Evolution in Our Understanding of Rhegmatogenous Retinal Detachment

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INTRODUCTION

Rhegmatogenous retinal detachment (RRD) remained an incurable, blinding condition until the early 1900's. Jules Gonin was the first to achieve reasonable anatomic reattachment rates with a procedure he developed called "ignipuncture".[1,2] His greatest contribution was to recognize that closure of the causative retinal break was essential for the management of RRD.[3] His procedure involved draining subretinal fluid while applying diathermy to the retinal break.[4] Gonin's contribution to the basic understanding of the underlying pathophysiology of RRD led to the era of scleral buckle (SB) surgery that started in the mid-1900's. Ernst Custodis, for the first time, reported the use of an exoplant, placed over the break to treat RRD. Another major contribution of Custodis was to recognize that subretinal fluid drainage was not necessary for RRD repair, as long as the causative break was addressed.[5] In the years that followed, there was substantial controversy regarding drainage vs non-drainage in SB surgery. Scleral buckle remained the dominant procedure for RRD repair throughout the late 1900's. However, in the 1980's, pneumatic retinopexy (PnR) was introduced by Alfredo Dominguez as an outpatient procedure that could achieve retinal reattachment in selected cases.[6] The procedure was popularized by Hilton & Grizzard,[7] and Paul Tornambe carried out the Pneumatic Retinopexy Trial, the results of which were published in the 1990's. The trial demonstrated superior visual acuity outcomes with PnR vs SB in fovea-off RRD with good anatomic reattachment rates.[8] However, although PnR gained acceptance in certain centers, particularly in some parts of North America, it did not gain significant traction worldwide. Instead, in the early 2000's we saw the rise and dominance of pars plana vitrectomy (PPV) in the management of RRD.[9,10] This was mainly driven by technological advancements and improved instrumentation that made PPV and elegant and efficient method of achieving retinal reattachment.[11] However, despite the rising popularity of PPV, randomized trials demonstrated not only no advantage but also a disadvantage in terms of visual acuity outcomes with PPV compared with SB.[12]

In 2019, we published the results of the PIVOT trial,[13] a randomized controlled trial comparing PnR vs PPV for RRD repair meeting specific criteria. The trial demonstrated superior visual acuity outcomes at all time points, including the one-year endpoint with PnR compared to PPV. Furthermore, PPV was associated with increased morbidity, with a greater risk of cataract and worse vision-related quality of life in the first 6 months. However, what was most compelling in the PIVOT trial, was that vertical metamorphopsia was more severe and more frequent in the PPV group vs the PnR group.[13] Vertical metamorphopsia is related to abnormalities in the foveal structure,[14] and it dawned on us that photoreceptor recovery could be influenced by surgical technique. This led to significant growth in research assessing anatomic biomarkers following RRD repair. The optical coherence tomography (OCT) scans from the PIVOT trial were assessed by a masked image reading center, and we found that discontinuity of the ellipsoid zone (EZ) and the external limiting membrane (ELM) in the central 3mm was more common following PPV vs PnR.[15] For the

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first time, this study demonstrated that the mechanism of reattachment impacted photoreceptor recovery. This led to more questions regarding other anatomic biomarkers following RRD repair, including outer retinal folds (ORFs) and retinal displacement. We carried out studies that demonstrated a greater risk of ORFs[16] and retinal displacement with PPV vs PnR,[17,18] and referred to patients with post-operative retinal displacement as having a low-integrity retinal attachment (LIRA).

