# scientific reports



## **OPEN** Thirteen year experience of vitrectomy and air tamponade for primary retinal detachment repair with clinical outcomes

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Purpose To report outcomes of pars plana vitrectomy (PPV) with air tamponade for primary rhegmatogenous retinal detachment (RRD) and investigate the impact of vitreous cortex remnants (VCR) on surgical outcomes.

Methods A retrospective review of 900 patients treated for uncomplicated primary RRD between 2007 and 2020. Exclusion criteria included axial length > 26 mm, prior retinal surgery, giant retinal tear, PVR grade > B, and inadequate follow-up. Primary outcomes were retinal reattachment rate and bestcorrected visual acuity (BCVA).

Results Of 900 patients, 397 met inclusion criteria. Primary reattachment rate was 88.4%, with significant BCVA improvement. Forty-six eyes experienced RRD recurrence. Complications included cataracts (38.8%), IOP rise (11.4%), and macular edema (8.3%). Better final BCVA was associated with preoperative macular non-involvement and absence of reinterventions. No significant association was found between RRD recurrence and various factors, including VCR removal.

Conclusion Air tamponade is a safe and effective option for primary RRD treatment. It has no negative effect on the environment and creates less discomfort for patients. VCR removal did not significantly reduce RRD recurrence in the overall number of cases. Further research will help determine the role of VCR in RD recurrence and define in which cases their removal might be beneficial.

Keywords Retinal detachment, Vitrectomy, Air, Tamponade, Vitreous cortex remnants

Retinal detachment (RD) occurs when the retinal neuroepithelium separates from the underlying retinal pigment epithelium (RPE). The adhesion of the retina to the RPE is essential for vision, and involvement of the fovea in RD can result in significant visual loss. Rhegmatogenous retinal detachment (RRD) is the most common form of RD, characterized by one or more retinal breaks that allow fluid to flow from the vitreous chamber into the subretinal space, leading to retinal separation. RRD can occur at any age, though it is most commonly observed in individuals aged 60 to 70, with a peak prevalence of 13 cases per 100,000 individuals.

With recent advancements, pars plana vitrectomy (PPV) is increasingly utilized for RRD treatment. However, the surgical technique is not yet fully standardized, leaving many aspects open to discussion. Factors such as the extent of vitrectomy, removal of vitreous cortex remnants (VCR), management of subretinal fluid (SRF), choice of intraoperative and final tamponade, and the patient's postoperative positioning can all influence surgical outcomes. In this study, we focused on the choice of tamponade and VCR removal, assuming that extensive vitrectomy was performed in all cases, and subretinal fluid was removed to the greatest extent possible.

Tamponade agents aim to create surface tension across retinal breaks, preventing further fluid entry into the subretinal space until retinopexy (photocoagulation or cryopexy) establishes a permanent seal. The most commonly used tamponades are sulfur hexafluoride (SF6), perfluoropropane (C3F8), and silicone oil (SO)<sup>1</sup>. Air is often used for exchanging and removing perfluorocarbon liquid (PFCL) and can serve as the final tamponade, especially when the risk of developing proliferative vitreoretinopathy (PVR) is low.

A recent theory by van Overdam suggests that VCR are present in many cases of primary RRD and play a critical role in retinal redetachment<sup>2</sup>. VCR may act as a scaffold for cell proliferation, thereby promoting the development of PVR<sup>3</sup>. Although VCR are transparent and difficult to visualize, they can be better identified

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with triamcinolone acetonide (TA) staining, though this procedure is not routinely performed during pars plana vitrectomy.

The primary end-point of this study is to evaluate, in a real-life setting, if the anatomical and functional results obtained with PPV and air tamponade for primary RRD repair compare favorably with published studies that involved the use of fluorinated gases. The secondary end-point is to assess the role of VCR staining and removal in affecting the surgical outcomes.

