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Title: Evaluation of the Vitreolenticular Interface with Intra-Operative OCT

Running Head: Intra-Operative OCT of the Vitreolenticular Interface

Dr. Arnout Vael¹

Dr. Luc Van Os¹

Kirsten Melis²

Prof. Dr. Marie-José Tassignon¹

¹ Department of Ophthalmology, University Hospital Antwerp, Belgium

²Independent researcher

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Prof. Dr. Tassignon has intellectual property rights to the bag-in-the-lens intraocular lens (U.S. patent 6 027 531; EU patent 009406794.PCT/120268), which is licensed to Morcher GmbH, Stuttgart, Germany. None of the other authors has a financial or proprietary interest in any material or method mentioned.

Abstract

Purpose

To determine the prevalence of anterior vitreous detachment (AVD) in routine bag-in-the-lens cataract cases and whether we could identify risk factors for its presence.

Setting

University Hospital of Antwerp, Belgium

Design

Prospective cross sectional study

Methods

Patients having routine bag-in-the-lens cataract surgery were included. Patients with traumatic cataract, prior intra-ocular surgeries, YAG-laser, intravitreal injection or medical conditions that might affect normal ophthalmologic anatomy were excluded. Several parameters were collected from the patients records and their surgical videos/photos/OCT were evaluated.

Results

99 Eyes of 99 patients were included. Detectable AVD was observed in 62 eyes (63%). AVD was not present in 37 eyes (37%). The difference in prevalence of AVD between males and females was not statistically significant ($P = 0.55$, Pearson Chi Square test). The Mann Whitney U test for axial length was not statistically significant ($P = 0.38$). The Mann Whitney U test for age was statistically significant ($P < 0.005$). A logistic regression model to ascertain the effect of

age on the likelihood that patients had AVD did reach statistical significance ($\chi^2(1) = 8.246$, $P < 0.005$).

Conclusion

The prevalence of AVD in a routine cataract population is 63%. We identified age as a risk factor, our model determined that the odds for AVD increase with 5.3% for each year patients age. This data allows for better pre- and postoperative assessment of complications. The bag-in-the-lens, by its mandatory PPCCC, does not increase the risk of postoperative ocular complications in the posterior segment of the eye.

Introduction

The vitreolenticular interface was first described in literature by Joseph von Hasner in 1851 and studied by Germain Wieger in 1883.¹ Later its existence was confirmed by anatomist Emil Berger in a post mortem specimen.² In 1985, Weidle showed the presence of Berger's space in the living human eye by filling it with an ophthalmic viscosurgical device (OVD).³ This Berger's space is now defined as a retrolental space delineated by the posterior crystalline lens capsule, the anterior hyaloid membrane and the Wieger ligament. The vitreolenticular interface encompasses this group of structures. Other terms such as the hyaloid-capsular interspace or patellar fossa are also used in literature.

During bag-in-the-lens cataract surgery a primary posterior continuous curvilinear capsulorhexis (PPCCC) is routinely performed to prevent reopacification of the visual axis. We noticed that the behaviour of the posterior lens capsule could vary significantly between patients, where in some patients the posterior lens capsule was very mobile, collapsed in folds or bulged anteriorly. Furthermore, we noticed in some eyes the presence of small particles in Berger's space after phacoemulsification, corresponding with crystalline lens fragments. Finally, the amount of OVD that needed to be injected into Berger's space to provide a stable and detached posterior lens capsule from the anterior hyaloid, allowing to perform a PPCCC without damaging the anterior hyaloid, was found inconsistent between patients. In addition, the distribution pattern of the OVD injected in Berger's space also showed some clinical differences. We hypothesized that these differences in behaviour corresponded to differences in morphology of this retrolenticular

space and could in some cases be explained by the presence of an anterior vitreous detachment (AVD).

