subject older than 50 years and Meuer et al. (2015) subjects older than 63 years of age. Several studies, including this analysis, reported that older age is linked to ERM presence using OCT technology and fundus photography for ascertainment (Mitchell et al. 1997; Miyazaki et al. 2003; McCarty et al. 2005; Kawasaki et al. 2008, 2009; You et al. 2008; Ng et al. 2011; Koh et al. 2012; Aung et al. 2013; Ye et al. 2015; Cheung et al. 2017). A recent meta-analysis confirmed this finding (Xiao et al. 2017). In addition to age, ethnic differences seem to play a role for ERM presence. The Multi-Ethnic Study of Atherosclerosis showed that ERM was more common in Chinese persons compared with whites, blacks and Hispanics in a direct comparison (Ng et al. 2011), while this finding could not be replicated in a recent meta-analysis including 12 population-based studies showing similar prevalence estimates

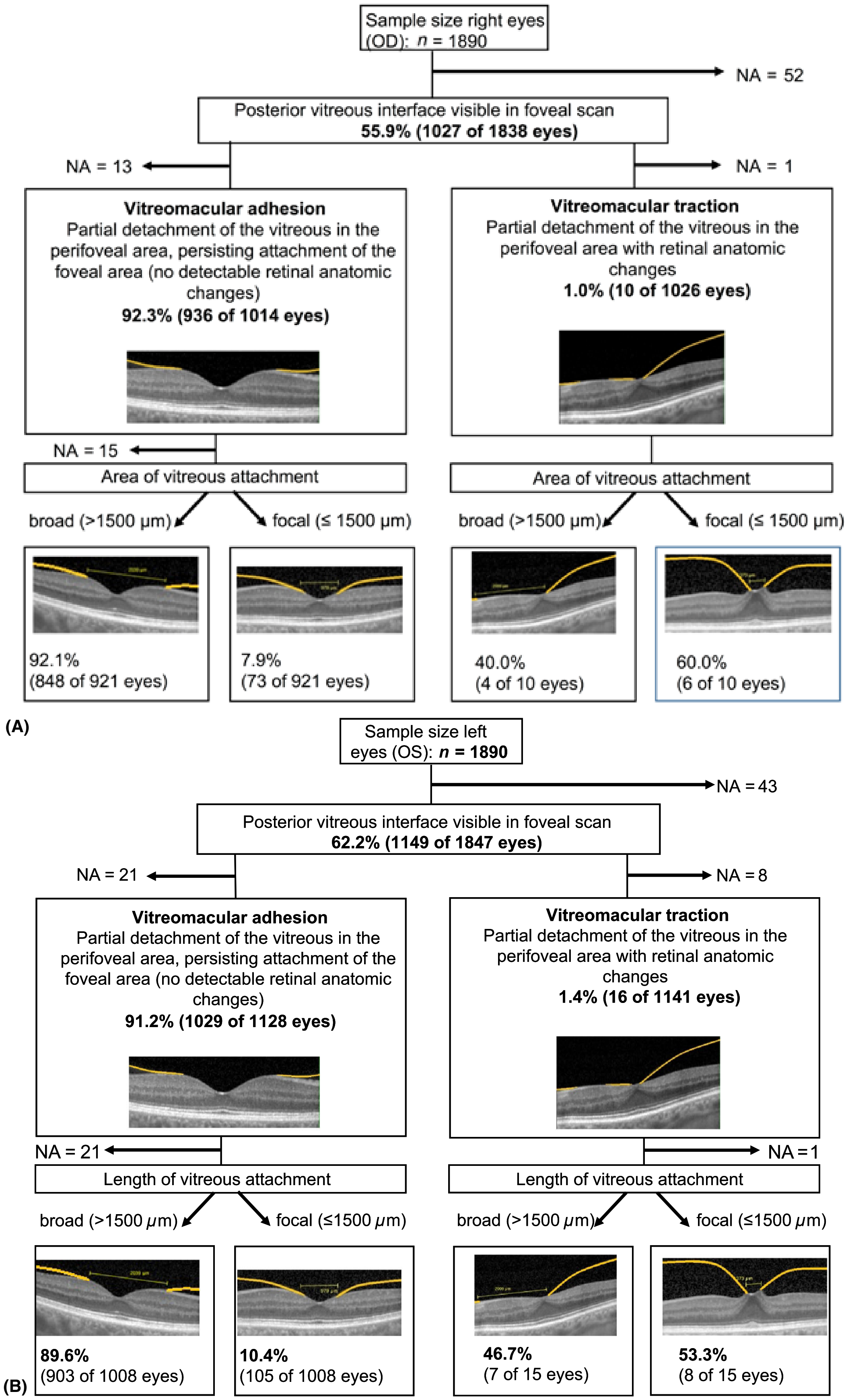

Fig. 1. Distribution of posterior vitreous detachment in macular volume scans in the Gutenberg Health Study (N = 1890). NA: not gradable or not available. (A) Right eyes (OD); (B) left eyes (OS).

