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CLINICAL INVESTIGATION

Clinical factors contributing to postoperative aqueous flare intensity after 27-gauge pars plana vitrectomy for the primary rhegmatogenous retinal detachment

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Abstract

Purpose To investigate the perioperative clinical factors, which contribute to the postsurgical aqueous flare intensity (AFI) following 27-gauge pars plana vitrectomy (27GPPV) for primary rhegmatogenous retinal detachment (RRD).

Study design Retrospective clinical study.

Methods We performed retrospective analyses of the medical records of 47 eyes of 47 patients with primary RRD who had undergone 27GPPV with a wide-angle viewing system. AFI was measured preoperatively and 1 week, 1 month, 3 months, 6 months, and 12 months after the surgery.

Results AFI was significantly increased 1 week after the surgery (p<0.01) and then decreased overtime. At 6 months after surgery it was still statistically significantly higher than preoperative AFI (p=0.03). There was no statistical difference between preoperative AFI and that at 12 months following surgery. Multiple regression analyses revealed that the number of retinal photocoagulations and the performance of scleral indentation had significant positive correlation with AFI at 1 week, 1 month, 3 months, and 6 months, and at 1 month and 3 months after the surgery, respectively.

Conclusion Intraoperative retinal photocoagulation and scleral indentation are probable causes of increased AFI after 27G PPV for RRD.

Keywords Rhegmatogenous retinal detachment · Aqueous flare value · Retinal photocoagulation · Scleral indentation · 27-Gauge

Introduction

Rhegmatogenous retinal detachment (RRD) is a severe sight threatening disorder. Current treatment modalities for RRD include pars plana vitrectomy (PPV) and scleral buckling [1, 2]. Because of the advantages of a small incision, self-sealing, decreased surgical trauma, less postoperative inflammation, better postoperative comfort for patients, less postoperative astigmatism, and an earlier visual recovery, PPV with a wide-angle viewing system has been gaining popularity as first-line therapy [3–10]. The primary anatomic success

rate after PPV with a wide-angle viewing system reportedly ranges from 85 to 93.8% with a 25-gauge system and from 90 to 96.7% with a 27-gauge (27G) system [11–14]. Unfortunately, the primary anatomic success rate is still not perfect even then and the retinal re-detachment due to miss-identification of retinal breaks, opening of old retinal breaks, new retinal break formation, and onset of proliferative vitreoretinopathy (PVR) are reported as one postoperative complication [15]. In particular, it is reported that PVR is one severe sight threatening postoperative complication and its development is related to the severity of the perioperative intraocular inflammation [16–18]. Therefore, it is important to elucidate perioperative clinical factors which can be a trigger for the postoperative intraocular inflammation after PPV.

In this study, primary RRD was managed with 27G PPV, and perioperative clinical factors, which contributed to the postsurgical aqueous flare intensity (AFI), were investigated.

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Subjects and methods

We performed retrospective analyses of the medical records of 47 eyes of 47 patients with primary uncomplicated RRD who underwent 27G PPV. Our study was performed after obtaining the approval of the institutional review board of Kobe University School of Medicine. The procedure used conformed to the Tenets of the Declaration of Helsinki. Patients' criteria included surgery performed at Kobe University Hospital from May 2016 through August 2017. Eyes with giant retinal tears, PVR, atopic dermatitis, and history of prior surgery for RRD were excluded. The patients were followed-up at least for 12 months after the surgery.

The following variables were analyzed: sex, age, the number of retinal breaks, locations of retinal breaks, the number of quadrants involved, the presence or absence of the macular detachment, lens status, preoperative best corrected visual acuity (BCVA), preoperative intraocular pressure (IOP), the perioperative AFI, the number of retinal photocoagulations, whether scleral indentations were performed during surgery, whether intensification anti-inflammatory therapy was performed postoperatively, the operation time, initial anatomical success and the final anatomical success. The AFI was measured preoperatively, and 1 week, 1 month, 3 months, 6 months, and 12 months after the surgery, with the laser flare meter (FM-600; Kowa) between 30 min to 1 h after the instillation of 0.5% tropicamide and 0.5% phenylephrine hydrochloride (Mydorin P; Santen Pharmaceuticals).

Whenever the sub-Tennon injections of 40 mg triamcinolone acetonide (STTA) (Kenacort; Bristol-Myers Squibb) were performed at the end of the surgery and the administration of postoperative 0.1% betamethasone sodium phosphate eye drops (Rinderon; Shionogi Pharmaceuticals) were increased from 4 times per day to 6 times per day, these cases were defined as postoperative intensification anti-inflammatory therapy.