Rosen E. reports that the anterior hyaloid membrane was historically a debated topic, as there are numerous negative reports, primarily of histopathologic origin, denying it exists. Notwithstanding many studies that confirm the reality of this membrane.⁴ Intraoperative OCT allows us to view these particular anatomical structures as never before, and has sparked a renewed interest in this region of the eye. The older concepts of the vitreolenticular interface were confirmed with the use of this technology in a recent case series.⁵

This study sought to further unravel the status of the vitreolenticular interface in the general population. We wanted to determine the prevalence of AVD in routine cataract cases and whether we could identify risk factors for the presence of AVD, which might lead to complications during surgery.

Methods

This prospective study comprised patients having routine cataract surgery following the bag-in-the-lens technique at Antwerp University Hospital between January 2016 through December 2019 (approval Ethics committee Antwerp University/Belgian registration number: B300201939794). The study adhered to the tenets of the Declaration of Helsinki. Only routine cataract surgeries in adults (>18 years old) were included, patients with traumatic cataract, prior intra-ocular surgeries, prior YAG-laser, prior intravitreal injection or medical conditions that might affect normal ophthalmologic anatomy were excluded. If both eyes of a patient were eligible for inclusion, one eye was randomly selected.

Patients' data was collected from their medical records. Collected parameters included sex, age at the time of surgery, medical history and laterality of lens opacification. Axial length (AL) measurements were recorded using an optical biometer (Lenstar, Haag-Streit AG), or A-scan echography (Ultrasound A by Righton).

Only cataract surgeries performed by the same surgeon (M.-J.T.) were included. This to avoid eventual surgeon related variations and because iOCT was systematically performed by M.-J.T. In all cases, BIL IOL implantation was planned, requiring a calibrated 5.0mm anterior and posterior capsulorhexis. During all surgical procedures, special attention was focused on avoiding excessive AC depth fluctuation. After phacoemulsification of the crystalline lens and stabilization of the anterior chamber with OVD, real-time iOCT, integrated into the surgical microscope (Rescan; Carl Zeiss Meditec), was performed. Video was recorded or screenshots were taken and the vitreolenticular interface was evaluated and classified as 'AVD present' or

‘AVD not present’. AVD was confirmed based on the absence of any contact between the anterior hyaloid and the posterior capsule. The posterior lens capsule was punctured in the centre with a 30-gauge needle and sodium hyaluronate 1.0% (Healon; Johnson&Johnson) was injected into Berger’s space to separate the posterior lens capsule and anterior hyaloid membrane. During this procedure, the status of the interface was again verified. Additional cases of AVD were confirmed at this stage because AVD is easier to diagnose after inflation of the Berger space with OVD. Next, a 5.0 mm PPCCC was created with Ikeda forceps (EyeTech Fr 2268) and a Morcher 89A intra-ocular lens (IOL) implant (Morcher GmbH) was injected into the eye (monofocal or toric). The anterior and posterior lens capsules were then placed within the IOL groove.

All data was imported into an SPSS statistics database (IBM Corp.) for statistical analysis. Descriptive statistics were performed to determine the distribution of sex, axial length and age at time of surgery. Shapiro-Wilk tests were performed for axial length and age to test for a normal gaussian distribution. A crosstabulation and Pearson chi-square test were performed for gender and a Man Whitney U test for axial length and age. Finally a binomial logistic regression was performed for age.

Results

Seven hundred forty-three cataract surgeries performed by prof. M.-J.T. at the University Hospital Antwerp during the study period (January 2016 through December 2019) were identified. After exclusion and anonymization the study included 99 eyes of 99 patients. Table 1 shows the distribution of age at time of surgery, sex and mean axial length in the subgroups with and without anterior vitreous detachment (AVD).

Detectable AVD (no contact between the anterior hyaloid and the posterior capsule) was observed in 62 eyes (63%). In cases with AVD the intraoperative OCT revealed a slightly wavy hyperreflective line identified as the posterior lens capsule. A second hyperreflective line could be seen more posteriorly and identified as the anterior hyaloid membrane (Fig 1 & Fig 2). The distance between these two structures could vary, this metric was not tracked in our study. We also noticed that when injecting OVD into Berger's space it would form 'spaghetti-like' strings until a sufficient volume had been injected.