#### Matherial and methods Patient selection

Overall, the methodology follows the approach used in a previous study conducted in our center<sup>4</sup>. This retrospective study involves a review of medical records from 900 consecutive patients who were treated for uncomplicated primary RRD at IRCCS Sacro Cuore-Don Calabria Hospital in Verona, Italy, between 2007 and 2020. The study included only patients who underwent pars plana vitrectomy (PPV) with air tamponade and had attended at least the baseline and 1-, 3-, and 6-month postoperative follow-up visits. The exclusion criteria were: (a) axial length > 26 mm; (b) vitreous hemorrhage affecting a reliable retina examination; (c) previous retinal surgery; (d) use of surgical techniques other than PPV with air tamponade for primary RRD; (e) presence of a giant retinal tear; (f) PVR grade greater than B, according to the 1991 updated Retina Society Classification; and (f) inadequate follow-up.

At baseline and each follow-up visit, a comprehensive ophthalmic examination was performed, including BCVA measurement, slit-lamp biomicroscopy, intraocular pressure evaluation, and dilated fundus examination with a 90D indirect lens. Additionally, baseline measurements included axial length in phakic eyes (IOLMaster 500; Carl Zeiss Meditec, Jena, Germany) and macular scans via optical coherence tomography (OCT) (Spectralis HRA-OCT; Heidelberg Engineering GmbH, Heidelberg, Germany). The number and location of retinal breaks were also documented at baseline, with breaks categorized as superior (between 8 and 4 o'clock) or inferior (between 4 and 8 o'clock). If both superior and inferior breaks were present, the break site was classified as inferior due to the greater clinical significance of inferior quadrants when air tamponade is utilized.

BCVA was assessed using a Snellen chart and converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analysis. The semiquantitative visual scales "counting fingers" and "hand motion" were converted to logMAR values of 2 and 3, respectively, according to Holladay (2004). The duration of RRD was defined as the time interval between the onset of central or peripheral vision loss and the surgery. Macular involvement by RRD was assessed via OCT at baseline.

#### Ethical aspects

All procedures adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all participants in the study. The experimental protocol and the informed consent were approved by the Institutional Review Board Committee of IRCCS Sacro Cuore-Don Calabria Hospital and by the Territorial Ethics Committee of South-West Veneto (Reference No. Prot. Negrar-2020 K).

#### Data availability

Raw data are accessible upon request to the corresponding author.

#### Surgical technique

All patients underwent the same surgical technique, previously described<sup>4</sup>. All surgical procedures were performed by experienced surgeons. The choice between general or local anesthesia was made based on patient preference and the anesthesiologist's recommendation. Local anesthesia was administered via retrobulbar nerve block. Cases performed before 2012 utilized 20-Gauge PPV, while those after 2012 used 23-Gauge PPV. Cataract surgery was performed concurrently if necessary.

During surgery, patients received a complete vitrectomy with peripheral vitreous shaving, and posterior hyaloid detachment from the retina was achieved when required. At the surgeon's discretion, triamcinolone acetonide (TA) was injected into the vitreous chamber to stain and identify any vitreoretinal traction (VCR); if present, the VCRs were removed using a diamond-dusted membrane scraper, the vitreous cutter, or microforceps and microscissors in a bimanual technique. Perfluorocarbon liquid (PFCL) was employed to reattach the retina, with subretinal fluid drained through the peripheral retinal breaks during the fluid-air exchange. The procedure was finalized with endolaser photocoagulation around the retinal breaks and on the peripheral retina. Postoperative positioning was determined based on the location of the retinal breaks: In the case of superior breaks, the patient was advised to maintain a semi-sitting position for the first postoperative day. In the case of inferior breaks, however, a supine position was recommended. Following surgery, patients were prescribed a tapering regimen of topical antibiotics and steroids for 4 weeks.

#### Statistical analysis

Demographic and clinical data were summarized through descriptive statistics, measures of precision and variability, depending on the type of variable (categorical or continuous).

Skewness and kurtosis tests were used to check the normality in distribution of continuous data.

Two sample t-tests for unpaired data were performed to compare mean BCVA between macula-on / maculaoff subgroups at different time point (baseline, 1-month, 3-month, 6-month and final follow-up).

