Original research

Prognostic factors of postoperative intraretinal cystoid spaces after primary pars plana vitrectomy for vitreomacular traction

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Abstract

Purpose: To study the anatomical and surgical prognostic factors related to developing postoperative intraretinal cystoid spaces (ICS) six months after 25-gauge pars plana vitrectomy (PPV) for vitreomacular traction (VMT).

Methods: The study is a retrospective case series of patients presenting with VMT treated primarily with PPV. All patients underwent 25-gauge PPV by the same retina surgeon. Intra-operative parameters were all recorded. Postoperative visual acuity (VA), foveal thickness, and ICS were collected over six months of follow-up. ICS were defined as hyporeflective cysts divided by hyperreflective septa on optical coherence tomography (OCT). Patients with ICS persistence 3 months postoperatively received topical treatment extension. The primary outcome measure was odds of preoperative ICS in patients with postoperative ICS compared to controls. Secondary outcome measures were odds of presence of an attached hyaloid to the optic disc, presence of pseudophakia, the use of intra-operative air, and the use of more than one intra-operative indocyanine green (ICG) injections in patients with postoperative ICS compared to controls.

Results: Two hundred and eighty treatment-naïve patients with preoperative diagnosis of epiretinal membrane (ERM) were reviewed. Thirty patients with VMT, confirmed both preoperatively on OCT and intra-operatively, were included. Postoperatively, 40% (n = 12) presented with ICS at 6 months. Among these, 83% (n = 10) had ICS prior to PPV. Patients presenting with preoperative ICS were significantly more at risk of having persistent ICS postoperatively (P < 0.05). The following factors did not statistically affect ICS occurrence: optic disc hyaloid attachment status, phakia/pseudophakia, intra-operative air vs. sulfur hexafluoride (SF6), and the number of intra-operative ICG injections.

Conclusions: Our data demonstrate a predictive relationship between the occurrence/persistence of ICS post-PPV for VMT and the initial foveal status. Specifically, having preoperative ICS is a major risk factor for its persistence postoperatively. Our data highlight the pathophysiological importance of the vitreous phase and its effect on visual prognosis.

Keywords: Vitreomacular traction; Macular edema; Pars plana vitrectomy
Introduction

The vitreous plays a crucial role in visual function. Age-related physiological changes in the vitreous gel start with liquefaction and lead to progressive destruction of the collagen-hyaluronic acid network. The latter will then focally weaken the vitreomacular adhesions and imbalance the overall integrity of vitreomacular interface. The presence of persistent tractional adhesions can lead to idiopathic vitreomacular traction (VMT) syndrome which may be associated with anatomic layer distortion in the fovea, foveal detachment, and/or intraretinal cystoid spaces (ICS).2

VMT predominately affects female patients in their 6th decade of life. VMT has an estimated prevalence of 22.5 cases per 100,000 and an incidence of 0.6/100,000 persons-year. Patients with persistent VMT often complain of symptomatic visual disturbances such as blurred and distorted vision; decreased visual acuity (VA) and metamorphopsia are often seen on exam. Spontaneous resolution of VMT occurs in 11–53% of cases. The remaining majority of symptomatic patients can be treated with pars plana vitrectomy (PPV) primarily or as a secondary intervention if other techniques such as intravitreal ocirplasmin or pneumatic vitreolysis fail. Currently, PPV is considered the most cost-effective option in treating VMT. Depending on the extent of VMT and other associated factors including epiretinal membrane (ERM) and macular holes, PPV can be offered to a specific subset of patients. In one report, 64.3–87.5% of patients who underwent PPV for VMT had their postoperative VA improve by > 1 line, and about 33% were found to have >2 lines of improvement.

PPV-related complications are well known and include cataract formation as well as macular edema (ME). The occurrence of postoperative ME ranges between 1% and 12.8% of cases. Even though ME is not an uncommon postoperative occurrence after any intraocular surgery, the exact inflammatory pathophysiology is still unknown. Two mechanisms have been proposed. The first is related to an iatrogenic weakening of retinal scaffolding due to damage to Müller cells following internal-limiting membrane peeling. This is then suspected to lead to formation of ICS mainly in the Henle fibers and inner nuclear layers. Interestingly, the absence of vascular leakage during fluorescein angiography of eyes with ICS confirms an intact blood-retinal barrier and reinforces the structural retinal pathophysiology. The second cause of inflammatory ME is related to disruption of blood-retinal barrier and subsequent leakage during fluorescein angiography.

