Original Article

Retinal shortening: Ultrasonic evaluation of proliferative vitreoretinopathy

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Purpose: To evaluate the effect of extraretinal proliferative vitreoretinopathy (PVR) on retinal shortening in eyes with rhegmatogenous retinal detachment (RD) using ultrasound (USG) and objectively prove the presence of intraretinal PVR (iPVR). **Methods:** This is a double-masked pilot prospective controlled case series. Patients with total RD planned for vitreoretinal surgery were included in the study. USG was used to determine retinal-to-choroidal length ratios (RCRs) in all the quadrants. Group 1 included 10 patients with preoperative PVR more than Grade B while Group 2 had 14 with PVR of Grades A or B. Severe retinal shortening was defined as RCR < 0.8. Primary outcome measures were severe retinal shortening and an early unexplained recurrence of RD within 15 days of surgery. **Results:** Mean RCRs were significantly low in all the four quadrants of Group 1 upon comparison with Group 2. The mean RCR had a good negative correlation with number of quadrants of PVR ($R = -0.66$, $P \leq 0.001$). Overall, severe quadrantic retinal shortening was detected in nine patients. In these 9 patients, 11 of the 36 retinal quadrants had severe retinal shortening in the absence of extraretinal PVR (ePVR). Six patients developed early unexplained RD, and all of these belonged to Group 1. Severe quadrantic retinal shortening had the highest odds ratio of developing early unexplained RD (odds ratio = 58, $P = 0.01$). **Conclusion:** Retinal shortening occurs both due to ePVR and iPVR, and iPVR occurs independently at least in some cases. Severe quadrantic retinal shortening indicates poor primary anatomical prognoses.

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Despite all preventive efforts and retinal screening for lesions, rhegmatogenous retinal detachment (RRD) remains a very frequent, if not the most common, indication for vitreoretinal surgery (VRS). Although VRS has had its generous share of conceptual and technical advancement, proliferative vitreoretinopathy (PVR) remains the surgeons' nemesis and its prevention is a challenge. Although techniques have been discussed for tackling preoperative PVR, the long-term results are not good.[1-3]

Recently, classification systems have been proposed to incorporate intraretinal PVR (iPVR) as an independent entity.[3] The need is evident if one considers the role of iPVR in causing recurrent retinal detachment (RD) following VRS/scleral buckling procedures.[4] iPVR has been a subjective diagnosis and may be oblivious to the naked eye examination.[4,5] In this regard, a new technique was introduced recently to quantify retinal shortening or iPVR with the help of ultrasound (USG) imaging.[4] The technique involves measuring retinal-to-choroidal length ratios (RCR). In that study, only patients with advanced ePVR were imaged. During the study, we noted, as also pondered by others, that the impact of epiretinal PVR (ePVR) and subretinal PVR (sPVR) on retinal shortening or iPVR cannot be negated entirely, and they may occur simultaneously.[4,6]

In this study, we compare RCR findings on USG between patients with and without ePVR. We aim to determine the extent of interaction between different forms of PVR in relation to retinal shortening. We also discuss the possibility of a critical RCR that may determine eyes prone to recurrent RRD.

Methods

Design

The study was conducted in accordance with the Declaration of Helsinki. Informed written consent had been obtained for surgery as well as the investigative procedures involved. This was a prospective investigative self-controlled study conducted at a tertiary eye care center of North India. Institute review board clearance had been obtained for the study. The methodology of this study has been briefly presented in Fig. 1 as a flowchart.

Patients

Consecutive patients undergoing primary VRS for total rhegmatogenous RD were included in the study. The exclusion criteria were similar to the parent study.[5] These included history of other ocular disease (apart from cataract), media haze >Grade 1,[7] giant retinal tears, and presence of choroidal detachment. All the patients underwent meticulous ocular workup with emphasis on duration of RD and grade and type of PVR. PVR, including grade, ePVR, and sPVR, was defined using Silicone Oil Study Classification system.[8] High myopia was defined as an axial length more than 26 mm or presence

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of posterior staphyloma. Optic disc was used as the landmark to clinically identify quadrant of PVR. This was done to have a common landmark between the two masked investigators for examination and USG.

Ultrasound and measurement of retinal shortening

The detailed methodology of performing the USG B-scan has been presented in the parent study.[4] In brief, preoperative USG B-scan of the involved eye was performed in all the patients and longitudinally sectioned images were obtained. Optic nerve head was present in each image.

