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Impact of the Time to Surgery on Visual Outcomes for Rhegmatogenous Retinal Detachment Repair: A Meta-Analysis

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• PURPOSE: To determine the relationship between time from symptom onset or presentation to repair and visual outcomes for macula-on and macula-off rhegmatogenous retinal detachment (RRD).

• DESIGN: Meta-analysis.

• METHODS: We searched MEDLINE, EMBASE, and Cochrane Library for randomized controlled trials and observational studies comparing best-corrected visual acuity (BCVA) based on time to RRD repair. Study identifiers, baseline characteristics, intervention characteristics, and visual outcomes were extracted. We conducted a random effects meta-analysis. Sensitivity analyses included leave-1-out and influence analyses. Primary outcomes included mean difference (MD) in final BCVA, MD between preoperative and final BCVA (ΔBCVA), and relative risk of final BCVA <0.4 logMAR for macula-off RRD repair in 0-3 vs 4-7 days and macula-on RRD repair in 0-24 vs >24 hours. Secondary outcomes assessed other time points.

• RESULTS: Twenty observational studies reported on 1929 patients. Macula-off RRD repair in 0-3 days from symptom onset was superior to 4-7 days for final BCVA (MD –0.06 [95% CI –0.09, –0.03], $P < .001$) but was not different for ΔBCVA ($P > .05$). Macula-on repair in 0-24 hours from presentation was superior to >24 hours for final BCVA (MD –0.02 [95% CI –0.03, –0.01], $P < .05$) but was not different for ΔBCVA ($P > .05$).

• CONCLUSIONS: Macula-off RRD repair in 0-3 days from symptom onset may have better final BCVA compared to repair in 4-7 days. Macula-on RRD repair in 0-24 hours of presentation may have better final BCVA compared to repair in >24 hours. These results were supported by moderate- and low-quality evidence, respectively, and may have been influenced by differences in baseline BCVA. (Am J Ophthalmol 2022;244: 19–29.

Modern surgical techniques achieve anatomic reattachment after repair of vision-threatening rhegmatogenous retinal detachment (RRD) in the majority of cases.[1,2] However, postoperative visual outcomes can be highly variable. Functional success after RRD repair is influenced by multiple factors, including patient age, macular status, presence of comorbidities, and RRD duration.[3,4] Of these factors, the duration from symptom onset and patient presentation to RRD repair are important predictors of future visual acuity outcomes.[4]

Immediate repair for every patient is ideal but may be limited by availability of operating rooms and on-site staff.[5] Emergent surgeries may also experience the "weekend" effect, an increase in the risk of intraoperative complications, duration of stay, and poorer outcomes that could result from limited staffing and physician coverage.[6,7] It is therefore useful to know how long RRD repair can be delayed without increased risk of adverse visual outcomes. A thorough understanding of the relationship between visual outcomes and time to repair will help determine how to best triage RRD patients.

The traditional approach recommends treating macula-sparing (macula-on) RRDs within 24-48 hours to avoid permanent central vision loss and macula-involving (macula-off) RRDs within 7 days.[8–12] However, disagreements in the literature have led to variability in recommendations. One case series found that macula-off RRDs had optimal final best-corrected visual acuity (BCVA) when repaired within 3 days,[13] whereas 3 case series found no significant difference in anatomic or visual outcomes when repair of macula-on RRDs was delayed.[14–16]

Clarifying the association between time to repair and visual outcomes for macula-on and macula-off RRDs is cru-

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cial in optimizing management. A previous meta-analysis was conducted by Van Bussel and associates assessing time to RRD repair and visual outcomes following scleral buckling (SB), which found that duration of macular detachment of 0-3 days was associated with the highest RR of final BCVA <0.4 logMAR.[17] To our knowledge, no existing meta-analysis has examined the relationship between time to RRD repair and visual outcomes across multiple interventions (SB, pars plana vitrectomy [PPV], combined SB and PPV [SB+PPV], or pneumatic retinopexy [PR]).

The primary objective of this study is to determine the relationship between time to surgery and visual outcomes for macula-on and macula-off RRDs. Secondary aims include analyzing this relationship in the context of varying intervention types and patient characteristics.

METHODS

• **SEARCH STRATEGY AND STUDY SELECTION:** We conducted a systematic literature search using Ovid MEDLINE (2000–April 2022), EMBASE (2000–April 2022), and Cochrane CENTRAL (inception up to April 2022). Randomized controlled trials or observational studies were included if they reported on BCVA or primary retinal reattachment rates following RRD repair and analyzed these outcomes according to time from presentation or symptom (ie, central vision loss) onset to repair. Both randomized and nonrandomized trials were included as only a small number of randomized trials were likely to be available for inclusion. Studies published in languages other than English, unpublished studies, case reports, narrative reviews, editorials, and articles with repeat data from the same patient sample were excluded.