In one study, the anatomic incidence of ICS was 47% at 1 month postoperatively when evaluation was conducted with OCT. There is no doubt that ICS can reduce vision following intraocular surgery. In fact, ICS can exert compressive forces on key retinal structures including photoreceptors and their ellipsoid zone, resulting in functional visual abnormalities and a lack of VA improvement postoperatively.

Currently, limited data exists on the incidence as well as the prognostic anatomical and surgical factors of postoperative ICS in patients presenting with VMT and who have been primarily treated with PPV.

Methods

A retrospective review of the medical records of 280 treatment-naive patients with preoperative diagnosis of ERM was initially done in order to identify patients with VMT as the surgical billing codes for VMT and ERM are the same in the province of Quebec, Canada. The study included all surgical cases of idiopathic ERM that consecutively underwent PPV with a 25-gauge system by the same surgeon (M.A.K), at the Jewish General Hospital, Montreal, Quebec, Canada. All operated patients had their internal limiting membrane (ILM) peeled. The peeling was confined to a 1.5–2.5 disc diameter area within the vascular arcades. The following pathologies associated with cystoid ME were excluded from the study: diabetic retinopathy, retinal vein occlusion, and uveitis (infectious, inflammatory and postoperative). The local research department confirmed the waiver of the ethical approval because there was no risk of deviation from the usual standard of care given the retrospective nature of the study. Direct written patient consent was not obtained for data collection and analysis, and as such, no identifying information has been included. Thirty patients were included in this study on the basis of the presence of VMT confirmed preoperatively by optical coherence tomography (OCT) and intra-operatively by direct visualization. Demographic data was abstracted including age and sex. Preoperative best corrected visual acuity (BCVA) in logMAR, phakic status, central subfield thickness as an indicator of central foveal thickness (CFT), horizontal vitreomacular adhesion (HVMA) diameter, and the presence of ICS on OCT were all recorded. ICS were defined using OCT as hyporeflective dark spaces divided or not by hyperreflective septa. Fig. 1 illustrates ICS in two of our patients pre and postoperatively. The HVMA diameter was measured using an electronic caliper within the spectral domain optical coherence tomography (SD-OCT) software. The diameter was defined by the maximum horizontal length of the vitreous attachment to the fovea, using the method described in another study. All intra-operative parameters were recorded including: the status of the hyaloid attachment to the optic disc, the type of tamponade used [air vs. sulfur hexafluoride (SF6)], and the number of indocyanine green (ICG) injections. Post-operatively, BCVA, CFT, and the presence of ICS (assessed by OCT) were recorded over a six-month followed period.

Patients were evaluated on postoperative day one, week one, month one, month three, and six months. All patients included in this study had a minimum follow-up period of six months. All patients received the same treatment post-operatively consisting of moxifloxacin QID for one week, diclofenac QID, and prednisolone acetate 1% on a tapering schedule over six weeks. Those with persistent ICS 3 months postoperatively received additional topical treatment extension of diclofenac or were switched to nepafenac 0.1% and prednisolone acetate 1% at a frequency equal to their use of nonsteroidal anti-inflammatory drugs (NSAIDs).
Surgical technique

All procedures were performed under retrobulbar anesthesia block of 2% lidocaine without epinephrine. In all surgeries, a wide-angle viewing system was used in combination with the Alcon Constellation system (Alcon Laboratories, Inc., Fort Worth, TX) using the ULTRAVIT 25-G vitreous cutter (Alcon). The surgical approach consisted of conjunctival displacement with insertion of a transconjunctival cannula using a beveled trocar in the inferotemporal, superotemporal, and superonasal quadrants. A 25-gauge infusion cannula was placed through the inferotemporal sclerotomy site. A sutured contact lens was used for visualization of the fundus. After assessment of the optic disc hyaloid attachment status, anterior and central vitrectomy was done followed by induction of a posterior vitreous detachment (where applicable). Peripheral vitreous shaving was performed with scleral indentation. ICG was used to enhance the ILM visualization and peel. SF6 gas, at a concentration of 20%, was only used for suspected foveal microhole or intra-operative peripheral retinal tear. In these cases, dilute gas was injected with a 30-gauge venting needle to adequately pressurize the eye. At the end of the procedure, the cannulas were removed, and the sclerotomies were assessed for leakage. When needed, 7.0 Vicryl was used to secure the sclerotomies.

