# Pars plana vitrectomy for vitreoretinal interface disorders coincident with intermediate stage age-related macular degeneration

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**Background and Aims.** Currently around 67 million people in Europe are affected by some form of age-related macular degeneration (AMD). As most known types of vitreoretinal (VR) interface disorders can coexist with AMD and as we can favourably affect the former with vitreoretinal surgery, our goal was to evaluate the results of vitreoretinal interface disorder surgery with macular peeling in relation to coincident intermediate stage AMD.
**Methodology.** This was a retrospective evaluation of eyes operated with 25-gauge pars plana vitrectomy (PPV). The monitored parameters were anatomical and functional findings and, safety of the procedure. The surface of the macula was stained with trypan blue and treated (peeling) with a disposable microforceps. 10% perfluoropropane, or the air tamponade was used. Distance visual acuity was examined on the ETDRS chart, the macular finding was monitored by OCT and photodocumented. The post-operative face-down position was 3-5 days. The follow-up period was 6 months.
**Results.** 17 eyes (14 patients, woman 86%) mean age 74 years. The primary indications for the procedure were: idiopathic macular hole (IMD) 59%, epiretinal membrane 29% and vitreomacular traction syndrome 12%. Ophthalmoscopic and OCT findings of intermediate dry form of AMD (100%), in 24% was drusoid ablation of the pigment leaf. In all cases of IMD, primary closure occurred. Input visual acuity 0.1–0.6 improved to 0.2–0.9 at the end of the follow-up period ($P<0.05$). No complications during surgery or progression of AMD in the follow-up period were observed.
**Conclusion.** PPV for vitreoretinal interface disorders have similar anatomical results, whether the outer part of the retina is disrupted by intermediate AMD or not. Functional results are affected by possible disruption of the RPE or the outer layers of the neuroretina by AMD. The PPV procedure has a standard security profile. It is safe and does not affect the progression of AMD in the short term.

**Key words:** pars plana vitrectomy, aged-related macular degeneration, vitreoretinal interface, visual acuity

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## INTRODUCTION

The vitreoretinal interface (VR interface) consists of the inner limiting membrane of the retina, the posterior cortex of the vitreous and the intervening extracellular matrix[1]. The VR interface is a dynamically evolving environment determined by the interaction of the posterior hyaloid membrane and the inner limiting membrane of the retina. The VR interface plays an important role in the pathogenesis and course of macular diseases[2-4].

Optical coherence tomography (OCT) is the best method for determining the details of the VR interface. Its introduction into clinical practice in 2011 as a routine examination has resulted in significant progress in the diagnosis and differential diagnosis of macular pathologies[2-4].

In connection with the expansion of OCT uses in diagnostics, an up-to-date classification of diseases of the vitreomacular interface has been created which distinguishes the basic findings on the macular surface[5].

Vitreomacular adhesion (VMA) is defined as the peripheral vitreous separation with remaining vitreomacular attachment and intact foveal morphological features. This is an OCT finding that is almost always the result of normal vitreous aging which can lead to pathological conditions[5].

Vitreomacular traction syndrome (VMTS) is characterized by anomalies of the posterior vitreous accompanied by anatomical distortion of the fovea which may include pseudocysts, macular schematics, cystoid macular oedema, and subretinal fluid. Vitreomacular traction can be subclassified according to the diameter of the vitreous attached to the macular surface, measured by OCT, with a connection of 1 500 μm or less defined as the focus and a connection of more than 1 500 μm as wide. If it is associated with another macular disease, VMTS is classified as concurrent[5].

The macular centre defect, the idiopathic macular hole (IMD), is defined as a foveal lesion with defects of all retinal layers from the inner limiting membrane to the retinal pigment epithelium. The full-thickness IMD is subclassified according to the hole size determined by the OCT and the presence or absence of the VMTS (ref.[5]).

The latter are the epiretinal membranes (ERM). The ERM is a thin layer of fibrous tissue that develops on the surface of the macula and can cause central vision problems[5].