Multivariate linear regression analysis was carried out to study the linear relation between BCVA at last visit (dependent variable) and a set of predictors variables.

Number of eyes	397
Age (years) mean (SD), [min-max]	63.1 (10.7), [29–93]
Gender n (M/F)	277/120
Eye n (right/left)	209/188
Macula involvement n (macula on/off)	162/186
<b>RRD duration (days)</b> mean (SD), [min-max]	1.5 (8.1), [0–150]
Baseline BCVA in logMAR mean (SD), [min-max]	1.0 (1.1), [-0.1–3.5]
Lens status at baseline n (phakic/pseudophakic)	217/178
Retinal breaks number mean (SD), [min-max]	1.6 (0.9), [1–5]
Retinal breaks site n (superior/inferior)	195/80
Follow-up (months) mean (SD), min-max	28.4 (30.7), [6–176]

**Table 1.** Baseline demographic and intraoperative characteristics of the patients included. SD = standarddeviation. M = male. F = female. BCVA = best standard visual acuity.

	BCVA (logMAR)				
	Baseline	1 month	3 months	6 months	Final
Macula-on mean (SD)	0.24 (0.58)	0.14 (0.19)	0.18 (0.31)	0.18 (0.44)	0.11 (0.27)
Macula-off mean (SD)	1.18 (1.03)	0.51 (0.52)	0.44 (0.45)	0.44 (0.31)	0.31 (0.43)
p-value	< 0.0001*	< 0.0001*	< 0.0001*	< 0.0001*	< 0.0001*

**Table 2**. Best-corrected visual acuity (BCVA) in comparison between macula-on and macula-off patients at baseline and 1,3, 6 months after surgery and at the end of the follow-up. SD = standard deviation. Asterisks indicate a statistically significant difference between the two groups (p < 0.05).

Two multivariate logistic regression analysis were also performed to explore the relation between RRD recurrence and EMC development (respectively considered as dependent variables) and a set of predictor variables.

A *p*-value of < 0.05 was considered for statistical significance.

StataSE software (Statistics and Data Science, SE-standard Edition, version 17.0, StataCorp, College Station, TX; https://www.stata.com) was used to run statistical analysis.

#### Results

The inclusion criteria were met by 397 eyes. In cases where a patient underwent surgery on both eyes, each eye was treated as an independent case. The demographic data and baseline characteristics of all eyes are summarized in Table 1. The mean follow-up was 28.4 months (SD=30.7), ranging from 6 to 176 months (median 21 months, interquartile range, IQR, 51.2). 144 patients (36.3%) reached the 6-month follow-up, while 125 (31.5%) completed over one year of follow-up. Forty-four eyes were excluded due to inadequate follow-up. 459 eyes were excluded because treated with other technique than PPV with air tamponade: 63 underwent PPV with SF6 tamponade, 104 PPV with SO tamponade and 292 scleral buckling.

One hundred and seven (26.9%) eyes were treated whit 20-Gauge PPV, while 290 (73.0%) with 23-Gauge PPV. Phacoemulsification was combined to PPV in 82 (25.4%) cases. During PPV, TA was injected in 144 (36.5%) cases and in 105 (26.7%) VCRs were found and removed.

BCVA changes during the follow-up are shown in Table 2. The difference between macula-on and macula-off cases was statistically significant at each time point.

Forty-six RRD recurrences (11.6%) were observed and need further reinterventions. Twenty-three recurrences were observed within 3 months (5.8%) and were considered early recurrences. The mean interval between surgery and recurrence was 52.1 days (SD=64.1), ranging from 6 to 227 days. Recurrences after 3 months (considered as late) were observed in 23 cases (5.8%). Recurrences were caused by new breaks formation in 56.3% and 36.4% of cases of early and late recurrences respectively, while by PVR in 43.7% and 63.6%. No statistically significant differences were found between early and late recurrences in term of age (p=0.93), RRD duration (p=0.84), retinal breaks number (p=0.57). No statistically significant association was found between the recurrence interval and preoperative macular involvement (p=0.72), retinal breaks site (p=0.81),

