TOP 10 LESSONS FROM THE PIVOT TRIAL

Post-hoc analyses are providing actionable pearls you can use in your management of rhegmatogenous retinal detachment.

BY RAJEEV H. MUNI, MD, MSC, FRCSC

The PIVOT trial was a randomized trial that compared pneumatic retinopexy (PnR) to pars plana vitrectomy (PPV) for the treatment of primary rhegmatogenous retinal detachment (RRD; Figure 1).[1] The trial demonstrated superior Early Treatment of Diabetic Retinopathy Study (ETDRS) visual acuity outcomes with PnR at each time point, including the 1-year endpoint. Patients who underwent PnR also experienced less vertical metamorphopsia and had a lower risk of cataract formation.[1] However, patients in the PnR group experienced a 12% lower primary reattachment rate (81% vs 93% in the PPV group).

Although the Scleral Buckling versus Primary Vitrectomy in Rhegmatogenous Retinal Detachment Study compared PPV versus scleral buckle for RRD repair, it did not use imaging modalities that could have provided information regarding postoperative anatomic abnormalities that may not have been visible clinically.[2] Therefore, the PIVOT trial provided the first randomized longitudinal prospective imaging dataset, which enabled us to answer questions not only about PnR versus PPV, but also about RRD repair in general. Based on post-hoc studies and analyses that emerged from the PIVOT trial, here are the top 10 lessons learned in the management of RRD.

10 PnR was associated with better vision-related quality of life in the first 6 months.

PIVOT was the first randomized trial in RRD repair that included an objective assessment of patient-reported vision-related quality of life. The National Eye Institute Visual Function Questionnaire 25 scores were superior at 3 months and 6 months in PnR versus PPV, with no significant difference at 1 year.[1] The difference between the two groups was attributed to higher scores for distance activities, mental health, dependency, and peripheral vision with PnR.[3] This suggests that patients undergoing PnR experience a faster functional recovery, supporting their mental health and overall well-being.

9 Subfoveal fluid blebs are not associated with a long-term reduction in visual acuity.

Patients may have residual subretinal fluid blebs following RRD repair. There was no statistically significant difference in the risk of subfoveal blebs between PnR and PPV,[4] although studies with larger numbers may find a difference. Retinal pigment epithelium (RPE) pump-based procedures, including PnR and scleral buckle, are more likely to have residual fluid blebs. It is worth noting that residual subfoveal fluid had no long-term effect on visual acuity, despite being present for months in some cases.[4] This is likely related to the persistence of some level of metabolic exchange between the RPE and photoreceptors, despite the presence of a thin film of fluid between the retina and the RPE. Therefore, in most cases, the surgeon can wait for subfoveal fluid to resolve on its own with no long-term effect on visual acuity.

8 En face OCT is useful for assessing postoperative outcomes.

Various post-hoc studies from the PIVOT trial have found that en face OCT was extremely useful at detecting outer retinal folds, subretinal fluid blebs, and disruption of the ellipsoid zone.[5,6] Assessment with en face OCT was superior and more efficient than assessment of the entire volume scan. En face OCT was also excellent at following these anatomic abnormalities and assessing recovery over time.

7 Ellipsoid zone recovery following macula-off RRD repair can take time.

We generally caution our patients that their visual acuity is unlikely to substantially improve after the first 1 to 2 years following RRD repair. Recent post-hoc data from the PIVOT trial demonstrated that ellipsoid zone recovery, best visualized with en face OCT, can gradually occur over many years (Figure 2).[6] We documented improvement up to 6 years postoperatively, suggesting that

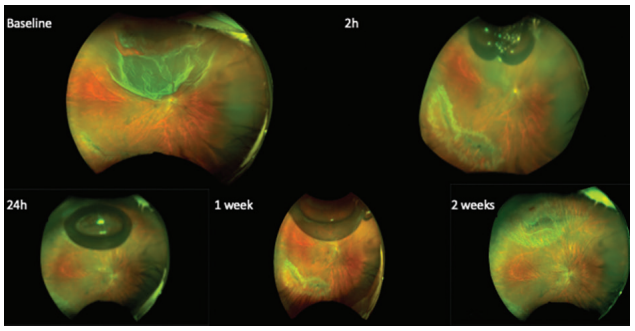

Figure 1. This phakic patient with a primary RRD and one superior break and inferior lattice in an attached retina underwent pre-PnR laser for the inferior lattice followed by anterior chamber paracentesis (0.3 cc) and intravitreal injection of pure SF_6 gas (0.6 cc). Initial face-down positioning was performed (followed by the steamroller maneuver) with substantial improvement at 2 hours. At 24 hours, the retina was fully attached and laser retinopexy was applied to the superior break. At 1 week, the retina was stable and fully attached. At 2 weeks, the gas bubble had dissolved, and the retina was attached with good laser around the break.