Statistical methods

Descriptive statistics were summarized by presenting the number and percentage for categorical variables, the average ± standard deviation (SD) for continuous variables with normal distribution and median and interquartile range (IQR) for variables without normal distribution. The data analysis was performed at the 6th month follow-up time point. The association between postoperative ICS groups and other categorical factors was carried out by using the Fisher’s exact test. Mann-Whitney U test was used to assess possible association between continuous variables. The binary logistic regression analysis was used to predict the odds of presence of postoperative ICS with different prognostic factors. The correlation between CFT change and baseline CFT was assessed by using scatter plots and Spearman’s rank correlation coefficient. The results were presented by the odds ratio (OR) and 95% confidence interval (CI). P-value less than 0.05 was used to indicate statistical significance. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS, version 22).

Results

Two-hundred eighty treatment-naïve patients with preoperative diagnosis of ERM underwent PPV with a 25-gauge system. Thirty patients had OCT-confirmed VMT preoperatively and intra-operatively by direct visualization with contact lens and wide-angle viewing systems.

Descriptive statistics

The descriptive analysis of the whole population is shown in Table 1. Postoperatively, 40% (n = 12) of patients presented with ICS at 6 months (PO-ICS) compared to 60% (n = 18) with no postoperative ICS at 6 months (NO-PO-ICS).
purpose of statistical analysis, the patients were divided into the PO-ICS and NO-PO-ICS groups (Table 2). The average age was 65\(\pm\)5 years old in the PO-ICS group and 63\(\pm\)5 years old in the NO-PO-ICS group. 75\% (n = 9) of patients in the PO-ICS group were female compared to 55.6\% (n = 10) in the NO-PO-ICS group. The relationship between age, sex, and the occurrence of postoperative ICS was not statistically significant (P = 0.44). The mean preoperative BCVA in the PO-ICS group was 0.47 \(\pm\) 0.24 compared to 0.54 \(\pm\) 0.25 in the NO-PO-ICS group. There was no statistically significant difference in the preoperative BCVA between the two groups (P = 0.49). The average postoperative logMAR VA change was 0.09 \(\pm\) 0.02 and \(-0.03 \pm 0.01\) for the PO-ICS and NO-PO-ICS groups, respectively. The statistical analysis showed no significant differences between the two groups (P = 0.20). The ICS were observed in the outer plexiform layer (OPL) in most patients (Fig. 1 provides examples of pre and postoperative OCT changes in two selected patients).

**Role of the vitreomacular adhesion diameter in the development of postoperative intraretinal cystoid spaces**

In order to investigate the role of the HVMA diameter on the occurrence of postoperative ICS, we measured the HVMA diameter on preoperative OCTs in both outcome subgroups. The median preoperative HVMA diameter in the PO-ICS group was 433.5 \(\mu\)m (455.8) compared to 422.5 \(\mu\)m (1917.0) in the NO-PO-ICS group. There was no statistically significant difference between the two groups (P = 0.66).

**Role of preoperative prognostic factors in the development of postoperative intraretinal cystoid spaces**

Fifty percent (n = 6) of patients with PO-ICS were pseudophakic compared to 61\% (n = 11) in the NO-PO-ICS group (Table 2). The odds of developing postoperative ICS in a pseudophakic patient was 1.57 (OR 1.57, 95\% CI: 0.36—6.86). The result was not statistically significant (P = 0.71).
Interestingly, 83.3% (n = 10) of patients with PO-ICS had preoperative ICS compared to 33.3% (n = 6) in the NO-PO-ICS group. The odds of having persistent postoperative ICS when preoperative ICS is present is 10 times higher (OR 10.00, 95% CI: 1.4–60.92). The result was statistically significant (P = 0.01).