The complete search strategy can be found in Supplemental Table S1. Three independent reviewers (A.S., A.E., A.S.D.) conducted title and abstract screening and subsequent full-text screening of included abstracts. Discrepancies were resolved through consensus with the input of a fourth author (M.M.P.). Reference lists of included papers were searched to ensure that no relevant studies were missed. The study protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database, CRD 42020204169.

• **DATA EXTRACTION AND QUALITY ASSESSMENT:** Two independent reviewers (A.S, A.E.) used standardized data collection forms to extract study identifiers (authors, journal, year of publication, study design, country of origin), baseline characteristics (number of eyes, age, gender, ethnicity, macula status, lens status, intraocular pressure, preoperative BCVA, duration of symptoms/delay to surgery), intervention characteristics (procedure type, vitrector gauge, and tamponade specifications), and outcomes (length of follow-up, BCVA at 3 months, 6 months, 12 months, and final follow-up, change in BCVA from baseline, primary reattachment rate, and adverse outcomes).

Two independent reviewers (A.S., A.E.) assessed the quality of included studies using the Risk of Bias in Nonrandomized Studies—of Interventions (ROBINS-I), which assesses bias in 9 domains: confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of reported results.[18] Quality of evidence for individual outcomes was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) tool.[19] All studies were also assessed for authorship conflicts of interest and industry sponsorship.

• **DATA SYNTHESIS AND DATA ANALYSIS:** Baseline demographics were reported as a proportion for categorical variables and means with SD for continuous variables. A random effects meta-analysis was conducted using an empirical Bayesian estimator for all outcomes. Studies were removed from meta-analysis of individual outcomes if the study did not report on that outcome, reported on the outcome but omitted a measure of dispersion (ie, SD, SE, or 95% CI), or was missing data for that outcome. Continuous outcomes were reported as a mean difference (MD) with a 95% CI, and binary outcomes as a relative risk [RR] with 95% CI.

Primary outcomes were final BCVA, change between preoperative BCVA and final BCVA (ΔBCVA), and relative risk (RR) of final BCVA <0.4 logMAR (better than 20/50 Snellen) between macula-off RRD repair in 0-3 vs 4-7 days and macula-on RRD repair in 0-24 vs >24 hours. Secondary outcomes examined other time points, the MD of operating time, the RR of primary reattachment, and the RR of complications. The most consistently reported time points in the included studies were selected for analysis.

Statistical heterogeneity was investigated using an I^2 statistic: I^2 <0.25 was considered low heterogeneity, I^2 equal to 0.25-0.50 was considered moderate heterogeneity, and I^2 >0.50 was considered high heterogeneity.[18,20] We performed sensitivity analyses by sequentially removing each study and reanalyzing the remaining studies (ie, leave-1-out analyses), by conducting diagnostic tests to identify outliers and highly influential studies on the results (ie, influence analyses), and by generating funnel plots and assessing publication bias. We aimed to conduct subgroup analyses within each outcome according to study design, duration of follow-up, surgery performed (PPV, SB, SB+PPV, PR), lens status (phakic vs pseudophakic), and endotamponade used. Studies that did not report duration of follow-up were excluded from subgroup analysis.

P values of ≤.05 were considered statistically significant for all analyses. Data extraction and description of baseline demographics were performed on Microsoft Excel (Redmond, WA). Meta-analysis was performed on R 4.0.2 (The R Project for Statistical Computing), using the metafor (version 2.4.0) and metaviz (version 0.3.1) packages.