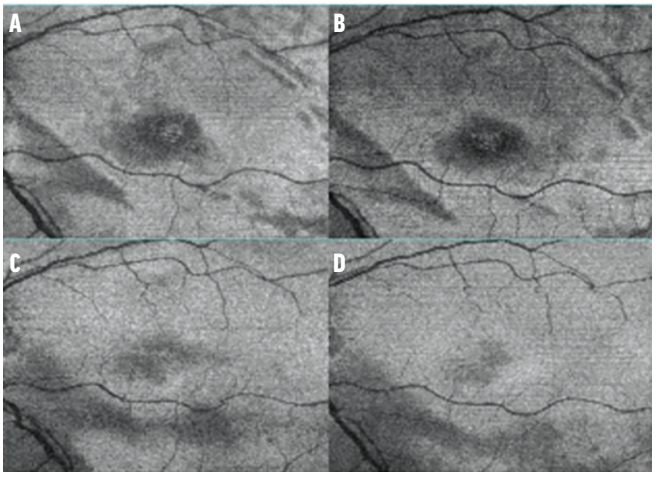

Figure 2. En face OCT of the ellipsoid zone slab at 3 (A), 6 (B), 12 (C), and 24 months (D) following macula-off RRD repair. There is an area of hyporeflectivity involving the fovea that gradually improved over time.

patients may experience *subtle* improvements in functional outcomes as photoreceptors continue to recover over many years.

6 The area of ellipsoid zone hyporeflectivity is associated with visual acuity.

The area of hyporeflectivity on the ellipsoid zone slab of the en face OCT provides a novel biomarker that is useful for assessing the extent of photoreceptor damage following macula-off RRD repair.[6] Change in the area of hyporeflectivity was associated with improvement in visual acuity. Patients who experience persistent functional deficits many years postoperatively can be assessed with en face OCT of the ellipsoid zone slab to demonstrate the extent of persistent photoreceptor disruption.

5 Speed of ellipsoid zone recovery was associated with time from presentation to surgery.

Historically, 1 week from presentation has been considered an acceptable timeframe for macula-off RRD repair, although recent data suggest that 3 days may be superior. We found that the speed of ellipsoid zone recovery was associated with duration of macula-off RRD to surgery.[6] Thus, performing the repair as soon as possible, rather than waiting up to 1 week, may be more beneficial from the perspective of photoreceptor recovery.

4 Retinal displacement is more common with PPV versus PnR.

Although retinal displacement was not assessed in the PIVOT trial, we assessed objective quantitative metamorphopsia between groups. We found that vertical metamorphopsia was more severe and occurred more frequently in PPV versus PnR. This led to our interest in determining whether there was a difference in the risk of retinal displacement between groups. Two subsequent studies demonstrated that retinal displacement is much more common in PPV compared with PnR.[7,8] Furthermore, one of the studies demonstrated that objective quantitative aniseikonia was more severe in PPV versus PnR and in patients with displacement versus without displacement. Further studies have increased our understanding of retinal displacement, and all evidence points to the large gas bubble used in most cases of primary PPV as the main culprit.[9]

3 Outer retinal folds are more likely with PPV versus PnR and are associated with reduced visual acuity.

A post-hoc analysis of the PIVOT trial identified a greater risk of outer retinal folds (ORFs) at 1 to 2 months following PPV versus PnR.[5] Furthermore, patients who had early ORFs experienced significantly worse VA by 9 ETDRS letters on average at 1 year. In addition, subgroup analysis of the PPV group alone found that patients with ORFs had significantly worse VA by 12 ETDRS letters compared with patients without ORFs, which are thought to occur when the retina is rapidly reopposed to the RPE prior to resolution of outer retinal corrugations.[10]

2 Postoperative photoreceptor integrity varies with surgical technique.

Until recently, it has been assumed that, regardless of surgical technique, a reattached retina was the only end goal of RRD repair. However, following macula-off RRD repair, patients' final functional outcomes are largely dependent on how well the photoreceptors have been reopposed and recovered over time. We now know from a PIVOT post-hoc study that postoperative photoreceptor integrity varies with surgical technique.[11] The post-hoc study found that the risk of external limiting membrane and ellipsoid zone discontinuity in the central 3 mm foveal scan was greater in

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PPV versus PnR and that these abnormalities had an effect on postoperative visual acuity. Our hypothesis is that the slower and more natural reattachment of the retina by the RPE pump in PnR leads to less photoreceptor damage compared with the forced active internal drainage technique used in PPV. Although further studies are required to determine the mechanisms at play, it appears that surgical technique does matter when it comes to postoperative photoreceptor integrity.

1 Let the RPE pump do the work.

The single most important lesson to learn from the PIVOT trial is that outcomes improved when we relied on the RPE pump to reattach the retina after the retinal break was closed. This applies to procedures like PnR and scleral buckle. Regardless of how the break is closed, allowing the RPE pump to reabsorb the fluid and minimizing the use of a large gas tamponade reduced the risks of postoperative complications, such as retinal displacement, ORFs, discontinuity of the ellipsoid zone, and external limiting membrane. By avoiding these outcomes, patients will experience improved visual acuity and less vertical metamorphopsia and aniseikonia. ■

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