	Regression coefficient [95% CI]	<i>p</i> -value
RRD duration	0.00 [-0.00-0.01]	0.324
Baseline BCVA	0.03 [-0.03-0.08]	0.327
Phacoemulsification combined to PPV	-0.03 [-0.17-0.11]	0.690
Retinal attachment 1 month after surgery	0.21 [-0.02-0.43 ]	0.070
Number of reinterventions	0.27 [0.16-0.39]	< 0.0001*
Retinal attachment at the end of FU	-0.02 [-0.43-0.38]	0.905
Macular involvement	-0.15 [-0.270.02]	0.020*
RRD recurrence	0.01 [-0.21-0.22]	0.944
ERM development	0.05 [-0.06-0.15]	0.383
EMC development	0.05 [-0.08-0.19]	0.442
Cataract development	-0.10 [-0.21-0.01]	0.079
IOP rising	-0.05 [-0.21-0.11]	0.543

**Table 3**. Multivariate linear regression model for BCVA at the end of the follow-up. RRD, reghmatogenous retinal detachment; BCVA, best corrected visual acuity; PPV, pars plana vitrectomy; FU, follow-up; ERM, epiretinal membrane; CME cystoid macular edema; IOP, intraocular pressure; CI, confidence interval. Asterisks indicate a statistically significant difference between the two groups (p < 0.05).

	OR [95% CI]	<i>p</i> -value
RRD duration	0.94 [0.75-1.19]	0.635
Breaks number	0.92 [0.65-1.28]	0.626
Breaks site	0.60 [0.20-1.80]	0.364
Combined phacoemulsification	0.90 [2.78-2.96]	0.870
Triamcinolone staining	0.95 [1.74-5.18]	0.953
VCR removal	1.10 [1.86-6.51]	0.916
Macular involvement	0.34 [0.11-1.15]	0.083
ERM development	1.54 [-0.06-0.15]	0.383

**Table 4**. Multivariate logistic regression model for RRD recurrence development during the follow-up.RRD, reghmatogenous retinal detachment; VCR, vitreous cortex remnants; ERM, epiretinal membrane; CI, confidence interval.

TA staining (p=0.68), or VCR removal (p=0.79). However, the association with the cause of recurrence was borderline significant (p=0.08). All cases of recurrence were successfully reoperated. Silicone oil was used in 36% of early recurrences and in 76% of late recurrences. In the remaining cases, air or SF6 was used, based on the surgeon's choice.

During the follow-up, 83 patients (38.8%) developed a significant cataract and underwent phacoemulsification. Forty-five eyes (11.4%) developed a increase in IOP, successfully treated with medical therapy in all cases. In 33 (8.3%) cases a macular edema was detected, that resolved after topical steroids were administrated with a tapering regimen.

A multivariate linear regression model showed that the final BCVA was directly associated with preoperative macular non-involvement (p=0.020) and inversely with reinterventions (p<0.0001) and, marginally, with cataract development (p=0.07) (Table 3). In a subsequent logistic model, none of the variables showed any significant association with the development of recurrent rhegmatogenous retinal detachment (RRD) (Table 4). The results from another logistic model showed no significant association between the development of epiretinal membrane (ERM) and any variables (Table 5). Finally, there were no statistically significant associations between the instruments gauge and retinal reattachment, visual recovery, and the development of recurrences.

#### Discussion

Tamponades act as barriers to prevent fluid passage between the vitreous cavity and the subretinal space. Once adhesion between the retina and the retinal pigment epithelium (RPE) is established, this barrier is no longer needed. Gas tamponade agents, after a complete gas-fluid exchange, resorb spontaneously over different periods: air in 5–7 days, 20% SF6 in about 2 weeks, and 14% C3F8 in about 8 weeks. Unlike gases, silicone oils are permanent until surgically removed. Air and gases have higher surface tension and buoyancy than silicone oils, with the tension exerted by air or gas being approximately 30 times greater than silicone oil<sup>5,6</sup>.