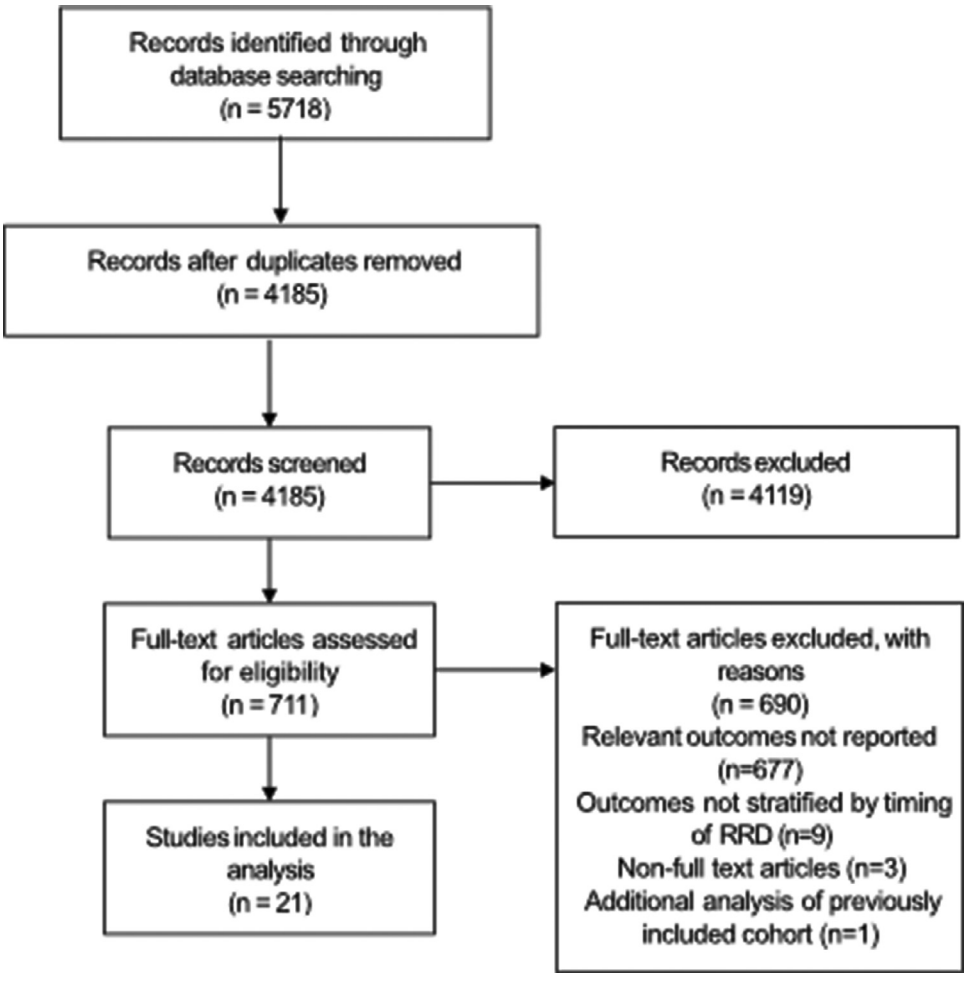

FIGURE 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

RESULTS

• **SEARCH RESULTS, STUDY SCREENING, AND BASELINE DEMOGRAPHICS:** The search yielded 4185 articles. After removing duplicates and screening titles and abstracts, 711 articles were advanced to full-text screening. Twenty-one studies (19 case series, 2 cohort studies) met all criteria after full-text screening (Figure 1). Seven studies were conducted in the United States,[11,14,16,21–24] followed by the United Kingdom ($k = 3$),[8,25,26] Germany ($k = 2$),[13,27] Japan ($k = 1$),[28] the Netherlands ($k = 1$),[29] Taiwan ($k = 1$),[30] Turkey ($k = 1$),[31] Canada ($k = 1$),[32] Italy ($k = 1$),[33] New Zealand ($k = 1$),[15] Pakistan ($k = 1$),[34] and Switzerland ($k = 1$).[35] Ten studies assessed multiple procedure types,[26] but 9 of them did not report results on time to repair stratified by procedure.[8,13,16,21-24,26,29,30]

A total of 1929 eyes were included at baseline. Individual study sample sizes ranged from 12 to 199 eyes. Thirty-nine percent of subjects were female (range: 18.8%-64.5%), the mean age of subjects was 58.2 (range: 39.2-64.9), and the mean postoperative follow-up time was 15.9 months (range: 3-55). Eighty percent of studies (16/20) assessed macula-off RRDs, of which 14 studies defined duration of RRD as time from symptom onset. Time from symptom onset was defined by 10 studies as central vision loss and not specified by 4 studies. Two studies did not specify whether duration of RRD was from symptom onset or presentation. Twenty percent of studies (4/20) assessed macula-on RRDs and all defined duration of RRD as time from initial examination to repair. Given limitations of available data, our analysis assessed time from symptom onset to RRD repair for macula-off RRDs and time from initial presentation to RRD repair for macula-on RRDs. A complete list of baseline characteristics can be found in Table 1.

