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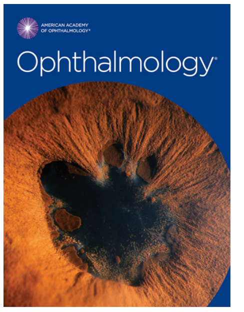

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Displacement Following Pneumatic vs Vitrectomy for Retinal Detachment (ALIGN)

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Running Head: Retinal Displacement after Pneumatic Retinopexy vs Vitrectomy for Retinal Detachment

Abstract

This multicenter non-randomized comparative trial demonstrates that PPV is associated with a higher risk of retinal displacement compared to PnR for macula-off rhegmatogenous retinal detachment. Furthermore, retinal displacement is associated with worse aniseikonia.

Trial Registration: NCT04089033

Retinal displacement is detected by the presence of retinal vessel printings (RVPs) on fundus autofluorescence (FAF) imaging[1,2] Although a high proportion of patients achieve anatomic reattachment following rhegmatogenous retinal detachment (RRD) repair, many patients experience post-operative metamorphopsia, aniseikonia, decreased visual acuity and poor vision-related quality of life.[3,4]. Retinal displacement, or a low integrity retinal attachment (LIRA) may provide an anatomic basis for suboptimal functional outcomes.

Pars plana vitrectomy (PPV) has been associated with increased risk of retinal displacement compared with pneumatic retinopexy (PnR) in a retrospective analysis.[4] This study compared the incidence of post-operative retinal displacement following PPV vs PnR in a prospective non-randomized comparative trial and determined the association of retinal displacement with post-operative functional outcomes.

This multicenter non-randomized comparative trial was carried out at three centers from June, 2018 to February, 2020. Patients were recruited at St. Michael's Hospital in Toronto, Canada, Newcastle Eye Centre in United Kingdom and Hamilton Regional Eye Institute in Hamilton, Canada. There were 10 experienced surgeons included at these sites with some surgeons preferring PnR and others preferring PPV for the same types of RRD. This methodology was carried out with a desire to achieve cohorts with similar baseline characteristics. The study was approved by the Research Ethics Board and adhered to the tenets of the Declaration of Helsinki.

Patients with primary macula-off RRD undergoing PnR or PPV were included. Exclusions included patients younger than 18 years, previous vitreoretinal surgery, significant proliferative vitreoretinopathy (PVR) (grade B or worse), significant media opacity or any pre-existing retinal pathology.

PnR was performed within 24 hours by 6 experienced surgeons with a technique used in the PIVOT trial.[5] All patients who underwent PnR were instructed to perform initial face down positioning and the steamroller maneuver. A standard 23- or 25-gauge PPV was performed within 72 hours by 10 experienced vitreoretinal surgeons. Subretinal fluid was drained via the retinal break or posterior retinotomy at the surgeon's discretion. While draining through the peripheral break, care was taken to minimize posterior displacement of subretinal fluid to the greatest extent possible. Isoexpansile sulfur hexafluoride (SF6), perfluoroethane (C2F6), perfluoropropane (C3F8), silicone oil (SO), and adjunct scleral buckle or perfluorocarbon liquid were used at surgeon discretion. Patients underwent immediate log-roll to face down following PPV for 24 hours followed by positioning based on location of the breaks.

Patients had ultra-widefield FAF (Optos California®, Optos Inc, Marlborough, MA, SA) and optical coherence tomography (OCT) (Zeiss Cirrus 500 HD, Carl Zeiss Meditec, Dublín, CA, USA; Spectralis, Heidelberg Engineering, Germany) (assessed by 2 masked graders with adjudication by a third senior grader) and Snellen BCVA using pinhole, objective measurements of metamorphopsia (M-CHARTS, Inami & Co Ltd) and aniseikonia (Awaya New Aniseikonia Tests, Handaya Co Ltd) at 3-months post-operatively. The primary outcome was proportion of eyes with retinal displacement detected on FAF at 3-months post-operatively in patients achieving successful reattachment with PPV vs PnR (Figure 1). We also compared the proportion of patients with retinal displacement based on initial treatment group (intention to treat). Secondary outcomes included the association of retinal displacement and treatment group with functional outcomes.

Sample size calculation used the following assumptions: minimal clinically important difference in risk of retinal displacement= 20%(35% in PPV and 15% in PnR), power 80% and alpha=0.05. We also accounted for patients with primary failure, lost to follow-up and ungradable images due to media opacity, yielding a total sample size of 204 patients (n=102 per group).

204 patients were enrolled (102 in PPV group and 102 in PnR group) (supplemental material 1 available at www.aaojournal.org). Of the 157 patients included in the final analysis, 47.1%(74/157) underwent PPV and 52.9%(83/157) underwent PnR as the primary procedure. Primary reattachment rate was 93.2%(69/74) with PPV vs 82%(68/83) with PnR. Baseline demographic or ocular characteristics were similar between groups (supplemental material 2 available at www.aaojournal.org).