AVD was not present in 37 eyes (37%). In these cases intraoperative OCT revealed a wavy hyperreflective double line which could be identified as the posterior lens capsule with the attached anterior hyaloid membrane (Fig 3). We also noticed when injecting the OVD into Berger's space that it would disperse homogenously in all directions.

Because all patients underwent bag-in-the-lens procedures the posterior lens capsule was punctured by means of a 30G needle dragging the posterior capsule until a small rupture occurs. This manoeuvre is best performed in the middle of the posterior capsule where the anterior

hyaloid is anatomically most remote from the posterior capsule. OVD was injected into Berger's space to separate the posterior lens capsule and the anterior hyaloid membrane (Fig 4).

The difference in prevalence of AVD between males and females was not statistically significant ($P = 0.55$, Pearson Chi Square test). Shapiro-Wilk tests for normality for age and axial length were statistically significant ($P < 0.005$), showing a non-gaussian distribution. The Mann Whitney U test for axial length was not statistically significant ($P = 0.38$). The Mann Whitney U test for age was statistically significant ($P < 0.005$), allowing us to conclude that age in the group with AVD was statistically significantly higher than in the group without AVD.

A binomial logistic regression was performed to ascertain the effect of age on the likelihood that patients had AVD. The logistic regression model was statistically significant ($\chi^2(1) = 8.246$, $P < 0.005$). The model explained 10.9% (Nagelkerke R^2) of the variance in the presence of AVD and correctly classified 69.6% of cases. The model predicts that the odds for AVD increase with 5.3% for each year a patient ages.

Discussion

Anterior vitreous detachment was first described and studied by Weber E. in 1942.⁶ It was later confirmed by Emanuel Rosen.⁷ Both researchers realized the possible complications that might arise from a detachment of the anterior hyaloid membrane and already reported links to ageing, retinal detachment and trauma. A recent study by Anisimova et al. confirmed anterior vitreous detachment in a series of 28 patients through the use of iOCT and reported it as a risk factor for intraoperative complications during phacoemulsification.⁸ Another study by Ikeda et al. described a surgical technique, using high pressure anterior chamber infusion, to separate the anterior hyaloid membrane from the posterior lens capsule.⁹ Torri et al. studied spontaneous anterior hyaloid membrane detachment in patients scheduled for pars plana vitrectomy with a fiberoptic endoscope.¹⁰ They reported not a single case of spontaneous anterior hyaloid detachment in their entire study population (n = 38). To our knowledge there is no data in the literature on risk factors or the incidence of anterior vitreous detachment in the general population.

A study performed by our group in 2018 reported on dysgenesis of this interface in pediatric cataract cases, confirming that this anterior interface is of utmost importance in the normal physiology of the eye.¹¹ Because the vitreolenticular interface in young patients is a topic on its own, we therefore did not include children in this study.

When training for lens-in-the bag implantation, a rupture or tear of the posterior capsule is considered an important surgical complication because it is often correlated with prolapse of the vitreous due to the high risk of anterior hyaloid damage. During a bag-in-the-lens procedure the

posterior lens capsule is punctured in a controlled fashion and Berger's space is filled with an OVD to separate both structures and allow for a PPCCC to be performed. This surgeon's controlled procedure presents an extremely low incidence of anterior hyaloid damage. It did not occur in any of the patients included in this case series. If the 2 capsule blades are properly fused in the circumferential groove around the BIL IOL optic, LECs cannot proliferate and cannot use the anterior vitreous membrane as a scaffold to migrate toward the visual axis.^{12, 13} By injecting an OVD in Berger's space we were able to confirm our assessment of AVD by means of the iOCT images. When there was no AVD, the OVD dispersed homogeneously in all directions when injected through the small puncture in the posterior lens capsule. If there was an AVD, the OVD would form 'spaghetti-like' strings until a large enough volume was injected into Berger's space.