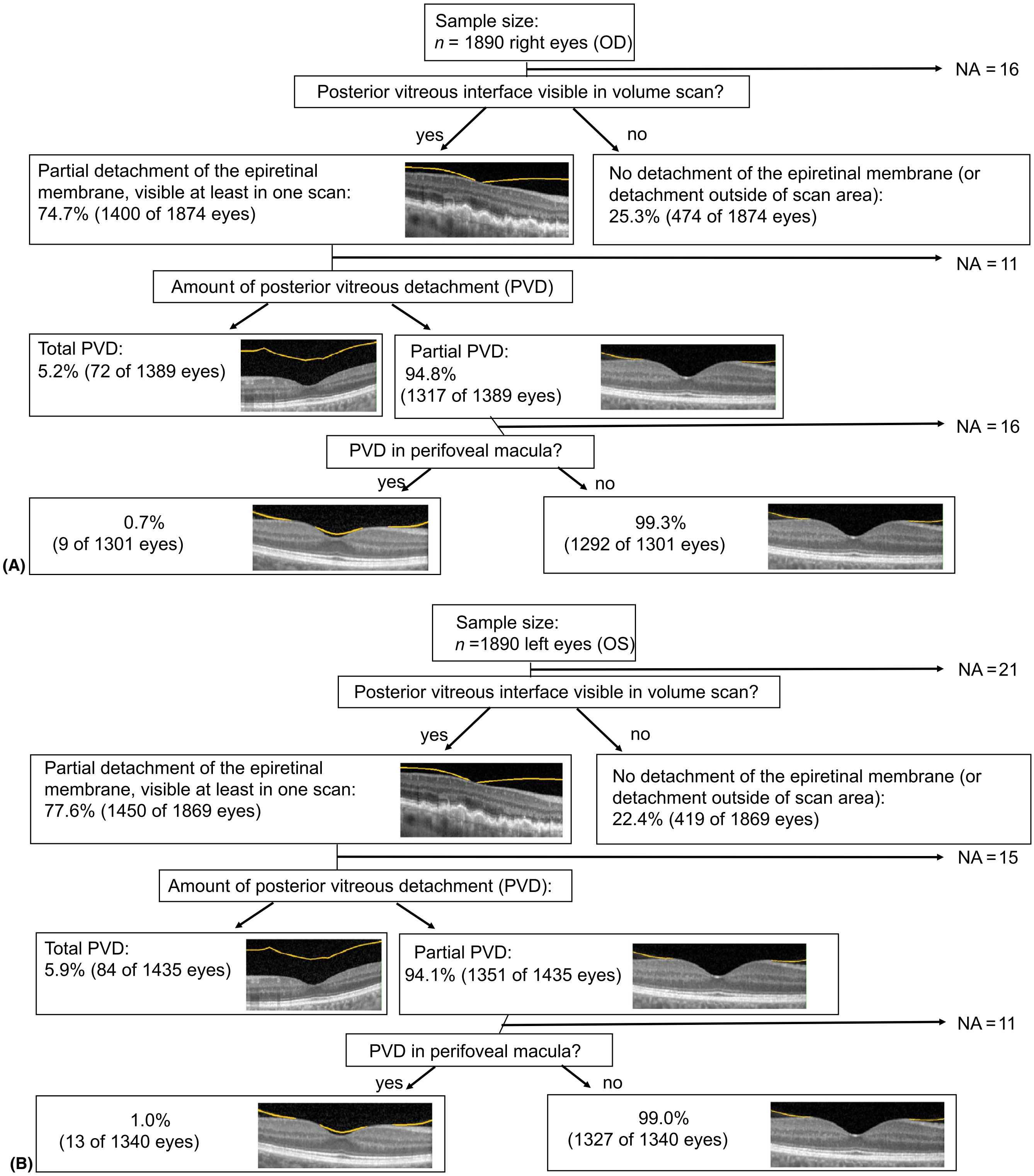

Fig. 2. Distribution of vitreo-macular adhesion and traction in foveal scans in the Gutenberg Health Study (N = 1890). NA: not gradable or not available. (A) Right eyes (OD); (B) left eyes (OS).