• **QUALITY ASSESSMENT:** Using the ROBINS-I tool (Supplemental Table S2), 55% (11/20) of observational studies had a low overall risk of bias, 40% (8/20) had a moderate risk of bias, and 5% (1/20) had a serious risk of bias. Studies received a more negative assessment for lack of statistical analysis to control for confounding (18/20), result selec-

TABLE 1. Baseline Characteristics of Included Articles

Study	Year	Study Design	Number of Eyes	Mean Age	% Female	Lens Status	Macula Status	Intervention type(s) (SB, PPV, PR, SB+PPV)	Definition of Duration Used by Study	Mean Follow-up, mo
Kim et al[21]	2013	Case series	81	63	33	Pseudophakic	Off	PPV	Symptom onset (central vision loss)	55
Doyle et al[26]	2007	Case series	185	63	38	Phakic: 137 Pseudophakic: 46 Aphakic: 2	Off	SB, PPV	Symptom onset (central vision loss)	7.9
Khanzada et al[34]	2014	Case series	170	51.5	44.1	Phakic	Off	SB	Symptom onset (central vision loss)	3
Mowatt et al[8]	2005	Case series	104	58.2	40.4	Phakic: 86 Pseudophakic: 15 Aphakic: 3	Off	SB, PPV, PR	NR	7.6
Henrich et al[35]	2009	Case series	62	64.9	64.5	NR	Off	SB	Symptom onset (central vision loss)	12.7
Geiger et al[22]	2019	Case series	131	62.5	32.8	Phakic: 80 Pseudophakic: 51	Off	SB, PPV, PR, SB+PPV	Symptom onset (central vision loss)	N/A (6-18 mo)
Diederen et al[29]	2007	Case series	202	60.9	39.2	Phakic: 158 Pseudophakic: 44	Off	SB	Symptom onset (central vision loss)	22.5
Hassan et al[11]	2002	Case series	94	61.5	40.4	Phakic: 52 Pseudophakic: 40 Aphakic: 2	Off	SB	Symptom onset	9.1
Çetin et al[31]	2013	Case series	28	55.9	44.4	Phakic: 14 Pseudophakic: 14	Off	SB, PPV	Symptom onset	23.2
Oshima et al[28]	2000	Retrospective cohort	55	54.3	47	Phakic: 49 Pseudophakic: 6	Off	SB, PPV	NR	24
Yang et al[30]	2004	Case series	93	39.2	34.4	NR	Off	SB	Symptom onset (central vision loss)	12.2
Frings et al[13]	2016	Case series	89	61	18.8	NR	Off	SB, PPV	Symptom onset (central vision loss)	6
Liu et al[27]	2006	Case series	96	62.5	40.6	NR	Off	SB	Symptom onset (central vision loss)	43.5
Lai et al[16]	2011	Case series	66	56.3	42.4	Phakic: 42 Pseudophakic: 24	On	SB, SB+PPV	Initial exam	13.1
Wykoff et al[14]	2010	Case series	199	54	44	Phakic: 122 Pseudophakic: 73 Aphakic: 4	On	SB	Initial exam	17
Gorovoy et al[23]	2014	Case series	96	52.5	52.4	Phakic: 43 Pseudophakic: 45	On	SB, PPV, PPV+SB	Initial exam	14.6
Ehrlich et al[15]	2013	Case series	114	57.8	34.2	Phakic: 65 Pseudophakic: 47 Aphakic: 2	On	PPV	Initial exam	7.6
Ross et al[32]	2005	Case series	52	60.5	30.8	Phakic: 26 Pseudophakic: 26	Off	SB, PPV, PR, SB+PPV	Symptom onset	9.4
Cavallini et al[33]	2007	Case series	12	62.8	50	Phakic	Off	SB	Symptom onset	6
Greven et al[24]	2018	Case series	79	61.5	29.1	Phakic: 55 Pseudophakic: 24	Off	PPV, SB+PPV	Symptom onset (central vision loss)	19.6
Yorston et al[25]	2021	Retrospective cohort	2074	<70	35.1	Phakic: 1386 Pseudophakic: 688	Off	PPV, SB+PPV	Symptom onset (central vision loss)	NR (2.5-3 mo)

NR = not reported, PPV = pars plana vitrectomy, PR = pneumatic retinopexy, SB = scleral buckling, SB+PPV = combined SB and PPV.