Statistical methods

We used Friedman's test, followed by post hoc analysis using Wilcoxon t-test with Bonferroni correction to examine differences in AFI at each time point. Multiple regression analysis was performed to determine the parameters significantly relevant to the AFI. The Landolt-decimal visual acuity was converted to the logarithm of the minimal angle of resolution (logMAR) for statistical analysis. Statistical analyses were performed using statistical software (MedCalc version 12.7.5.0; MedCalc Software). Statistical significance was determined at $p < 0.05$.

Surgical procedures

Sub-Tenon anesthesia by approximately 4 mL of 2% lidocaine was performed. 27G PPV with a wide-angle non-contact viewing system (Resight®; Carl Zeiss Meditec AG) was performed using the Constellation Vision System (Alcon Laboratories, Inc.). Three cannulas were created with conjunctival displacement and oblique-angled sclerotomies in the inferotemporal, superotemporal, and superonasal quadrants 3.0–4.0 mm posterior to the limbus. 27G chandelier illumination fibers (Oshima vivid, Synergetics) were placed at 4.0 mm behind the limbus for wide-angle intraocular illumination. Before vitrectomy, phacoemulsification and intraocular lens implantation with 2.4 mm bent transconjunctival single-plane sclerocorneal or clear corneal incision were performed using the same machine for all phakic eyes. Following the core vitrectomy, vitreous gel was visualized by the injection of triamcinolone acetonide (MaQaid, Wakamoto Pharmaceutical) during midperipheral vitrectomy. Then, the peripheral vitreous gel was shaved for 360°. Scleral indentations under a wide-angle non-contact viewing system were performed whenever necessary. No internal drainage retinotomy was made. Subretinal fluid was evacuated from original breaks and followed by a complete fluid–air exchange. All retinal detachments were restored intraoperatively. Retinal photocoagulations was applied to completely surround all retinal breaks (Purepoint® endoocular probe, Alcon Laboratories, Inc) (180 mW, 200 ms). At the end of surgery, all eyes were flushed with 50 mL of mix of nonexpansile gas (20% SF6) to assure a complete exchange. Additional gas mixture was injected through the pars plana to adjust IOP if necessary. Scleral buckling and perfluorocarbon liquid were not used for any of the surgery in this study. Any sclerotomy sites that were found to leak at the end of the surgery were sutured with 8-0 vicryl suture. IOP was checked by tactile examination. Subconjunctival corticosteroids were injected and antibiotic ointment was administered at the end of the surgical procedure.

Results

Table 1 summarizes patients' perioperative demographic data. Forty-seven eyes of 47 patients were included in the study. We evaluated time-course changes in AFI during the follow-up period. The AFI was significantly increased 1 week after the surgery ($p<0.01$) and then decreased overtime. AFI at 6 months after the surgery was still statistically significantly higher than preoperative AFI ($p=0.03$). There was no statistical difference between preoperative

Table 1 perioperative demographic data for the patients

Number of eyes (eyes)	47
Sex, male/female	25/22
Age (years), mean±SD	58.3±8.8
No. of retinal breaks, mean±SD	1.8±1.6
Location of retinal breaks, superior/inferior/3 or 9 o'clock	9/22/16
Quadrant of retinal detachment, 1/2/3/4	16/28/3/0
Macular detachment, macular on/macular off	22/25
Combined cataract surgery (yes/no)	41/6
Preoperative visual acuity (logMAR), mean±SD	0.29±0.57
Preoperative intraocular pressure (mmHg), mean±SD	14.5±3.3
Preoperative aqueous flare intensity, mean±SD	12.6±12.1
The number of retinal photocoagulation, mean±SD	307.0±199.4
Scleral indentation (yes/no)	31/16
Intensification anti-inflammatory therapy (yes/no)	33/14
Operative time (min), mean±SD	85.0±46.2
Initial anatomical success (eyes)	46
Final anatomical success (eyes)	47