(Asian: 10.5%; Caucasian 11.0%) (Xiao et al. 2017).

A recent analysis of the Beijing Eye Study showed that the 10-year cumulative incidence of epiretinal membranes (8.4%) is related to older age, previous cataract surgery and complete posterior vitreous detachment (Yang et al. 2018). In cross-sectional analysis, we were not able to show an expected association between cataract surgery and epiretinal membrane, but our cohort design will allow to investigate this in subsequent longitudinal analyses.

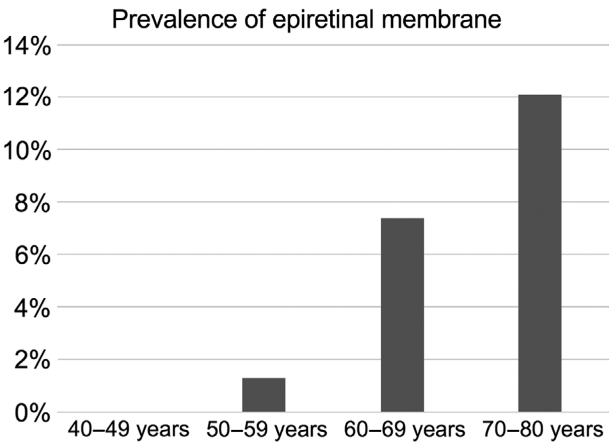

Fig. 3. Prevalence of epiretinal membrane in the Gutenberg Health Study, as determined on OCT imaging. Cases were defined as having prevalent epiretinal membrane in at least one eye.

Table 2. Association analysis of the presence of an epiretinal membrane with demographic and anthropometrical parameters, as well as general ocular parameters (N = 3687 eyes), data from the Gutenberg Health Study.

Logistic regression analysis with GEE modelling (multivariable)	Odds Ratio	95%-CI	p-value
Sex [female]	1.01	[0.56–1.83]	0.97
Age [years]	1.12	[1.09–1.14]	**<0.0001**
Body height [cm]	1.02	[0.99–1.06]	0.18
Body weight [kg]	1.00	[0.98–1.01]	0.54
Smoking	0.64	[0.28–1.46]	0.28
Intraocular pressure [mmHg]	1.06	[0.98–1.14]	0.14
Spherical equivalent [dpt]	0.84	[0.78–0.91]	**<0.0001**
Prior cataract surgery	1.15	[0.63–2.09]	0.65
Prior severe ocular inflammation	0.72	[0.20–2.56]	0.61
Prior retinal laser treatment	3.09	[1.56–6.13]	**0.0012**

Bold values indicate statistically significant.

Table 3. Association analysis of the presence of an epiretinal membrane with biometric parameters (N = 2.209 phakic eyes with biometric measurement), data from the Gutenberg Health Study.

Logistic regression analysis with GEE modelling (multivariable)	Odds ratio	95%-CI	p-value
Central corneal thickness [μm]	1.00	[0.99–1.01]	0.55
Anterior chamber depth [mm]	0.21	[0.07–0.67]	**0.0082**
Axial length [mm]	2.58	[2.01–3.32]	**<0.0001**
Lens thickness [mm]	0.80	[0.22–2.89]	0.74
Intraocular pressure [mmHg]	1.00	[0.91–1.11]	0.94
Mean corneal power [dpt]	1.27	[1.00–1.61]	0.053

Statistical analysis is adjusted for age and sex.
Bold values indicate statistically significant.

Our data show that longer axial length is linked to ERM presence; this is in complete agreement with the Handan Eye Study (Duan et al. 2009), the Singapore Indian Eye Study (Koh et al. 2012), the Jiangning Eye Study (Ye et al. 2015) and the Melbourne VIP Study (McCarty et al. 2005). A possible explanation for the myopia and ERM association is the increased PVD probability in myopic eyes, PVD being a risk factor for ERM (Yang et al. 2018). Several studies report an association with myopia (Koh et al. 2012; Ye et al. 2015), as we found. Epiretinal membranes (ERMs) were more likely in subjects with prior retinal laser therapy in our study, which is consistent with clinical studies (Mester et al. 1988; Saran & Brucker 1995) but has not been shown yet in a population-based study setup.