**Role of the preoperative central foveal thickness in the development of postoperative intraretinal cystoid spaces**

The mean preoperative CFT in the PO-ICS group was 521.42 ± 205.37 μm compared to 449.67 ± 178.24 μm in the NO-PO-ICS group. The difference was not statistically significant (P = 0.28). At 6 months, the change in CFT postoperatively compared to the preoperative value was −304.08 ± 288.3 μm in the PO-ICS group compared to −199.89 ± 193.5 μm in the NO-PO-ICS group (Table 1), a difference that was also not statistically significant (P = 0.27).

There was, however, a statistically significant linear correlation between preoperative CFT and postoperative CFT change (r = −0.75, P < 0.0001). Specifically, patients presenting with larger preoperative CFT would have a larger reduction in their postoperative CFT.

**Role of intra-operative prognostic factors in the development of postoperative intraretinal cystoid spaces**

In the PO-ICS group, 100% (n = 12) of patients had an attached hyaloid to the optic disc preoperatively, compared to 77.8% (n = 14) in the NO-PO-ICS group (Table 2). An OR could not be calculated in this case. In regard to endotamponade, 75% (n = 9) and 50% (n = 9) of patients in the PO-ICS and NO-PO-ICS groups underwent tamponade with air and with SF₆, respectively. The odds of developing postoperative ICS when air was used compared to SF₆ was 3.00 (OR 3.00, 95% CI: 0.61–14.86). This result was not statistically significant (P = 0.26). 100% (n = 12) and 88.9% (n = 16) of patients in the PO-ICS and NO-PO-ICS groups received one ICG injection, respectively. In the NO-PO-ICS group, 11.1% (n = 2) received 2 ICG injections. An OR could be calculated in this case.

**Discussion**

Our study describes the prognostic factors related to developing postoperative ICS after 25-gauge primary PPV for VMT. The presence of ICS was correlated with a statistically significant ten-fold increase in the risk of persistence ICS postoperatively, despite the surgical release of the VMT. This result is consistent with the findings of Frisina et al. highlighting that the presence of preoperative ICS was associated with its persistence following PPV for ERM. The latter finding was associated with a significantly worse VA after surgery. 

In our study, there was mild VA worsening in the PO-ICS group at six months (ΔlogMAR of +0.09) that is likely explained by the persistent presence ICS. Patients without postoperative ICS had a modest VA improvement (ΔlogMAR − 0.03), but the difference was not statistically significant. Our study results are similar to those by Frisina et al., who analyzed a cohort undergoing PPV for VMT with a baseline VA of 0.45. VA modestly improved to 0.37 logMAR at the six-month follow-up.

Patients presenting with a large preoperative CFT had a larger reduction in their CFT as shown on their postoperative OCT. The correlation was linear and statistically significant. In other words, patients presenting with more severe and larger ICS had a greater reduction in their foveal thickness, but ICS did not necessarily resolve as we have shown earlier. Because the presence of preoperative ICS was a major risk factor for its postoperative persistence, we expected a similar correlation with baseline CFT given the interdependence between CFT and ICS as indicators of foveal status in patients with VMT. However, our data fails to show a relationship between baseline CFT on OCT and the development of postoperative ICS. This is likely related to our small sample size which resulted in a statistically significant result for a categorical variable (in this case the presence/absence of ICS) and not for a continuous variable (in this case the CFT).

Despite being not statistically significant, more patients with PO-ICS had an attached hyaloid to the disc preoperatively and thus required mechanical detachment intraoperatively. This observation could raise the possibility of an important effect of persistent optic disc hyaloid attachment on the development of postoperative ICS. This is likely due to the chronic tractional forces exerted by an attached hyaloid and its resultant structural anatomical retinal alterations. This finding is in concordance with previous publications showing a reduction or regression of ICS in patients where a posterior vitreous detachment occurred, or in other words, where the hyaloid was detached from the optic nerve. While the estimate did not yield statistical significance in our study, a repeat study with a larger sample size could provide a more precise estimate of this potential association.

While the development of postoperative ICS following cataract surgery is well-known and documented (Irvine-Gass Syndrome), the relationship between lens status and post-PPV ICS is not very well understood. In our study, we investigated whether pseudophakia predisposes to a higher risk of postoperative ICS. The statistical analysis did not show significant correlation between pseudophakia and the incidence of postoperative ICS. However, more patients with postoperative ICS were pseudophakic. This observation could be explained by a higher tendency in pseudophakic to show postoperative mechanical alterations at the vitreomacular interface.