Although this was a single-center/single surgeon study with a limited patient population, this study is to our knowledge, the first to report the incidence of AVD in routine cataract patients and to assess the influence of sex, axial length and age on the detachment of the anterior hyaloid membrane. Unfortunately not all cataract cases that were treated with BIL IOL implantation at the Antwerp University Hospital during our study period could be included. Since it is a tertiary referral hospital, many patients had prior surgery or comorbidities resulting in exclusion from the study. In addition there were two reasons for missing data: OCT images of bad quality in patients who were unable to fixate the light source or poor records of the status of the anterior hyaloid membrane. There was no bias to disclose in the selection of patient's inclusion to record their AVD. The male – female ratio in our study group was balanced and a wide spectrum of axial length and age was present. We were only able to include two cases under the age of 21 years and no cases between the ages of 21 and 43. This was within our expectations as uncomplicated

cataract in young adults is rare and clear lens exchange is not performed at the University Hospital Antwerp.

With the current OCT devices it was not possible to visualize Berger's space and the anterior hyaloid membrane preoperatively. It was only possible after removal of the crystalline lens. A study by Pavan Kumar et al. used anterior segment OCT to assess the status of the posterior capsule preoperatively in posterior polar cataract, they reported a sensitivity of 100% and a specificity of 94.9% for detecting posterior capsule dehiscence but they were unable to specify anterior hyaloid malformation.¹⁴

To allow for an accurate assessment of the vitreolenticular interface, our study required phacoemulsification of the lens first, while simultaneously ensuring the stability of the anterior chamber. The act of performing a phacoemulsification has the potential of causing AVD and being a confounding factor for defining spontaneous from acquired AVD.^{9, 15, 16} To our knowledge there is currently no method to accurately visualize the vitreolenticular interface in vivo without removing the crystalline lens.

No statistically significant correlation was found between the presence of AVD and sex or AVD and axial length. We initially hypothesized that AVD would occur earlier in eyes with longer axial length as the tractional forces within the vitreous are stronger in large eyes.^{17, 18} However our study contradicts this. This does not exclude the presence of variations in size of Berger's space, which can be extremely big in high myopes but with an intact Wieger's ligament.

Anterior vitreous detachment was present in 60% of the total study population. This prevalence does not correspond with the findings of Torii et al.¹⁰ A possible explanation for this disparity is the difference in study populations. Firstly, Torii et al. performed their study in Japan, secondly

they included patients who were planned for pars plana vitrectomy, some of which had rhegmatogenous retinal detachment or proliferative diabetic retinopathy. This could lead to existing changes in the vitreous anatomy which might affect the natural history of AVD. Finally their study population was limited (n = 38).

We found no AVD in both of our young adult cases. This was to be expected as anatomical studies and studies concerning intracapsular cataract extraction in children and young adults demonstrated a strong adhesive quality between the posterior lens capsule and the anterior hyaloid membrane.^{6, 7} The youngest patient in our study group with AVD was 43 years old. However, some patients over the age of 80 years old still did not have AVD. The same variation is found in PVD.¹⁹ An interesting study to perform would be to demonstrate the relation between AVD and PVD in the same patient.

Knowledge of the status of the vitreolenticular interface can prove to be invaluable in the prevention of complications during cataract surgery. The most common complication during cataract surgery is a posterior capsular tear, which can result in reduced visual outcome and increased patient morbidity.²⁰ Anisimova et al. have recently demonstrated that AVD can cause excessive Berger's space hydration, leading to anterior displacement of the posterior capsule, increasing the risk of instrument touch and a posterior capsule tear. This same mechanism can also increase the risk of iris prolapse.⁸ Framme et al. describe in their review the increased risk of retinal tears, retinal detachment, posterior vitreous detachment and cystoid macular oedema following disruption of the anterior hyaloid barrier.²¹