The insights gained from multimodal imaging led to significant advances in our understanding of the mechanisms involved in both retinal detachment and reattachment. We described the stages of both retinal detachment and reattachment[19,20] and understood the importance of outer retinal corrugations and their pathophysiology.[21] It is clear that unresolved outer retinal corrugations lead to ORFs and that these folds can impact functional outcomes. We were able to demonstrate that a slow natural reattachment of the retina, rather than a rapid forced drainage was less likely to lead to ORFs.[20] We also understood in greater detail the mechanism underlying retinal displacement, and the central role of the large gas fill being directly responsible for retinal displacement in almost all patients following PPV. The large gas fill in PPV applies significant buoyant force to the retina and causes a displacement of any residual subretinal fluid, usually to the inferior periphery. This leads to a stretching of the retina that is visualized with fundus autofluorescence imaging by the presence of retinal vessel printings (RVPs).[22,23] We also demonstrated RVPs/retinal displacement with other techniques where fluid was being forcibly displaced at the time of surgery, such as with fluid-fluid exchange during vitrectomy/scleral buckle[24] or with external drainage with SB where the iatrogenic flow of subretinal fluid leads to a stretch of the retina which then gets fixed in position on the SB when the drainage ceases.[25] We learned that using a small gas bubble and not draining fluid with procedures such as PnR reduced the risk of retinal displacement and associated aniseikonia that likely occurs because of a stretching of the macular cone mosaic.[26] Although FAF has allowed us to diagnose retinal displacement in more severe cases, we have demonstrated that FAF greatly underestimates the presence and extent of retinal displacement. Using a novel image analysis method called homography, we found that although FAF had a specificity of 100%, it had a sensitivity of only 43.7%.[27] This suggests there are many false negatives, likely related to imaging technique and image quality.

Almost a century after critical concepts were introduced by Gonin and then Custodis, we seem to be migrating back to techniques and procedures where subretinal fluid may not need to be actively drained (internally or externally) and where large gas tamponades may not be required. The basic principle of closing the retinal break and allowing the retinal pigment epithelium to do the rest may lead to the best outcomes. On the other hand, techniques meant to rapidly reattach the retina with emphasis on single operation success rate may lead to worse outcomes in terms of anatomic integrity and visual function. Although PnR was originally introduced for selected cases with retinal breaks within a single clock hour in the detached retina, above the 8 and 4 o'clock meridians,[8] the PIVOT trial expanded these indications to include cases with any number, location or size of retinal breaks or lattice degeneration in the attached retina, that can be treated with laser retinopexy prior to the gas bubble injection.[13] There is also the potential of using PnR in even more complex cases, such as those with breaks in multiple quadrants, large breaks, giant retinal tears (GRTs), choroidal detachment, inferior retinal breaks and pediatric RRDs.[28,29,30,31] A significant concern with PnR is the lower single-operation reattachment rate. However, it is important to understand that there is an art to PnR, much like with SB, and improved outcomes can be achieved with more complex cases by modifications in technique. Understanding how to counsel patients regarding positioning, how much gas to inject, how to utilize laser retinopexy and cryopexy treatments and when to inject more gas are all critical to improving outcomes.

Another critical element of RRD repair relates to timing of surgery. The current standard of care for fovea-off RRDs is to perform surgery within one week. However, recent studies seem to suggest that surgery for fovea-off RRDs within three days may yield better outcomes.[32,33,34,35] One of the challenges is in knowing how long someone has had a fovea-involving RRD. Patients are generally not completely aware of when their fovea detached, and the reported duration of fovea-off seems to be inconsistent with the morphological appearance of the RRD with OCT. We recently described the morphological stages of RRD and demonstrated their association with both reported duration of central vision loss and postoperative visual acuity.[19] More recent data suggest that the morphology of the retina on OCT at baseline may provide a more objective assessment of the status of the retina, and this may allow for better decisions regarding the urgency of RRD repair for each individual case.[36] We also recently described bacillary layer detachment (BALAD) in fovea-off RRD for the first time and demonstrated that this is a key step in the pathophysiology of full-thickness macular hole (FTMH) in RRD. Therefore, patients presenting with a BALAD should have surgery relatively soon to prevent progression to FTMH.[37]

In summary, there has been tremendous growth in our understanding of rhegmatogenous retinal detachment and its repair. We have refined our understanding of the mechanisms involved in retinal detachment and reattachment, and this has led to great insights into anatomic abnormalities that are present in RRD either before or after repair. These abnormalities impact functional outcomes, and we are starting to learn how to avoid them. There is compelling evidence that procedures that close the retinal break without draining subretinal fluid and without using a large gas tamponade such as pneumatic retinopexy and non-drainage scleral buckle yield the best functional outcomes once the retina has reattached. The era of only focusing on single-operation reattachment rate is coming to an end, and it is imperative that the current and future generations of retinal surgeons learn all RRD repair techniques so that they can choose the best procedure for each individual that will maximize the integrity of reattachment and functional outcomes..

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