TABLE 2. Baseline Best-Corrected Visual Acuity (BCVA) of Meta-analysis Groups

Meta-analysis Outcome	Group 1 Baseline BCVA, logMAR, Mean (SD)	Group 2 Baseline BCVA, logMAR, Mean (SD)
Macula-off RRD repair in 0-3 d vs 4-7 d		
Final BCVA	Could not be calculated	
Change from preoperative to postoperative BCVA	1.26 (0.64)	1.50 (0.78)
Relative risk of final BCVA <0.4 logMAR	1.69 (0.39)	1.94 (0.32)
Macula-off RRD repair in 0-7 d vs >7 d		
Final BCVA	Could not be calculated	
Change from preoperative to postoperative BCVA	1.58 (0.73)	1.60 (0.80)
Relative risk of final BCVA <0.4 logMAR	Could not be calculated	
Macula-off RRD repair in 0-10 d vs >10 d		
Final BCVA	1.78 (0.70)	1.76 (0.61)
Change from preoperative to postoperative BCVA	1.78 (0.70)	1.76 (0.61)
Macula-off RRD repair in 0-15 d vs >15 d		
Final BCVA	Could not be calculated	
Change from preoperative to postoperative BCVA	1.46 (1.04)	1.54 (0.93)
Macula-on RRD repair in 0-24 h vs >24 h		
Final BCVA	0.28 (0.48)	0.22 (0.32)
Change from preoperative to postoperative BCVA	0.28 (0.48)	0.22 (0.32)
Relative risk of final BCVA <0.4 logMAR	0.12 (0.10)	0.18 (0.11)

BCVA = best-corrected visual acuity, RRD = retinal rhegmatogenous detachment.

tion likely based on multiple analyses (10/20), insufficient description of intervention groups (5/20), unclear selection process (4/20), and possible effect of outcome risk on intervention group classification (1/20).

The GRADE evaluation (Supplemental Table S3) identified that the final BCVA outcome for macula-off RRD repair in 0-3 vs 4-7 days and all outcomes for macula-off RRD repair in 0-7 vs >7 days were supported by moderate quality evidence; RR of BCVA <0.4 logMAR for macula-on RRD repair in 0-24 vs >24 hours, and all outcomes for macula-off RRD repair in 0-15 vs >15 days were supported by very low quality evidence; and all other outcomes and endpoints were supported by low quality evidence. One study reported an author conflict of interest, and no included studies received industry sponsorship.

Baseline BCVA could not be calculated for all outcomes because of inconsistent reporting across studies. A difference in baseline BCVA was noted for the analysis of RR of final BCVA <0.4 logMAR for macula-off RRD repair in 0-3 days vs 4-7 days (1.69 ± 0.39 logMAR vs 1.94 ± 0.32 logMAR). A similar difference in baseline BCVA was noted for the analysis of RR of final BCVA <0.4 logMAR for macula-on RRD repair in 0-24 hours vs >24 hours (0.12 ± 0.10 logMAR vs 0.18 ± 0.11 logMAR). Baseline BCVA for individual outcomes can be found in Table 2.

• **MACULA-OFF RRDS:** Meta-analysis revealed that macula-off RRD repair within 0-3 days from symptom onset was superior to 4-7 days for final BCVA (MD –0.06 [95% CI –0.09, –0.03] logMAR, $P < .001$), but was not different for ΔBCVA (MD 0.03 [95% CI –0.18, 0.25], $P > .05$) or for the RR of BCVA <0.4 logMAR (RR 1.27 [95% CI 1.09, 1.49], $P < .01$) (Figure 2). Macula-off RRD repair in 0-7 days was superior to >7 days for final BCVA (MD –0.20 [95% CI –0.30, –0.10], $P < .001$), ΔBCVA (MD –0.29 [95% CI –0.46, –0.13], $P < .001$), and RR of BCVA <0.4 logMAR (RR 1.49 [95% CI 1.33, 1.67], $P < .001$) (Supplemental Figure S1). Macula-off RRD repair in 0-10 days was superior to >10 days for final BCVA (MD –0.48 [95% CI –0.65, –0.31], $P < .001$; ~5 Snellen lines) and ΔBCVA (MD –0.42 [95% CI –0.66, –0.17], $P < .001$) (Supplemental Figure S2). Macula-off RRD repair in 0-15 days was not different from >15 days for final BCVA (MD –0.06 [95% CI –0.23, 0.11], $P > .05$) or ΔBCVA (MD –0.02 [95% CI –0.43, 0.38], $P > .05$) (Supplemental Figure S3).

• **MACULA-ON RRDS:** Macula-on RRD repair in 0-24 hours from presentation was superior to >24 hours for final BCVA (MD –0.02 [95% CI –0.03, –0.01], $P < .01$), but was not different for ΔBCVA (MD 0.00 [95% CI –0.02, 0.02], $P > .05$) or for the RR of BCVA <0.4 logMAR (RR 1.09 [95% CI 0.91, 1.31], $P > .05$). Macula-on RRD repair in 0-24 hours was not different from >24 hours for primary reattachment (event rate: 0.90 [95% CI 0.83, 0.97], 0-24 hours; 0.89 [95% CI 0.80, 0.99], >24 hours; RR 0.97 [95% CI 0.90, 1.03], $P > .05$; mean follow-up: 11.8 months) (Figure 3). Primary reattachment rate for other time points, operating time, and complications could not be assessed because of insufficient data. A full list of results may be found in Table 3.