The proportion of eyes with retinal displacement on FAF imaging was 50.7%(35/69) for PPV and 14.7%(10/68) for PnR in patients with primary reattachment (difference=36%,RR=3.49,95%CI=1.86–6.39,P< .001). In the intention-to-treat analysis, based on the initial procedure, the proportion of eyes with retinal displacement was 50.0%(37/74) for PPV and 25.3%(21/83) for PnR(difference=24.7%,RR=1.97, 95%CI=1.28–3.05,P=0.001); of the 21 patients with retinal displacement in the PnR group, 48%(10/21) failed the initial procedure and underwent secondary PPV.

OCT analysis revealed that there were no significant differences between the PPV and PnR groups in regard to the presence of significant ERM(PPV=6.9%(5/72); PnR=7.4%(6/81);P=0.91, CME(PPV=8.3%(6/72);PnR=6.2%(5/81);P=0.61) and residual

SRF(PPV=1.4%(1/72);PnR=7.4%(6/81);P=0.75). Furthermore, there were no differences among patients with vs without displacement with respect to the presence of ERM(with displacement=12.1%(7/58);without displacement=4.2%(4/95);P=0.068), CME(with displacement=8.6%(5/58);without displacement=6.3% (6/95);P=0.060) and SRF(with displacement=1.7%(1/58);without displacement=6.3%(6/95);P= 0.187).

BCVA (logMAR) among patients who achieved successful reattachment was 0.50±0.44 in PPV vs 0.33±0.33 in PnR (mean difference=0.16;95%CI=0.27–2.95;*P=0.019*). Aniseikonia scores were worse in eyes following successful PPV versus PnR (PPV=4.22+/-5.45 vs PnR=2.03+/-3.77)(difference=2.19;95%CI=0.51–3.86; *P=0.011*). The vertical (PPV=0.37±0.41;PnR=0.33 ± 0.33;difference=0.04;95%CI=-0.09–0.17;*P=0.564)* and horizontal (PPV=0.31±0.33;PnR=0.34±0.33;difference=-0.02; 95%CI=-0.14–0.09;*P=0.665*) MCHARTS scores were similar between groups. Mean aniseikonia scores were worse in patients with retinal displacement (with retinal displacement=4.52±6.05; without retinal displacement=2.31±3.51;difference=2.21; 95%CI=0.41–4.01;*P=0.017*). When assessing baseline factors that could have contributed to retinal displacement, there was a 7.7% higher proportion of RRDs that were four quadrants in the PPV group and a 7.9% higher proportion of RRDs that were one quadrant in the PnR group. Although these differences were not statistically significant, to adjust for it, a Poisson Regression with robust variance was performed which demonstrated that the size of the detachment did not impact the risk of retinal displacement. The relative risk of retinal displacement was 2.0(95%CI=1.3-3.1,P=0.002) in patients undergoing PPV compared to those undergoing PnR after adjusting for quadrants of detachment.

As a sensitivity analysis, a subgroup analysis excluding patients with SO or SB, found that the proportion of eyes with retinal displacement was 50%(34/68) for PPV vs 23.5%(19/81) for PnR(P=.001) in the intention-to-treat analysis and 51%(32/63) for PPV vs 14.7%(10/68) for PnR(P=<.0001) when assessing patients with primary reattachment. Furthermore, when excluding patients with SB and/or SO, aniseikonia scores remained significantly different (PPV=4.07+/- 5.1;PnR=2.03 +/- 3.77;difference=2.04;*P=0.016*).

There is a greater risk of retinal displacement in patients undergoing PPV compared to PnR and patients with retinal displacement had worse aniseikonia scores compared to patients without retinal displacement. Furthermore, among patients with a successful primary procedure, aniseikonia scores were significantly worse in the PPV group. This was the first prospective study to formally assess aniseikonia in the setting of retinal displacement with an objective quantitative test and to the best of our knowledge, no previous studies have demonstrated an association between retinal displacement and objective aniseikonia scores. Many patients complain of micropsia following RRD repair. We hypothesize that retinal stretch may lead to increased spacing between photoreceptors and this could be perceived as a change in image size (Animation Video as supplemental material 2 available at www.aaojournal.org). These findings will likely stimulate future studies on potential variations in the management of RRD that can minimize the risk of retinal displacement, such as drainage method and the use of minimal gas during PPV.[6,7]

In conclusion, this non-randomized comparative trial (the ALIGN study) found that PPV was associated with a greater risk of retinal displacement compared to PnR and that retinal displacement was associated with worse aniseikonia.