Post phacoemulsification rhegmatogenous retinal detachment is an important complication that is not yet fully understood. The general consensus in literature is that this might be associated with

an earlier posterior vitreous detachment.²² However it may be that AVD is also a possible mechanism. A study performed by Schäffer et al. demonstrated that pseudophakic eyes, after a standard lens in bag procedure, with rhegmatogenous retinal detachment had a significantly lower prevalence of AVD compared to pseudophakic control eyes. They concluded that the persistent attachment of the anterior hyaloid membrane to the posterior lens capsule probably indicates a strong vitreoretinal adherence, which plays a crucial role in the development of post-phacoemulsification rhegmatogenous retinal detachment.¹⁸ Van den Heurck et al. reported a lower incidence of rhegmatogenous retinal detachment using the bag-in-the-lens technique and Morcher 89A implant (Morcher GmbH), compared to reported values in the literature of standard lens-in-the-bag procedures.²³ A possible explanation for this lower incidence of detachment when using the bag-in-the-lens technique is that the BIL procedure more often induces AVD if not yet present. However, it is important to stress that by injecting OVD into Berger's space, the loss in volume inherent to the removal of the crystalline lens content, will be partially compensated. Consequently, there is very little anterior displacement of the anterior hyaloid and the vitreous body in the immediate postoperative period. Further studies would be required to confirm the eventual protective role of using OVD to inflate Berger's space on posterior segment complications after cataract surgery.

Our study now gives surgeons information on the prevalence of AVD in a routine cataract population. We identified age as a risk factor, our model determined that the odds for AVD increase with 5.3% for each year patients age. This knowledge allows for better preoperative assessment of the risk of complications during and after cataract surgery. These data also corroborate on previous papers that the bag-in-the-lens, by its mandatory PPCCC, does not

increase the risk of postoperative ocular complications in the posterior segment of the eye but might prevent them to a certain degree.

We did not consider performing PPCCC using femtosecond laser capsulotomy. Future studies will tell whether this technique might be instrumental in performing a safe and reproducible PPCCC²⁴.

Acknowledgement

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Value Statement

What Was Known

- Anterior vitreous detachment is present in some patients.
- Anterior vitreous detachment is a risk factor for intraoperative complications.
- Absence of anterior vitreous detachment may be a risk factor for rhegmatogenous retinal detachment in pseudophakic patients

What This Paper Adds

- Prevalence of anterior vitreous detachment in age group 19 to 87 in routine bag-in-the-lens cataract surgery (60%).
- Age is a risk factor for anterior vitreous detachment as observed peroperatively.
- Posterior capsulorhexis does not cause but might eventually prevent posterior segment postoperative ocular complications.

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Figure legends

Fig 1. Screenshot of the iOCT after phaco-emulsification. The anterior lens capsule (AC), posterior lens capsule (PC) and anterior hyaloid membrane (AHM) are visible. The distance between the PC and AHM is relatively small. Also note the vitreous floaters (VF).

Fig 2. Screenshot of the iOCT after phaco-emulsification. The posterior lens capsule (PC) and anterior hyaloid membrane (AHM) are visible. Note the larger distance between both structures.

Fig 3. Screenshot of the iOCT after phaco-emulsification. The anterior lens capsule (AC), posterior lens capsule (PC) and anterior hyaloid membrane (AHM) are visible. Note the close approximation between the PC and AHM.

Fig 4. Screenshot of the iOCT, of the same patient as fig. 3 after OVD injection in Berger's space (BS). The anterior lens capsule (AC), posterior lens capsule (PC) and anterior hyaloid membrane (AHM) are visible. Note the clear separation between the PC and AHM.

Table 1. Distribution of age at time of surgery, sex and mean axial length in the subgroup with and without anterior vitreous detachment.

Parameter	AVD		<i>P</i> value
	Yes (n = 62)	No (n = 37)	
Age (years)			< 0.005
Median	73	67	
Range	43 - 87	19 - 84	
Sex			0.55
Male	29	17	
Female	33	20	
Mean AL (mm) ± SD	24,48 ± 2,36	24,23 ± 2,28	0.38

AL: Axial length, AVD: anterior vitreous detachment, SD: standard deviation