• **SENSITIVITY AND SUBGROUP ANALYSES:** I^2 calculation demonstrated high heterogeneity for the final BCVA out-

TABLE 3. Meta-Analysis Outcomes for Macula-Off and Macula-On RRDs

Comparison Groups	Number of Studies	Mean Duration of Follow-up, mo	Group 1 Mean (SD) [logMAR]	Group 2 Mean (SD) [logMAR]	Mean Difference (95% CI) [logMAR]
Final BCVA					
Macula-off RRD: 0-3 d vs 4-7 d from symptom onset	3	20.6	0.35 (0.30) [Snellen 20/44]	0.47 (0.39) [Snellen 20/59]	–0.06 (–0.09, –0.03)*** [∼3 Snellen letters]
Macula-off RRD: 0-7 d vs >7 d from symptom onset	8	22.4	0.34 (0.32) [Snellen 20/44]	0.55 (0.49) [Snellen 20/71]	–0.20 (–0.30, –0.10)*** [∼2 Snellen lines]
Macula-off RRD: 0-10 d vs >10 d from symptom onset	2	15.8	0.42 (0.40) [Snellen 20/53]	0.85 (0.59) [Snellen 20/142]	–0.48 (–0.65, –0.31)*** [∼5 Snellen lines]
Macula-off RRD: 0-15 d vs >15 d from symptom onset	3	28.6	0.32 (0.34) [Snellen 20/42]	0.49 (0.44) [Snellen 20/62]	–0.06 (–0.23, 0.11)
Macula-on RRD: 0-24 h vs >24 h from presentation	3	11.8	0.28 (0.55) [Snellen 20/38]	0.20 (0.23) [Snellen 20/32]	–0.02 (–0.03, –0.01)** [∼1 Snellen letter]
			Group 1 Mean (SD) [logMAR]	Group 2 Mean (SD) [logMAR]	Mean Difference (95% CI) [logMAR]
Change from preoperative to final postoperative BCVA (ΔBCVA)					
Macula-off RRD: 0-3 d vs 4-7 d from symptom onset	3	19.6	–0.94 (0.65)	–1.07 (0.81)	0.03 (–0.18, 0.25)
Macula-off RRD: 0-7 d vs >7 d from symptom onset	5	21.1	–1.32 (0.80)	–0.99 (0.90)	–0.29 (–0.46, –0.13)*** [∼3 Snellen lines]
Macula-off RRD: 0-10 d vs >10 d from symptom onset	2	15.8	–1.33 (0.75)	–0.92 (0.81)	–0.42 (–0.66, –0.17)*** [∼4 Snellen lines]
Macula-off RRD: 0-15 d vs >15 d from symptom onset	2	15.4	–1.07 (1.09)	–0.98 (1.08)	–0.02 (–0.43, 0.38)
Macula-on RRD: 0-24 h vs >24 h from presentation	3	11.8	0.00 (0.71)	–0.02 (0.37)	0.00 (–0.02, 0.02)
			Group 1 Proportion (95% CI)	Group 2 Proportion (95% CI)	Relative Risk Ratio (95% CI)
Relative risk ratio (RR) of final BCVA <0.4 logMAR					
Macula-off RRD: 0-3 d vs 4-7 d	4	16.2	65% (61%, 68%)	50% (46%, 54%)	1.27 (1.09, 1.49)**
Macula-off RRD: 0-7 d vs >7 d	3	20.5	57% (55%, 60%)	38% (34%, 41%)	1.49 (1.33, 1.67)***
Macula-on RRD: 0-24 h vs >24 h	2	15.8	80% (72%, 88%)	73% (65%, 80%)	1.09 (0.91, 1.31)

BCVA = best-corrected visual acuity, RRD = retinal rhegmatogenous detachment.

*$P < .05$, **$P < .01$, ***$P < .001$.

Mean (SDs) and proportions for each group are calculated from raw data. Mean differences and relative risk ratios were calculated from models accounting for study weighting and between-study variance.