Postoperative ICS after PPV could possibly be multi-factorial due to baseline previous ICS secondary to cataract surgery or tractional forces secondary to VMT. A multivariate analysis on those prognostic factors could have mitigated this problem. However, the small sample size of our study would have rendered such analyses insignificant. Hence, the influence of cataract remains debatable, as Frisina et al. also suggested.

Previously, Koizumi et al. suggested that the HVMA diameter is inversely related to foveal deformation and thus its related pathophysiological changes such as ICS. In fact, a
smaller HVMA diameter precludes more anteroposterior traction for the same force: a larger HVMA diameter dampens the traction and spreads along a larger surface. Our sample size does not permit a definitive statement about the relationship between HVMA diameter and ICS, but we strongly believe, however, that such a correlation is real and could lead to clinically significant visual disturbances.

In 2014, Emrani et al. showed that the use of gas tamponade (air or SF6) during ERM surgery significantly improved outcomes. However, we strongly believe that such a correlation is real and could lead to clinically significant visual disturbances.

In 2014, Emrani et al. showed that the use of gas tamponade (air or SF6) during ERM surgery significantly improved outcomes.20 More recently, Chabot et al. compared air and SF6 endotamponade on VA after ERM surgery. Their study showed similar outcomes for VA, quality of life, and central retinal thickness21 for the two type of gases used. In our study, we did not find any statistically significant relationship between the use of air or SF6 and the development of postoperative ICS, in keeping with those two abovementioned studies.

In regard to the intra-operative staining of the ILM, our study did not show a statistically significant relationship between the number of ICG injections and postoperative ICS. Particularly, the number of ICG injections did not appear to be correlated with the development of postoperative ICS. A double injection was performed only twice and was likely due to surgeon preference.

Additionally, our data highlights the pathophysiological importance of the vitreous phase and its effect on ICS persistence and visual prognosis. Normally, PPV and ILM peeling should have beneficial therapeutic effects on foveal deformation because they remove tangential traction and allow intraretinal fluid evacuation from the macula to the vitreous cavity if edema is present.22 However, our data demonstrates a predictive relationship between the occurrence and persistence of ICS after PPV for VMT and the initial foveal status. Having preoperative ICS is a major risk factor for its persistence postoperatively despite surgical treatment. While the mechanism of development and persistence is not fully understood, Frisina et al. proposed a mechanical hypothesis.12 They suggest that ICS can occur in the absence of inflammation and breakdown of blood-retinal barrier through damage and weakening of the scaffolding effect by Müller cells. Structural retinal damage can possibly occur during surgery, further worsening the presence and/or persistence of ICS. Based on this hypothesis, Frisina et al. recommended that PPV should be performed as soon as possible and even before the occurrence of intraretinal cysts in patients with VMT.

Our study has some limitations. Given the retrospective nature of this study, intra-operative factors such as number of ICG injections and the size/extent of ILM peeling and type of tamponade used depended on surgeon preferences and intra-operative findings; therefore, our data does not capture potential confounding intra-operative variables. Furthermore, all patients included in this study underwent ILM peeling, which could cause ICS postoperatively,12 in predisposed patients. Due to the small sample size, the data could not be standardized with respect to age, gender, and preoperative parameters including hyaloid and phakic status. A repeat study with a larger sample size could better characterize the risk associated with this prognostic factor. Furthermore, the observed ICS postoperatively could not be differentiated from degenerative changes. Fluorescein angiography would be needed for that purpose. However, taking into account the exclusion of major pathologies related to the development of ICS, it is more likely that the observed ICS were the result of postoperative changes.

Nonetheless, our work suggests that in patients with VMT undergoing PPV, a high index of suspicion for the occurrence and persistence of ICS is warranted when preoperative ICS is present. We believe that some patients with VMT could benefit from an earlier surgical intervention to prevent permanent foveal alternations stemming from chronic tractional vitreous forces.