SD: standard deviation; logMAR: logarithm of the minimal angle of resolution

AFI and that at 12 months after the surgery ($p=0.08$) (Fig. 1). For multiple regression analysis, we entered the following clinical factors as explanatory variables: age, the number of quadrants involved, the presence or absence of the macular detachment, lens status, preoperative IOP, the preoperative AFI, the number of retinal photocoagulation, whether scleral indentations were performed during the surgery, whether the intensification anti-inflammatory therapy was performed postoperatively, the operation time, the initial anatomical success. Multiple regression analyses revealed that the number of retinal photocoagulations and preoperative IOP had significant positive correlation and the performance of intensification anti-inflammatory therapy had significant negative correlation with AFI at 1 week after surgery (Table 2). At 1 month after surgery, the number of retinal photocoagulations (std B= 0.473, $p= 0.009$) and the performance of scleral indentations (std B=0.528, $p=0.004$) had significant positive correlation with AFI. At 3 months after surgery, the number of retinal photocoagulations (std B= 0.561, $p< 0.001$) and the performance of scleral indentations (std B= 0.497, $p= 0.002$) had significant positive correlation and the performance of intensification anti-inflammatory therapy (std B= -0.322, $p= 0.008$) had significant negative correlation with AFI. Other factors were not associated with AFI at
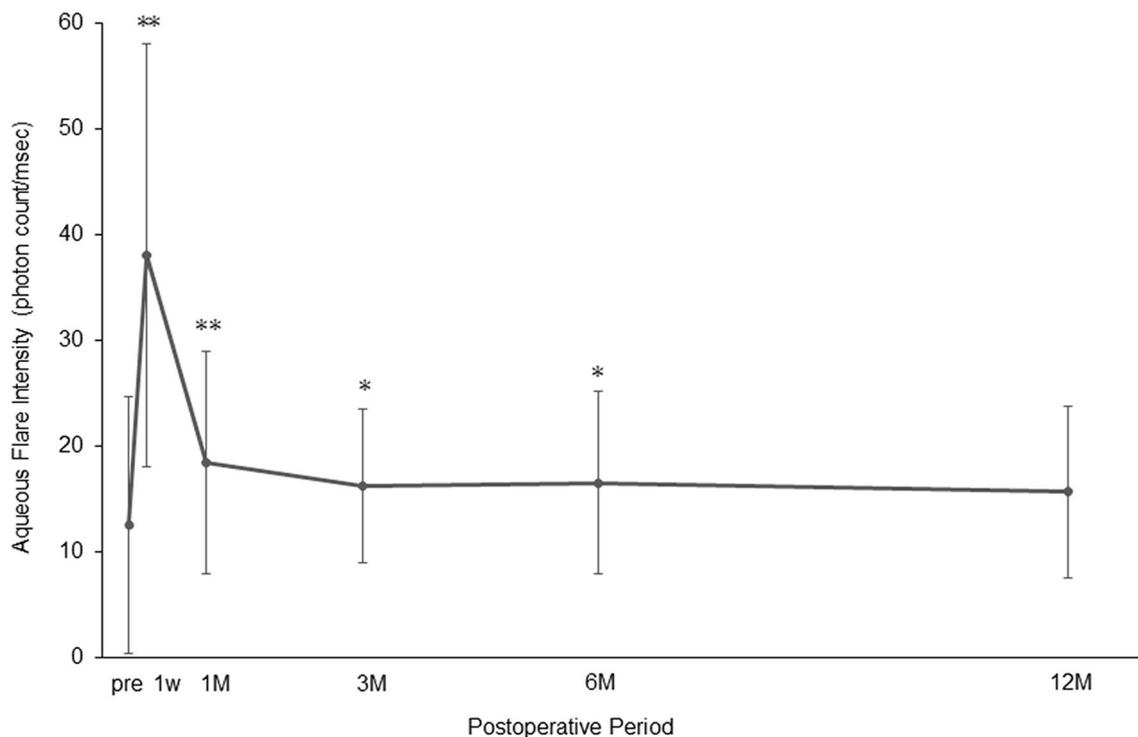

Fig. 1 Time course changes in aqueous flare intensity. The mean aqueous flare intensity (AFI) (photon count / msec) at baseline was 12.57 ± 12.09. At 1 week (1W), 1 month (1M), 3 months (3M), 6 months (6M), and 12 months (12M) postoperatively, the AFI was 38.05 ± 19.95, 18.47 ± 10.55, 16.29 ± 7.28, 16.57 ± 8.59, and 15.70 ± 8.11, respectively. AFI statistically significantly changed during the follow-up period ($p<0.01$). AFI at 1W, 1M, 3M, and 6M after the surgery was significantly higher than pre AFI (**$p<0.01$, *$p<0.05$)

Table 2 The result of multiple regression analysis for the establishment of the relationships between explanatory variables and aqueous flare intensity at one week after the surgery

Independent variables	Std B	p-value
Age	0.047	0.731
Quadrant of retinal detachment	0.071	0.628
Macular detachment	-0.040	0.784
Combined cataract surgery	0.110	0.384
Preoperative intraocular pressure	-0.307	0.031
Preoperative aqueous flare intensity	-0.013	0.937
The number of retinal photocoagulation	0.515	0.002
Scleral indentation	0.130	0.392
Intensification anti-inflammatory therapy	-0.258	0.038
Operative time	-0.112	0.510
Initial anatomical success	0.100	0.404

Table 3 Details on patients with postoperative complications

Complication	Number of eyes	Second treatment
Retinal redetachment	1	27GPPV+SF6 tamponade
Epiretinal membrane	3	27GPPV+epiretinal membrane peeling+ ILM peeling

27GPPV: 27-gauge pars plana vitrectomy; SF6: sulphur hexafluoride; ILM: internal limiting membrane

any time point. Table 3 summarizes details on patients with postoperative complications. We experienced a case of retinal re-detachment and 3 cases of epiretinal membrane. We performed additional 27G PPV for the treatment of these complications.