Retina-RPE adhesion begin theoretically within 24 h without subretinal fluid (SRF)<sup>7</sup>. Thus, the effectiveness of tamponade agents in closing retinal breaks is most critical within the first 24 h post-surgery. Residual SRF around tears can interfere with adhesion. For superior tears, gravity helps isolate the tears from SRF, making long-acting tamponade excessive. Conversely, short-acting gases like air might be inappropriate for inferior

	OR [95% CI]	<i>p</i> -value
RRD duration	1.10 [0.75-3.79]	0.132
Breaks number	0.94 [0.73-1.24]	0.708
Combined phacoemulsification	1.68 [0.75-3.79]	0.205
VCR removal	0.74 [0.31-1.73]	0.486
Macular involvement	0.60 [0.26-1.36]	1.37

**Table 5**. Multivariate logistic regression model for CME development during the follow-up. RRD,reghmatogenous retinal detachment; VCR, vitreous cortex remnants; CI, confidence interval.

breaks<sup>8</sup>. However, studies have shown that air can be as effective as long-lasting gases for inferior breaks<sup>9,10,3,11-14</sup>, given adequate SRF drainage<sup>15</sup>.

Our SRF drainage technique includes thorough vitreous base shaving and around breaks, filling the eye with PFCL to push away SRF, and passive drainage through retinal tears. Drainage through a posterior retinotomy is avoided due to potential complications like PVR.

In a prospective series of 15 patients, Martínez-Castillo's group first reported that PPV with air tamponade effectively managed pseudophakic RRDs with inferior breaks without postoperative facedown positioning<sup>10,15</sup>. Singh et al. described 236 eyes treated for primary RD: one third receive SF6 gas tamponade and the others air tamponade. The authors demonstrated air's safety in treating RRDs with a success rate of 88.5% for superior, inferior, and multiple breaks<sup>16</sup>. More recently, Han confirmed the effectiveness of air as a tamponade for retinal detachment with inferior breaks<sup>17</sup>. Although our study did not include a gas tamponade control group, our data confirm the overall reported results in terms of retinal reattachment. We did not find any association between surgical failure and the number of quadrants involved in the RD, contrary to what was reported by Chuandi Zhou et al., although this association was independent of the choice of air or gas<sup>9</sup>. Taken together, the reports above confirmed our results and suggest that air tamponade is generally adequate for both superior and inferior retinal detachments and is, at least, as effective as long-lasting gas tamponade, especially if complete removal of vitreous traction, aspiration of SRF, and sealing of all retinal breaks are routinely performed.

In addition, the use of SF6 and other fluorinated gases in RRD surgery poses significant environmental risks due to their high global warming potential. These gases are extremely stable and can persist in the atmosphere for thousands of years, thereby contributing to long-term climate change. Although the release of these gases during medical procedures is minimal compared to other industrial uses, it still adds to the overall environmental burden. In a retrospective analysis of 3,239 eyes treated for RRD, Moussa et al. evaluated the mass of gas used per operation and its CO2 equivalent across three different gas delivery systems (SF6, C2F6, and C3F8). Their study provides real-world data on the environmental impact of fluorinated gases and air tamponade in the management of RRDs, highlighting the potential benefits of utilizing air in the majority of cases to reduce the carbon footprint of vitreoretinal surgery<sup>18</sup>.

Moreover, it is important to pay attention to the gas concentrations used: expandable concentrations can, on one hand, compensate for potential losses due to leakage from the sclerotomies, but on the other hand, they can lead to potentially dangerous IOP increases<sup>19</sup>.