References

1. Los LI, van der Worp RJ, van Luyn MJ, Hooymans JM. Age-related liquefaction of the human vitreous body: LM and TEM evaluation of the role of proteoglycans and collagen. Investig Ophthalmol Vis Sci. 2003;44(7):2828−2833.
2. Duker JS, Kaiser PK, Binder S, et al. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. Ophthalmology. 2013;120(12):2611−2619.
3. Steel DH, Lotery AJ. Idiopathic vitreomacular traction and macular hole: a comprehensive review of pathophysiology, diagnosis, and treatment. Eye (Lond). 2013;27(Suppl. 1):S1−S21.
4. Jackson TL, Nicod E, Simpson A, Angelis A, Grimmaccia F, Kanavos P. Symptomatic vitreomacular adhesion. Retina. 2013;33(8):1503−1511.
5. Charalampidou S, Nolan J, Beatty S. The natural history of tractional cystoid macular edema. Retina. 2012;32(10):2045−2051.
6. Hikichi T, Yoshida A, Treme CL. Course of vitreomacular traction syndrome. Am J Ophthalmol. 1995;119(1):55−61.
7. Flynn Jr HW, Relhan N. The charles scheepens lecture: management options for vitreomacular traction: use an individualized approach. Ophthalmol Retina. 2017;1(1):3−7.
8. Chang JS, Smiddy WE. Cost-effectiveness of retinal detachment repair. Ophthalmology. 2014;121(4):946−951.
9. Garcia-Layana A, Garcia-Arumi J, Ruiz-Moreno JM, Arias-Banquet L, Cabrera-Lopez F, Figueroa MS. A review of current management of vitreomacular traction and macular hole. J Ophthalmol. 2015;2015:909640.
10. Sonmez K, Capone Jr A, Trese MT, Williams GA. Vitreomacular traction syndrome: impact of anatomical configuration on anatomical and visual outcomes. Retina. 2008;28(9):1207−1214.
11. Kim SJ, Martin DF, Hubbard 3rd GB, et al. Incidence of postvitrectomy macular edema using optical coherence tomography. Ophthalmology. 2009;116(8):1531−1537.
12. Frisina R, Pinackatt SJ, Sartore M, et al. Cystoid macular edema after pars plana vitrectomy for idiopathic epiretinal membrane. Graefes Arch Clin Exp Ophthalmol. 2015;253(5):47−56.
13. Hassan TS, Williams GA. Counterpoint: to peel or not to peel: is that the question? Ophthalmology. 2002;109(1):11−12.
14. Kozumi H, Spade RF, Fisher YL, Freund KB, Klancnik Jr JM, Yannuzzi LA. Three-dimensional evaluation of vitreomacular traction and epiretinal membrane using spectral-domain optical coherence tomography. Am J Ophthalmol. 2008;145(3):509−517.
15. Odrobina D, Michalewska Z, Michalewski J, Dziegielewski K, Nawrocki J. Symptomatic vitreomacular traction syndrome evaluated by ocular coherence tomography (OCT) retinal mapping. Acta Ophthalmol Scand. 2004;82(6):691−694.
16. Hikichi T. Time course of development of posterior vitreous detachments after phacoemulsification surgery. Ophthalmology. 2012;119(10):2102−2107.
18. Mirshahi A, Hohn F, Lorenz K, Hattenbach LO. Incidence of posterior vitreous detachment after cataract surgery. *J Cataract Refract Surg*. 2009; 35(6):987–991.

19. Ripandelli G, Coppe AM, Parisi V, et al. Posterior vitreous detachment and retinal detachment after cataract surgery. *Ophthalmology*. 2007; 114(4):692–697.

20. Emrani E, Matlach J, Guthoff R, Goebel W. Morphologic and functional outcome of epiretinal membrane surgery with and without gas tamponade - a pilot study. *Investig Ophthalmol Vis Sci*. 2014;55(13), 3829-3829.

21. Chabot G, Bourgault S, Cinq-Mars B, Tourville E, Caisse M. Effect of air and sulfur hexafluoride (SF6) tamponade on visual acuity after epiretinal membrane surgery: a pilot study. *Can J Ophthalmol J Can Ophtalmol*. 2017;52(3):269–272.

22. Romano V, Angi M, Scotti F, et al. Inflammation and macular oedema after pars plana vitrectomy. *Mediat Inflamm*. 2013;2013:971758.