Figure 1: Ultra-widefield color photo and fundus autofluorescence (FAF) imaging after retinal detachment repair.

A and B) Color photo (A) and FAF (B) imaging of a patient demonstrating anatomic reattachment (A) and a high integrity retinal attachment (HIRA) with no retinal displacement on FAF (B).

C and D) Color photo (C) and FAF (D) imaging of another patient demonstrating anatomic reattachment (C) with a low integrity retinal attachment (LIRA) with retinal displacement on FAF (D); retinal vessel printings are seen (arrowheads), indicating that the retina has been displaced compared to its original location.

Supplemental Material 1: Patient Flow Diagram

Supplemental Material 2: Baseline Patient and Study Eye Characteristics

Supplemental Material 3: Animation video demonstrating proposed pathophysiology of post-operative aniseikonia with retinal displacement following rhegmatogenous retinal detachment repair

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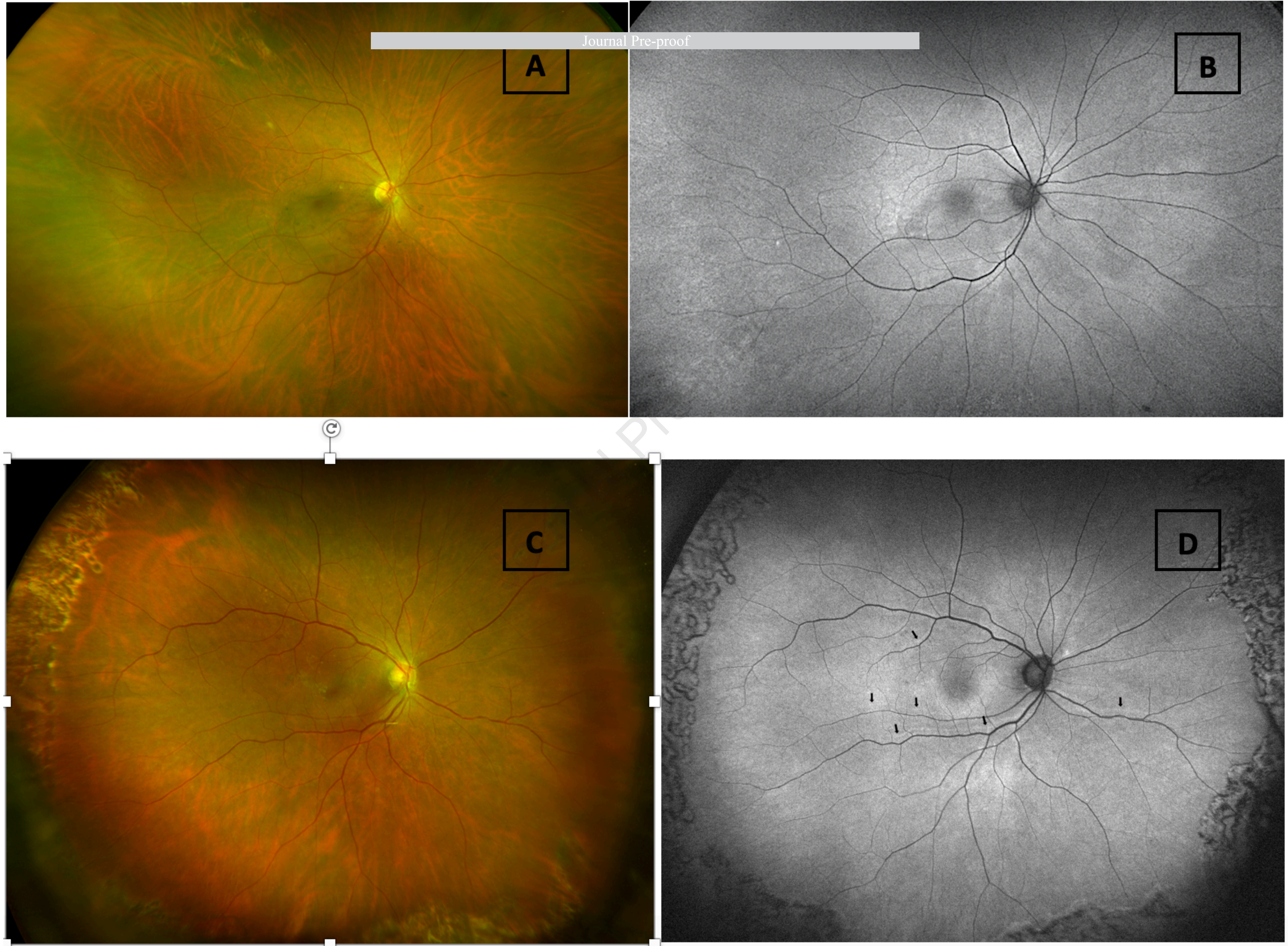
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