All the USG-based measurements were performed using "freehand line tool" of the ImageJ software (http://imagej. nih. gov/ij/). With the help of the software, distance between two end points on a structure can be measured while moving the cursor's locus along the contour of the structure [Fig. 2]. Thus, the retina was measured starting from the optic nerve head till its point of fusion with the choroid. The choroid was measured similarly between these end points. If the ora serrata could not be localized in a USG image, the end point for choroid was determined by drawing a perpendicular from the end of the retina toward the choroid.[4] These measurements were done 5 times for each image and mean was taken after excluding measurements deviating more than 0.5 mm from the median for each measurement. RCR was calculated for each quadrant separately along with a mean ratio for each patient.

Surgery

Surgery was done on the day following USG imaging in every case. Standard 3-port 25-gauge VRS was performed in all the patients. Encirclage was used as per surgeons' choice. Fluid-air exchange with active fluid extrusion at 40 mmHg air pressure, laser retinopexy, 360-degree endolaser photocoagulation, and C3F8 gas/silicone oil injection was done. Membrane peeling and subretinal band removal were performed as needed, but no patient underwent relaxing retinectomy. The VRS was not combined with cataract surgery or lensectomy in any patient. Routine postoperative care and head positioning for 7 days were advised to all patients.

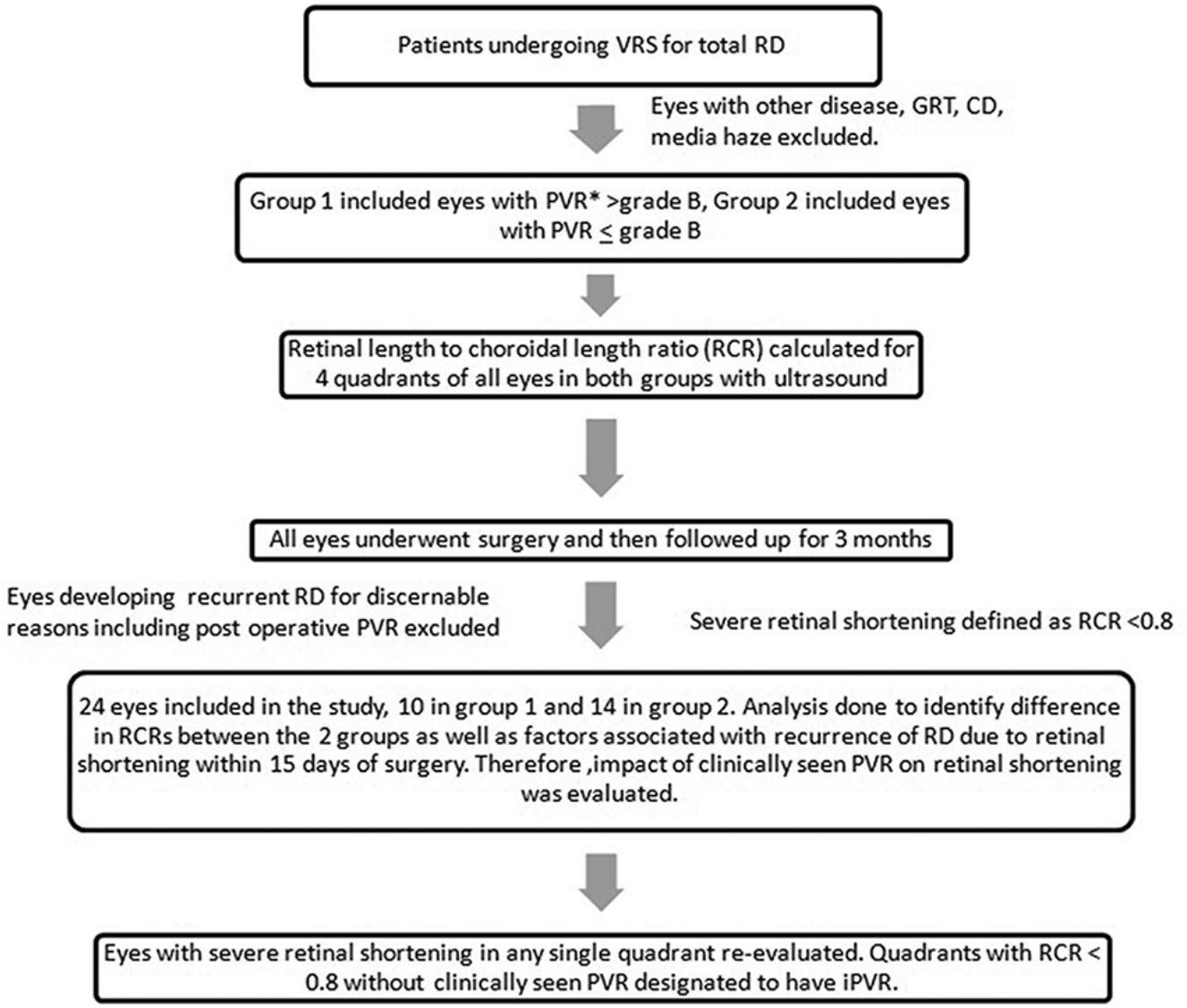

Figure 1: Flowchart depicting the study methodology. *PVR was assessed as per Silicone Oil Study Classification.[8] VRS: Vitreoretinal surgery, RD: Retinal detachment, GRT: Giant retinal tear, CD: Choroidal detachment, PVR: Proliferative vitreoretinopathy, iPVR: Intraretinal PVR

Outcomes

All patients were followed till 3 months. Patients who developed recurrent RD during this period for discernable reasons such as missed retinal break, postoperative ePVR, postoperative sPVR, and poor oil/gas fill were excluded from the study. Finally, 24 patients and 96 images (~1000 measurements) were included for analysis. The study hence was designed to address if recurrent "unexplained" RD during the first 15 days of surgery could be attributed to severe retinal shortening.