Age-related macular degeneration (AMD) is a major cause of visual impairment and severe vision loss. Clinically classified as early stage (defined by the presence of many small (<63 microns, "hard") or medium (≥63 microns, but <125 microns, "soft" drusen), middle stage (macular disease characterized by either extensive small or medium drusen (≥125 microns – 124 microns is the average diameter of the retinal vein at the edge of the optic disc) and advanced stage (defined by the presence of either geographical atrophy or choroidal neovascular membrane). AMD is a multifactorial disorder with dysregulation in lipid, angiogenic, inflammatory and extracellular pathways[2,6].

More than 50 loci of genetic susceptibility have been identified, the most important of which are in the CFH and ARMS2 genes. The main non-genetic risk factors are smoking and low dietary antioxidant intake (zinc and carotenoids) (ref.[2,6]).

There are currently around 67 million people in Europe affected by some form of AMD, and as the population ages, this number is expected to increase around 15% by 2050 (ref.[7]).

Virtually all known types of VR interface disorders can be present at the same time as AMD. In most cases, we can favourably affect the former with vitreoretinal surgery.

In 1969, David Kasner first described vitrectomy using the "open-sky" technique[8]. Subsequently, in 1971, Robert Machemer created the first closed vitrectomy system (which allowed intraocular pressure regulation) using a 17-gauge (G) approach through the pars plana[9,10]. This dates back to the beginnings of pars plana vitrectomy (PPV), which we know now. The latest technology is mini-invasive, micro-invasive, suture-free 25G (or even 27G) PPV. Its advantages are: reduction of postoperative pain, reduced induced corneal astigmatism, shorter operation time and better healing of surgical wounds and visual rehabilitation. There are also possible complications and disadvantages of the surgical method: risks of rhegmatogenic retinal detachment and retinal tears in the periphery of the retina, endophthalmitis, sclerotomy leakage and hypotension, and last but not least, higher financial costs[11].

Peeling membrana limitans interna is the most technically demanding part of the surgical procedure. With single-use instruments, the surgical procedure increases, and the risk of iatrogenic damage is possible. Visualization agencies (indocyanine blue, trypan blue) are used as prevention against iatrogenic disease of the macula[12].

The development of OCT and the progression of retinal surgical procedures together with the beginning awareness of the influence of VR interface on the development of AMD led us to assess the current impact of these disorders. For this reason, our goal was to evaluate the most common operations of the most frequent VR interface disorders in relation to the dry form of AMD.

**Table 1.** Information about patients.

| Order | Eye | Year Dg | | AMD | BCVA before | BCVA 3M | BCVA 6M | LogMAR before | LogMAR 3M | LogMAR 6M |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | OP | 72 | IMD (3) | confluent druses | 20/125 | 20/50 | 20/40 | 0.8 | 0.4 | 0.3 |
| 2 | OL | 72 | VMTS | drusoid ablation RPE | 20/32 | 20/25 | 20/25 | 0.2 | 0.1 | 0.1 |
| 3 | OP | 77 | ERM | drusoid ablation RPE | 20/40 | 20/25 | 20/25 | 0.3 | 0.1 | 0.1 |
| 4 | OP | 76 | IMD (2) | drusoid ablation RPE | 20/32 | 20/32 | 20/25 | 0.2 | 0.2 | 0.1 |
| 5 | OL | 76 | IMD (3) | confluent druses | 20/100 | 20/100 | 20/100 | 0.7 | 0.7 | 0.7 |
| 6 | OL | 76 | IMD (3) | drusen, focal atrophy RPE | 20/200 | 20/63 | 20/50 | 1.0 | 0.5 | 0.4 |
| 7 | OP | 76 | ERM | drusoid ablation RPE, hyalosis asteroides | 20/100 | 20/40 | 20/40 | 0.7 | 0.3 | 0.3 |
| 8 | OP | 79 | IMD (4) | drusen, focal atrophy RPE | 20/125 | 20/63 | 20/50 | 0.8 | 0.5 | 0.4 |
| 9 | OP | 73 | VMTS | confluent druses | 20/50 | 20/40 | 20/32 | 0.4 | 0.3 | 0.2 |
| 10 | OL | 73 | ERM+VMTS | drusen, focal atrophy RPE | 20/63 | 20/50 | 20/40 | 0.5 | 0.4 | 0.3 |
| 11 | OL | 68 | IMD (3) | drusen | 20/50 | 20/40 | 20/50 | 0.4 | 0.3 | 0.4 |
| 12 | OP | 54 | IMD (2) | drusen | 20/63 | 20/32 | 20/25 | 0.5 | 0.2 | 0.1 |
| 13 | OP | 79 | VTMS+IMD (2) | small drusen, pigment transfers | 20/125 | 20/40 | 20/32 | 0.8 | 0.3 | 0.2 |
| 14 | OP | 80 | ERM | multiple drusen | 20/63 | 20/50 | 20/50 | 0.5 | 0.4 | 0.4 |
| 15 | OL | 69 | ERM after amotio surgery | multiple drusen | 20/50 | 20/32 | 20/25 | 0.4 | 0.2 | 0.1 |
| 16 | OL | 80 | IMD (3) | multiple drusen | 20/63 | 20/40 | 20/25 | 0.5 | 0.3 | 0.1 |
| 17 | OL | 75 | IMD (4) | drusen | 20/100 | 20/63 | 20/63 | 0.7 | 0.5 | 0.5 |