Other pathologies of the vitreo-macular interface pathologies such as FTMH, lamellar hole and pseudohole were rare in our study. Sen et al. (2008) reported in an adult South Indian population a FTMH prevalence of 0.17% using slit-lamp examination and fundus photography, while The Beijing Eye Study found the prevalence of 0.09% (Wang et al. 2006); both are comparable to our findings. In contrast, the Blue Mountain Eye Study (Mitchell et al. 1997) reported a much lower prevalence (0.02%) but only had fundus photography for detection.

Using SD-OCT technology, the Beaver Dam Eye Study (Meuer et al. 2015) found a much higher FTMH prevalence of 0.4% and 3.6% for lamellar holes; these are even higher than in our study; again, the difference age range of the participants is likely to be the most important contributing factor.

Bilateral pathologies of the vitreomacular interface were rare in our study. 0.5% (n = 10) had an epiretinal membrane in both eyes, that were 11% of all subjects with an epiretinal membrane, and one subject had a lamellar hole in both eyes. Cheung et al. (2017) report that 23% of subjects with epiretinal membranes had this condition in both eyes, while Meuer et al. (2015) report a proportion of 30% with epiretinal membranes in both eyes and with respect to lamellar holes of 17.9%.

There are methodological limitations to our study: first, macular SD-OCT imaging was limited to the central 15 × 15° and characteristics of the vitreo-macular interface were only evaluated on this area; therefore, ERM at the macular periphery might not have been visible on our images. Other studies used different volume scan size and different OCT devices (Meuer et al. 2015; Ye et al. 2015). Second, correct classification of the different vitreo-macular interface characteristics is crucial. Only one observer graded the scans, and if there was doubt, a second grading from the supervisor was performed. Additionally, a random sample of OCT scans was also graded by the supervisor. As inter-observer reliability showed fairly low kappa statistics, misclassification cannot be ruled out. Nevertheless, in 25% of the eyes the posterior hyaloid membrane could not be detected and was therefore excluded from further analysis. A categorization into complete PVD versus complete posterior vitreous attachment could not be achieved in these eyes. Differentiation of PVD stages (0–4) according to (Kakehashi et al. 1997; Stalmans et al. 2013) could not be achieved due to missing data on the mid-peripheral retina. Defining the lens status by using ocular biometry measurements might have led to misclassification of aphakic subjects as well. Nevertheless, aphakia is a very rare condition in Germany, as previously described (Schuster et al. 2017). Panretinal laser coagulation and retinal laser treatment for retinopexy could not be differentiated in our data, as well as eyes with different underlying diseases (diabetic retinopathy, peripheral vascular diseases, uveitis, other inflammatory conditions), which further represents a limitation.

Only 46% of the underlying cohort did receive OCT imaging with subsequent grading. Non-responder analysis revealed that these subjects were of slightly lower age (58.8 versus 60.9 years), while gender and ocular parameter were comparable. Furthermore, we did not measure objective refraction under cycloplegic conditions; therefore, findings regarding hyperopia might be underestimated. However, our study cohort had an age range from 40 to 80 years, and in the older age groups accommodation was limited. As most of our study participants were Caucasians, our results should be regarded valid for this ethnicity but cannot be generally applied to other genetic or ethical backgrounds.

In summary, we demonstrate that ERMs have a prevalence of 4.7% and are more frequent in older and myopic subjects and in those with prior retinal laser therapy. Due to an ageing society and the myopic epidemic, ERM will probably gain in importance as cause for visual impairment in future. Other pathologies of the vitreo-macular interface such as VMT, FTMH, lamellar hole and pseudohole are currently rare in our population.

Informed consent

The study protocol and study documents were approved by the local ethics committee of the Medical Chamber of Rhineland-Palatinate, Germany (reference no. 837.020.07; original vote: 22.3.2007, latest update: 20.10.2015). According to the tenets of the Declaration of Helsinki, written informed consent was obtained from all participants prior to entering the study.

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Brief summary statement: 4.7% of the German population aged 40-80 years had an epiretinal membrane in at least one eye, 0.1% a full-thickness macular hole, 0.6% a lamellar hole and 0.6% a pseudohole. The presence of an epiretinal membrane was associated with higher age, myopic refractive error and prior retinal laser therapy.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Non-responder analysis with respect to OCT-image grading: data from the Gutenberg Health Study.