Analysis

This was a double-masked study. Patient workup was performed by a single surgeon (ST) while all USG-related measurements were done by another (BT). These authors were blinded to each other's findings throughout the study period.

Data were entered into Microsoft Excel sheets, and statistical analysis was performed (SPSS software, version 22.0, IBM Corporation, New York). Retinal shortening was categorized as severe when RCR was measured to be <0.80. Fisher's exact test was used for parametric comparisons, and a two-tailed *P* value <0.05 was defined as significant. Comparison was done between eyes with PVR >Grade B (Group 1) and <Grade B (Group 2). Therefore, patients with clinically visible ePVR and sPVR were categorized into Group 1 and Group 2 was used as control group. Mann–Whitney U-test was done for comparison of means between these two groups. Pearson's coefficient was used for assessing correlation among variables. RCRs were evaluated separately for eyes with unexplained recurrent RD. Odds ratio (OR) was calculated for variables associated with unexplained recurrent RD within the first 15 days, and all the confidence intervals (CIs) described here after are true for 95% of population. iPVR was later objectively identified in the eyes which had severe quadrantic retinal shortening in the absence of preoperative ePVR in that quadrant.

Results

The mean age of the 24 patients was 49.58 ± 16.76 years, 9 were female, and the right and left eyes were equally affected, 12 cases each. Three cases were found to have high myopia. Mean duration of RD (defined from vision loss) was 2.76 months. Ten cases had PVR greater than Grade B. Among these 10 patients, average number of quadrants with PVR was 2.2. All these cases had ePVR while sPVR was present in one patient only. Encirclage was used in 13 cases. C3F8 gas was used as vitreous substitute in 8 cases while silicone oil was used in 16 cases.

The RCRs of the 24 cases have been presented in Table 1. The mean RCR overall was 0.85 (range: 0.69–1.00). Quadrant-based RCRs ranged from 0.62 to 1.36. Overall three RCR values were found to be in excess of 1; all these three cases had bullous RD. The mean quadrant-based RCRs in superior-temporal,