The table consists of numbers of patient and their data with we statistically evaluated.
Dg, Diagnosis; AMD, Aged-related macular degeneration; BCVA, Best-corrected visual acuity; LogMAR, Logarithm of the Minimum Angle of Resolution.

## MATERIAL AND METHODOLOGY

In retrospective follow-up, a set of standard 25G PPV operated eyes was evaluated by a single surgeon (L.H.). The surface of the macula was stained with trypan blue and treated with a disposable Eckardt microforceps. Each epimacular membrane as well as ILM in all cases were peeled off. In IMD surgery, perfluoropropane (10%) was used as a tamponade at the end of the procedure, in other cases air tamponade only. Best-corrected visual acuity (BCVA) was examined on the ETDRS charts. The macular finding was monitored biomicroscopically on a slit lamp, details using an OCT instrument (Zeiss AngioPlex) and photo-documented on a ZEISS Clarus 700 instrument. The postoperative position was face down and the length of positioning depended on the macular involvement (3–5 days). The follow-up period is 6 months. The statistics were processed by Excel and we used paired t-tests for comparison of before and after the surgery.

## RESULTS

The group consisted of 17 eyes (14 patients) aged 54–80 years (mean 74 and median 76 years). The majority of the group consisted of women (12 patients, 86%), men made up a smaller percentage (2 patients, 14%).

The primary indications for retinal surgery were: the presence of IMD (10 cases, 59%), ERM (5 cases, 29%) and VMTS (2 cases, 12%). All patients had an ophthalmic examination on a slit lamp and an OCT macular examination, where the dry form of AMD was diagnosed in the intermediate stage (multiple drusen, medium, size <125 μm) in 100% of patients before the procedure. Of these, drusoid ablation of the pigment leaf was found in 4 cases, representing 24%. In all cases of IMD, primary closure occurred after surgery (100% healing). The baseline BCVA of 0.1 to 0.6 (mean and median 0.3) improved to 0.2 to 0.9 (mean and median 0.6) at the end of the follow-up period. The improvement in BCVA was statistically significant ($P$<0.05).

There were no known complications of the following: perioperative retinal rupture, rhegmatogenic retinal detachment, endophthalmitis, and there was no progression of the macular finding when assessing the development of moderate AMD at the time of follow-up

## DISCUSSION

Macular pathology, which consists of a combination of VR interface disorders and some degree of advanced AMD, is found relatively often in clinical practice. In our group, we focused only on situations where the coincident disability of the VR interface is an intermediate (risky) form of AMD. Approximately 26% of patients with this form of AMD progress to a higher stage (atrophy, or choroidal neovascularization) within 5 years. We monitored the possible progression of the dry form into the wet form by biomicroscopic examination on a slit lamp, fundus photos and OCT examination of the retina, which we compared with each other. During the follow-up period, there was no acceleration of specifically significant changes of the type: development of atrophy of neuroretina and RPE, change of distribution (increase or decrease of drusen) or development of CNV. The finding of AMD manifestations before and after surgery remained stable in our cohort and half-year follow-up period.