Discussion

In the current study, the AFI peaked at 1 week, decreased overtime, but kept a significant increase for 6 months after surgery. Hoshi, et al. report that after 20-gauge (20G) PPV, the AFI peaked at 1 week and remained significantly higher than that in the contralateral normal eyes for 12 months following surgery [19]. They suggest several mechanisms responsible for the increase in AFI, including a reduction in the aqueous bulk flow and disruption of the blood-retinal barrier (BRB) caused by RRD and surgical intervention, and dispersion of subretinal protein into the vitreous and aqueous cavities. Their postoperative time course of change in AFI is highly comparable with our results although the surgery method is different. This may suggest that mechanisms active after 20G PPV also influence the postoperative increase in AFI after 27G PPV with a wide-angle viewing

system, which is a minimally invasive vitreous surgery for the treatment of RRD [20].

To investigate the clinical factors contributing to the postoperative AFI levels, multiple regression analysis was performed. As a result, the number of retinal photocoagulations, the performance of scleral indentation, and preoperative IOP had significant positive correlations; at the same time the performance of intensification anti-inflammatory therapy had significant negative correlation with postoperative AFI. Especially, the number of retinal photocoagulations was identified as the strongest contributing clinical factor for 3 months after the surgery. A previous report also suggests that the number of retinal photocoagulations was significantly associated with the increase in AFI at 3 months after 20G PPV for RRD [19]. It is known that retinal photocoagulations can induce disruption of the blood-aqueous barrier (BAB) and BRB [21], and that a damaged BRB results in production of inflammatory cytokines into the vitreous cavity [22]. Moreover, the breakdown in BRB due to surgical intervention after the treatment of RRD is a factor in the pathogenesis of PVR [16–18]. It will be an important project to investigate effective methods of decreasing the number of retinal photocoagulations during surgery resulting in the decrease of postoperative intraocular inflammation.

Our results show that the performance of scleral indentation also affected the postoperative increase in AFI at 1 and 3 months. It's believed that excessive scleral depression is involved in postoperative intraocular inflammation due to ocular deformation and rapid changes in IOP during scleral indentation can induce inflammation in the ciliary body. However, no studies have investigated postoperative intraocular inflammation based on whether scleral indentation was performed or not, because, during the 20G PPV era it had been an imperative technique for the observation of the peripheral retina. Moreover, nobody knows whether scleral indentation under PPV with a wide-angle viewing system could still induce significant inflammation postoperatively. We believe that this is the first report suggesting that scleral indentation is in fact involved in postoperative intraocular inflammation. All vitreoretinal surgeons should attempt to avoid excessive scleral indentations even when using 27G PPV with a wide-angle viewing system.

Postoperative intensification anti-inflammatory therapy using high-dose steroid treatment significantly reduced postoperative AFI. Yamada, et al. also report that pretreatment of STTA can reduce AFI in eyes with NPDR after panretinal photocoagulation using pattern scan laser [23]. It is reported that STTA and an intravitreal triamcinolone acetonide injection (IVTA) suppresses inflammatory cytokines including VEGF, interleukin-6, intercellular adhesion molecule-1, and monocyte chemotactic protein-1induced after laser treatment [24]. Takamura, et al. report that IVTA at the end of vitrectomy for vitreous hemorrhage related to proliferative

diabetic retinopathy can also reduce postoperative AFI [25]. These results suggest that postoperative intensification anti-inflammatory therapy using high-dose steroid treatment may contribute to a further reduction in postoperative intraocular inflammation even after PPV for RRD.

This study has some limitations. First, this is a retrospective study. There may have been a bias in patient selection. Additionally, the sample size was relatively small. The results of large-scale, randomized, prospective studies in the future may be warranted.

In summary, we evaluated the time course change of perioperative AFI and contributing clinical factors for postoperative AFI after 27G PPV for RRD. Our results indicate that surgeons should consider the risk/benefit ratio regarding the number of intraoperative photocoagulations and avoid scleral indentations as much as possible even with 27G PPV under a wide-angle viewing system for less postoperative intraocular inflammation.

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