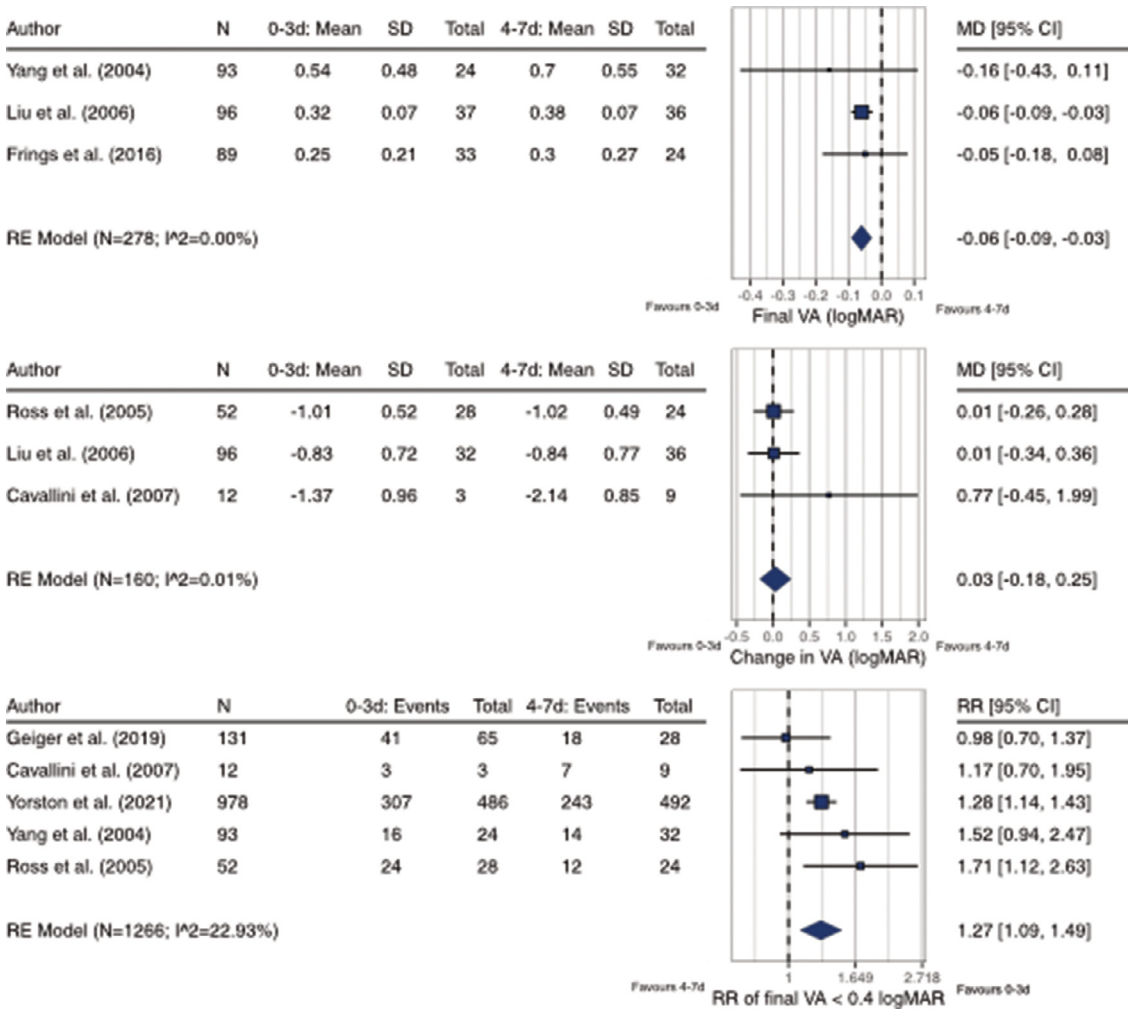

FIGURE 2. Forest plot of visual outcomes for macula-off RRD repair in 0-3 vs 4-7 days.

comes of 0-7 days vs >7 days and 0-15 days vs >15 days, and moderate heterogeneity for ΔBCVA at 0-7 days vs >7 days, and RR of BCVA <0.4 logMAR at 0-3 days vs >3 days and 0-24 hours vs >24 hours. All other outcomes had low heterogeneity.

Leave-1-out analyses identified changes in magnitude and direction of effect when removing Liu and associates in the analysis of final BCVA for macula-off RRD repair in 0-3 vs 4-7 days (MD –0.07 [95% CI –0.19, 0.05], $P = .24$), Geiger and associates in the analysis of RR of final BCVA <0.4 logMAR for 0-3 days vs 4-7 days (RR 1.48 [95% CI 1.13, 1.95], $P < .01$), Lai and associates in the analysis of final BCVA for macula-on RRD repair in 0-24 vs >24 hours (0.01 [95% CI –0.08, 0.09], $P > .05$), and Liu and associates and Yang and associates in the analysis of RR of final BCVA <0.4 logMAR for macula-off RRD repair in 0-7 days vs >7 days (0.32 [95% CI –0.21, 0.84], $P > .05$, and 0.19 [95% CI –0.14, 0.52], $P > .05$, respectively).

Additional sensitivity analyses did not identify any highly influential studies, outliers, or funnel plot asymmetry. No differences relative to the main analysis were identified in subgroup analysis for the duration of follow-up (0-3 months, 3-12 months, >12 months) in any outcome. We were unable to conduct a subgroup analysis based on endotamponade, intervention type, or lens status because of insufficient reporting of outcomes in relevant patient cohorts across studies.