Table 1: Summary of 24 cases analyzed

Case number	Age (years)	Duration (months)	Quadrants with PVR	Recurrent RD within 15 days	Superior-temporal RCR	Inferior-temporal RCR	Superior-nasal RCR	Inferior-nasal RCR	Mean RCR
Case 1	48	3	3	Yes	0.79	0.62	0.73	0.63	0.69
Case 2	52	2.5	4	Yes	0.80	0.75	0.71	0.71	0.74
Case 3	55	2	1	No	0.81	0.78	0.82	0.84	0.81
Case 4	72	4	1	Yes	0.81	0.75	1.00	0.77	0.83
Case 5	56	1	3	Yes	0.80	0.83	0.81	0.77	0.80
Case 6	66	5	1	No	0.68	0.76	0.91	0.74	0.77
Case 7	60	0.75	0	No	0.87	0.63	0.97	0.80	0.82
Case 8	64	1.5	3	Yes	0.71	0.79	0.84	0.78	0.78
Case 9	10	12	1	Yes	0.85	0.79	0.86	0.88	0.84
Case 10	60	0.75	0	No	0.93	0.91	0.98	0.88	0.93
Case 11	60	1	0	No	0.84	0.81	0.81	0.83	0.82
Case 12	23	9	4	No	0.86	0.81	0.88	0.80	0.84
Case 13	30	1	0	No	0.91	0.89	0.97	1.10	0.97
Case 14	27	6	0	No	0.83	0.86	0.91	0.85	0.86
Case 15	45	1	1	No	0.81	0.90	0.89	0.88	0.87
Case 16	47	2	0	No	1.15	0.93	0.89	0.85	0.96
Case 17	65	1	0	No	0.85	0.81	0.91	0.82	0.85
Case 18	52	1	0	No	0.84	0.81	0.83	0.89	0.84
Case 19	22	0.33	0	No	0.91	0.89	0.88	0.90	0.89
Case 20	45	0.25	0	No	0.91	1.36	0.95	0.80	1.00
Case 21	59	2	0	No	0.88	0.91	0.85	0.87	0.88
Case 22	76	7	0	No	0.92	0.82	0.98	0.99	0.93
Case 23	42	0.25	0	No	0.86	0.85	0.93	0.83	0.87
Case 24	54	2	0	No	0.97	0.93	0.88	0.88	0.91

PVR: Proliferative vitreoretinopathy (includes both ePVR and sPVR), RD: Retinal detachment, RCR: Retina-to-choroidal length ratio, ePVR: Epiretinal PVR, sPVR: Subretinal PVR

inferior-temporal, superior-nasal, and inferior-nasal quadrants were 0.86, 0.84, 0.88, and 0.84, respectively, thus slightly lower in the inferior quadrants. The mean RCR was 0.82 in the three patients with high myopia. The mean RCR had a good negative relation with number of quadrants with PVR (combined ePVR and sPVR), correlation coefficient being 0.66 ($P \leq 0.001$). However, there was no statistically significant relation between mean RCR and age of the patient ($R = -0.16$, $P = 0.45$) and duration of RD ($R = -0.06$, $P = 0.78$).

Group 1 (patients with preoperative PVR >Grade B) had 10 patients while Group 2 had 14. The mean duration of RD was significantly more in Group 1 than Group 2 (4.1 months vs. 1.8 months, $P = 0.03$). The mean RCR was significantly less in Group 1 (0.8 ± 0.07) as compared to Group 2 (0.89 ± 0.05) ($P < 0.001$). All the quadrantic RCRs were also significantly lower in Group 1 than Group 2 ($P < 0.05$ for all quadrants). Overall, six patients had unexplained RD within the first 15 days. All these patients belonged to Group 1.

The details of the patients with recurrent RD attributable to retinal shortening have been presented in Table 1 (cases 1, 2, 4, 5, 8, 9). The mean RCR of these 6 patients was 0.78 whereas the mean number of quadrants with ePVR was 2.5. More interestingly, all these 6 cases had RCR <0.8 at least in 1 quadrant of retina, whereas 4 had in 2–4 quadrants [Table 1]. Apart from these 6 patients, there were 3 more patients who had RCR <0.8 in at least in a single quadrant but did not develop unexplained RD in the first 15 days [cases 3, 6, and 7 in Table 1]. One of these patients had thick-taut adherent posterior hyaloids, as noted during surgery and which may have led to underestimation of RCR, one had a healthier mean RCR of 0.82, while the third developed RD in the 2nd month of follow-up.