We compared our results (discussed according to individual subtypes of VR interface failure) with the work of other authors.

The mechanisms of VMA that modify mechanical and biochemical factors in AMD continue to be the subject of clinical and laboratory research. The presumed action of the tightly adhering vitreous is the formation of a barrier to the diffusion of oxygen and biochemical nutrients into the retina. This condition, along with traction changes, promotes relative retinal ischemia and the accumulation of other cytokines, including VEGF. Hypoxia is also induced by retinal elevations (vitreoretinal traction) (ref.[13]).

We did not indicate VMA pathology to PPV and therefore we do not evaluate it here. As a reminder, however, VMA is associated with AMD and progresses more frequently to VMTS in eyes with wet AMD. In the work of Mojana et al. VMTS was more strongly associated with advanced AMD ($P$=0.0082). VMTS patients who underwent surgery showed a slight improvement in BCVA and a reduction in retinal thickness[14]. This was confirmed by our results where all patients with VMTS experienced an improvement in BCVA.

ERM in the macular landscape is a relatively common condition, with seniors being at higher risk. The incidence, similar to AMD, increases to 15.1% in people over the age of 70 (ref.[15]). The age range of patients with ERM was 54–80 years (mean 74).

Morphological (histopathological) differences between AMD with ERM and idiopathic ERM have been identified. The AMD group with ERMs had more likely ERMs with smooth surface, less severe surface traction, thinner central retinal thickness, and greater photoreceptor layer disruption than idiopathic ERMs. BCVA improved and central retinal thickness decreased in both groups 1 year after surgery. Ellipsoid zone baseline integrity and preoperative BCVA correlated significantly with vision outcome in the AMD group with ERM. PPV led to significant anatomical and visual improvements in eyes with AMD with ERM, but the final visual outcome was worse in these eyes due to AMD than in eyes with only idiopathic ERM (ref.[16]). The PPV surgical method for ERM is a benefit for eyes with relatively good preoperative vision[17].

BCVA after PPV for ERM improves during the first 3 years after surgery and remains stable. Improved anatomical integrity of the outer retinal layers correlated with improved BCVA (ref.[18]).

In our cohort, we had 5 patients after PPV for ERM. BCVA improved in all our patients. This confirmed the results of the other authors[16-18].

In a publication of Rao et al., the incidence of IMD is reported to be higher in eyes with dry AMD than in

wet with AMD. The degree of surgical closure was comparable in the groups with dry AMD, compared to the second group with wet AMD. However, the improvement in BCVA was statistically significant only in the group with the dry form of AMD (ref.[19]). The improvement of BCVA after PPV for IMD also continued during the first 3 years. It was subsequently maintained in a substantial percentage of patients, with the final BCVA correlating with better preoperative BCVA and better postoperative OCT parameters[20].

The largest percentage of our group consisted of 10 patients with IMD. All had AMD dry form confirmed by OCT examination. Each of our patients had either improved or at least stabilized BCVA after surgery during a 6-month follow-up period. There was an anatomical improvement in the macular finding according to OCT examination, which confirmed the results of other authors[19,20].

The question of whether macular peeling PPV can prevent the progression of AMD (into the wet form) is so far speculative. Further studies are needed to define the role of vitreoretinal surgery in such cases[14].

## CONCLUSION

Vitreoretinal surgery for VR disorders has similar anatomical results whether or not the outer retina is damaged by intermediate AMD. Functional results are naturally affected by the eventual disruption of the retinal pigment epithelium or photoreceptors by an age-related process. In our case, there was a statistically significant improvement in BCVA. We explain this by timely indicating and performing surgery. At a later stage, when age-related changes are already clinically significant, there may not be statistically significant improvements in BCVA and the course of the operation could be risky for both the patient and the surgeon.

At the same time, we also know that approximately 26% of patients with moderate AMD progress to a higher stage (atrophy or choroidal neovascularization) within 5 years and that patients with the wet form have more frequent signs of VMA (detectable on OCT). The question of whether macular peeling during PPV can prevent the progression of AMD (into wet form) is still speculation. The procedure is safe and does not affect the progression of AMD in the short term.

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