We also investigated the role of VCRs in influencing the outcomes of PPV and air tamponade for primary RRD. Several authors have suggested that VCRs, which can occur as a consequence of PVD with vitreoschisis<sup>3</sup>, may contribute to PVR membrane formation, critical in retinal redetachment<sup>2</sup>. Sebag's theories distinguish between full-thickness PVD, which does not involve VCRs, and partial-thickness PVD, which includes vitreoschisis with VCRs<sup>3</sup>. Van Overdam expanded on these theories by noting that anomalous PVD with vitreoschisis can result in VCRs over the retina, which can act as a scaffold for fibrocellular proliferation<sup>20</sup>. In such cases, RPE cells from retinal tears and hyalocytes in VCRs, along with other known PVR risk factors, can combine to form PVR membranes<sup>2</sup>. Triamcinolone staining is used to reveal VCRs, which are often underestimated when not routinely used<sup>2</sup>. Van Overdam conducted a pilot study comparing two cohorts of patients who underwent PPV for RRD in 2016 and 2018. The 2018 group, which had more extensive triamcinolone staining and consequent VCR removal, showed a lower rate of RD relapse<sup>21</sup>. Recently, Rizzo et al. described a series of eyes that underwent PPV for RRD, with the presence of VCRs confirmed intraoperatively using triamcinolone acetonide (TA), observing that the presence of VCRs is associated with a higher incidence of PVR development<sup>22</sup>.

In our study, we didn't observe any significant association between VCR removal and RRD recurrence. A possible explanation could be that cases with a potential high risk of PVR were excluded from the study, having generally been operated using long-lasting tamponade. For this reason, we do not feel that TA staining and VCR removal are completely irrelevant for anatomical success: in fact, our surgical experience suggests that VCR presence is a relatively frequent finding in eyes treated for RRD recurrence with PVR development. However, VCR removal can sometimes be extremely time-consuming and does not represent a completely riskless procedure: iatrogenic retinal breaks can occur, and this can be a problem especially in case of posterior breaks due to their potential in PVR promoting.

In addition to RD relapse, other possible postoperative complications are represented by IOP rising, cataract development, macular edema, and retinal displacement. No differences in IOP rising between air and long-acting expansile gas were previously found, even if the air group had a lower IOP on the first postoperative day<sup>9</sup>. Another study reported about 11% of cases of early IOP rising (within 3 days after PPV and air tamponade), normalized by using anti-glaucoma medication within 3 days<sup>23</sup>. We reported similar results and no further surgeries for IOP rising were required.

Macular edema after RRD repair is believed to stem from subclinical low-grade inflammation that breaks down the blood-aqueous barrier<sup>24</sup>. Anti-inflammatory agents like corticosteroids and NSAIDs have been successfully used for treatment<sup>25,26</sup>. Chatziralli reported a 16.3% CME rate post-PPV for RRD<sup>27</sup>. Our previous study showed a 6.5% CME rate post-PPV with air tamponade, and this larger series observed an 8% rate<sup>4</sup>. No significant association was found between CME and any variables, including combined phacoemulsification. Discrepancies may be due to different sample sizes and exclusion of patients with preoperative PVR and long-standing RRD.

Retinal displacement is reported in about a third of RRD cases treated with PPV. Blue fundus autofluorescence identifies retinal displacement via lines of increased autofluorescence, which closely reflect the adjacent retinal vessels that occur in metamorphopsia and vertical diplopia<sup>28</sup>. Given the retrospective nature of our study, blue fundus autofluorescence images could not be acquired for all patients, and so it was not possible for us to describe the retinal displacement prevalence in our cohort. In conclusion, our data suggest that air represents a safe and effective tamponade for primary RRD treatment and is adequate for both superior and inferior retinal breaks. Accurate traction release through a complete vitreous base shaving and as complete as possible SRF drainage represent the key elements for a successful RRD surgical repair. A faster tamponade resorption compared to long-standing gas is associated with lower visual disturbance, quicker normal lifestyle recovery, and probably a lower inflammation grade without any impact on the environment.

VCR removal does not seem to affect anatomical results, even if its role should be better investigated, especially in cases with a higher PVR risk. A prospective randomized study on large multicentric series would likely clarify these aspects.

#### Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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#### Author contributions

M.M.: research design, data interpretation, manuscript preparationE.M.: research designG.P., E.B., G.M., S.T: data acquisitionN.D.S. and M.G.: data analysisG.P.: research design, data interpretation, manuscritp revisionAll authors reviewed the manuscript.

### Declarations

#### **Competing interests**

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