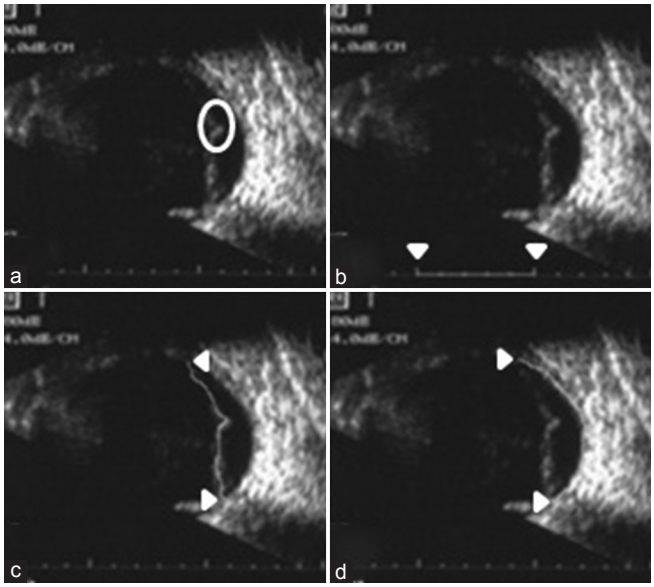

Figure 2: Ultrasonic measurement of retinal shortening. (a) Ultrasound B-scan of an eye with retinal detachment and proliferative vitreoretinopathy. A retinal fold (encircled) with overlying adherent vitreous can be seen. (b) Figure depicts setting up a scale for further measurements. Note the yellow line, indicated by arrowheads, placed over the vector scan. This pixel distance was set as 10 mm, and future measurements were done accordingly. (c) The process of retinal length measurement. The measuring yellow line has been drawn along the retinal contour, the end points being the optic disc, and point of fusion of neurosensory retina with the retinal pigment epithelial-choroid (arrowheads). In this case, the retinal length was measured as 12.44 mm after taking 5 readings. (d) The process of choroidal length measurement. The end points used for retinal length (arrowheads) were used for measuring the choroidal length, drawn as a curved yellow line along its length. In this case, the choroidal length was measured as 15.95 mm after taking 5 readings. The retinal-to-choroidal length ratio was hence measured as 0.78

Univariate analysis for factors associated with recurrent RD attributable to retinal shortening has been presented in Table 2. The presence of ePVR, mean RCR <0.8, or presence of RCR below 0.8 in 1 quadrant was significantly associated with the occurrence of unexplained RD in the first 15 days. OR was calculated to ascertain impact of these 3 factors on unexplained RD in the first 15 days. Quadrantic RCR <0.8 had the highest OR (57.57, CI = 2.58-1279.96), followed by the presence of ePVR (41.88, CI = 1.95-897.66) and mean RCR < 0.8

Table 2: Factors associated with unexplained recurrent retinal detachment within the first 15 days

	Recurrent RD (%)	*P*
Age >50 years		
Yes (14)	4 (28)	1.00
No (10)	2 (20)	
Duration of RD >3 months		
Yes (7)	3 (43)	0.3
No (17)	3 (18)	
Presence of ePVR		
Yes (10)	6 (60)	0.001
No (14)	0	
Mean RCR <0.8		
Yes (5)	4 (80)	0.004
No (19)	2 (11)	
RCR <0.8 in 1 quadrant		
Yes (9)	6 (67)	<0.001
No (15)	0	

RD: Retinal detachment, ePVR: Epiretinal proliferative vitreoretinopathy, RCR: Retinal-to-choroidal length ratio

Table 3: Relation between location of epiretinal proliferative vitreoretinopathy and severe quadrantic retinal shortening

Case number	Superior-temporal		Inferior-temporal		Superior-nasal		Inferior-nasal	
	RCR	ePVR	RCR	ePVR	RCR	ePVR	RCR	ePVR
Case 1	0.79	Yes	0.62	Yes	0.73	No	0.63	No
Case 2	0.80	Yes	0.75	Yes	0.71	No	0.71	No
Case 3	0.81	No	0.78	No	0.82	Yes	0.84	No
Case 4	0.81	Yes	0.75	No	1.00	No	0.77	No
Case 5	0.80	Yes	0.83	No	0.81	No	0.77	Yes
Case 6	0.68	Yes	0.76	No	0.91	No	0.74	No
Case 7	0.87	No	0.63	No	0.97	No	0.80	No
Case 8	0.71	No	0.79	Yes	0.84	Yes	0.78	Yes
Case 9	0.85	No	0.79	Yes	0.86	No	0.88	No

ePVR: Epiretinal proliferative vitreoretinopathy, RCR: Retinal-to-choroidal length ratio

(34, CI = 2.43–474.57). Although the CI of all these variables was very large, the lower confidence bound was 2 or more in all cases.

Discussion

In the current study, we aimed to identify the impact of ePVR on retinal shortening using USG-based RCRs. We have found a strong statistically significant relationship between quadrantic RCR <0.8 and ePVR, and mean RCR correlated well with the amount of ePVR. Retinal shortening has been quantified with USG recently.[4] In that study, it was speculated that as retina is an elastic structure, the RCR is likely to fall to some value below 1 after RD and that ePVR and sPVR are likely to coexist with iPVR, therefore the term mixed PVR.[3,4] Like the previous study, in the current study also, we found unexplained early recurrent RD to have high odds of occurring in cases with quadrantic RCR below 0.8.

Although minute fall in RCR is likely to be related to elasticity of neurosensory retina (NSR) as discussed above, severe retinal shortening is more likely to be due to structural changes. This is reflected in significantly lower RCR in the group with advanced PVR and the negative correlation between number of quadrants with ePVR and mean RCR values. iPVR, with the help of immune markers such as glial fibrillary acidic protein, has been proven to be due to glial proliferation within the detached NSR.[4,5] This is different from the traditional retinal pigment epithelial (RPE) cell theory advocated for ePVR.[9,10] However, one should remember that ePVR by virtue of fibrotic contraction would result in fall of RCR.[10] This reflects in strong association ePVR with severe retinal shortening below RCR of 0.8. During surgery, manual dissection or removal of this ePVR would result in favorable intraoperative RCR that should allow for flattening of the retina along the choroidal contour and future surgical success. However, in cases where "enough" iPVR has set in, recurrent "unexplained" RD would occur defying the high fluid/air pressure used during surgery. This is more likely to occur as soon as patient positioning is stopped, and before NSR-RPE, microstructure bonding has occurred.[4,11] That is why we chose 15 days as the cutoff duration. After this time, postoperative PVR can also come into play.

Further, to objectively identify iPVR and prove it as an independent cause of retinal shortening, we analyzed the location of ePVR vis-a-vis severely low RCRs. Data of all patients with at least 1 quadrantic RCR below 0.8 along with location of ePVR have been presented in Table 3. It can be seen that of the 36 quadrantic RCRs, in 11 cases (30%), there was severe retinal shortening in the absence of ePVR. As this is a pilot technique, direct comparisons cannot be drawn with previous data. The lack of studies on iPVR is related to the subjective difficulty in its preoperative identification and need for immunohistochemistry.[4,5] However, we are not the first to speculate on the importance of iPVR. A lot of work has been done by Pastor *et al*.,[3] who have emphasized the role of iPVR in staging PVR in general. The author group has evaluated previously published studies using PVR classification systems and has discussed the need for including iPVR in grading techniques.[3,4,12] The authors have also done a study on 60 patients of retinal shortening. In that study, iPVR was defined as inability to achieve intraoperative retinal flattening despite removing extraretinal PVR after perfluorocarbon liquid (PFCL) injection.[6] However, only nine out of sixty patients had needed retinectomy.[6]

Our study has some limitations. We are taking a single dimension per quadrant into account for calculating RCR, and ideal would be retinal area to choroidal area ratio, but current technology eludes such an analysis. Our sample size was low (24 cases) and we did not have enough patients with sPVR (only 1). It would also be interesting to analyze the RCR values in eyes with early RD and no clinical PVR in a larger sized study as RCR is expected to fall below 1 in most cases [Table 1]. Although a single surgical team operated, there was no fixed protocol on the use of explants or vitreous substitutes. Patients with bullous RD do not seem to be good candidates for this imaging technique. In the older study, 7 of the 40 images analyzed needed perpendicular method (explained in methodology section to judge RCR).[4] In the current study, 11 out of 96 images needed this method for calculating RCR. We believe that if blinding is removed and the sonographer is aware of the clinical findings, this ratio will further lessen. We could not study the angle subtended by the detached retina on the choroid as a function of retinal shortening because the retina was curved in most cases and was not straight like a chord is to an arc.

Gold standard for the presence of iPVR would be histopathological analysis, but as relaxing retinectomy was not done, such tissue was not available. In this regard, future study on preoperative planning of site of retinectomy based on lowest RCR can be undertaken where retinectomy would increase intraoperative RCR and tackle retinal shortening and also provide tissue for analysis. Thus, deciding a critical threshold for planned retinectomy is an interesting surgical option and needs appropriate evidence before bringing to surgical practice.[4]

Conclusion

USG-based calculation of RCR is a good method of documenting retinal shortening. While ePVR is an important cause of retinal shortening, in some cases, iPVR may exist independent of it. Retinal shortening is an important indicator of poor anatomical prognoses in patients with RD. Severe retinal shortening in any single quadrant should prompt appropriate measures.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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