DISCUSSION

Time to repair of macula-on and macula-off RRDs has been shown to impact visual outcomes.[10,11] The conventional approach, which recommends treating macula-on RRDs within 24-48 hours and macula-off RRDs within 7 days, has been questioned by several recent studies.[14–16] This meta-analysis explored the relationship between time to RRD repair and visual outcomes, analyzing 1929 eyes from 20 studies, which were collectively of low-moderate quality.

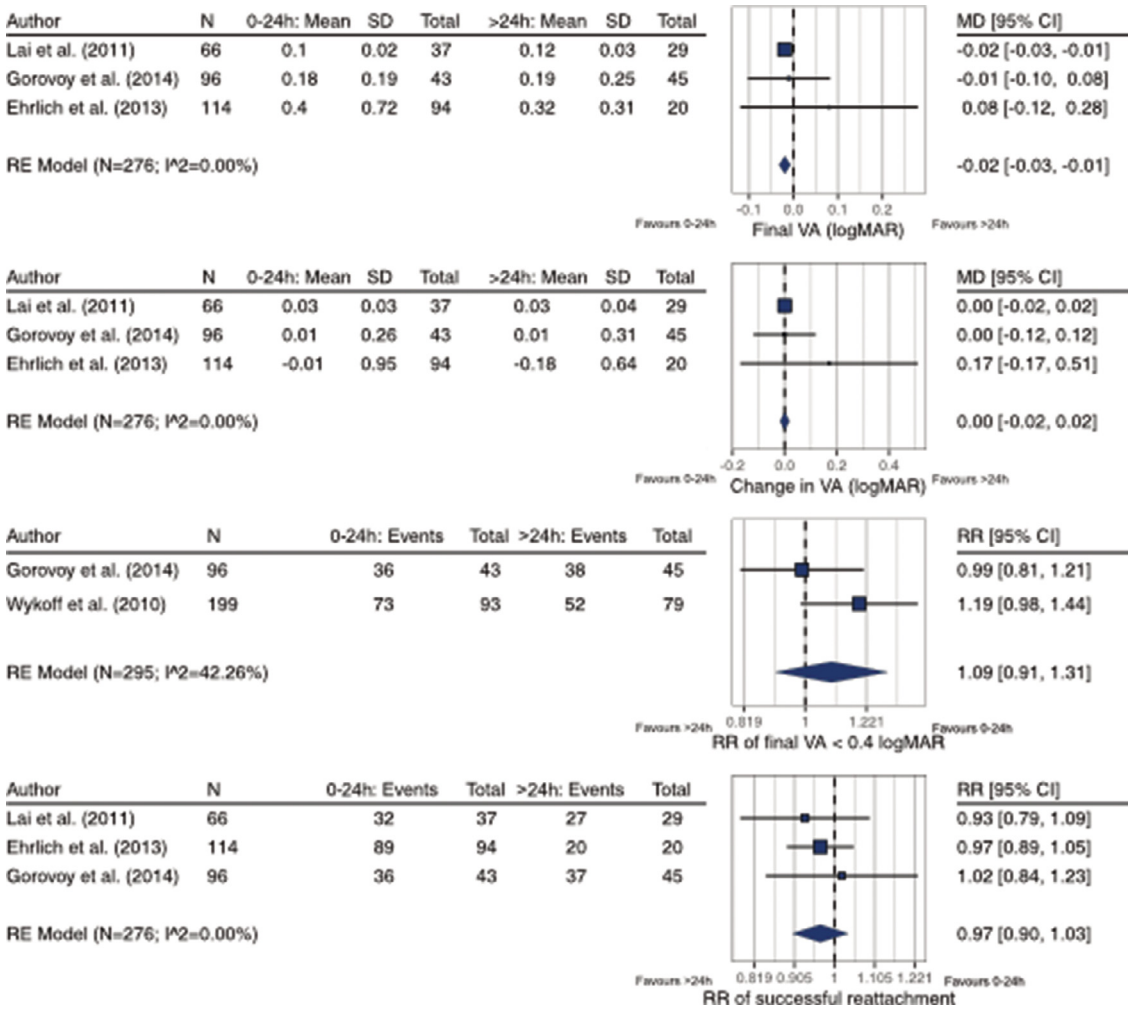

FIGURE 3. Forest plot of visual outcomes for macula-on RRD repair in 0-24 vs >24 hours.

Macula-on RRDs are treated urgently to prevent detachment of the fovea preoperatively, whereas macula-off RRDs are thought to have already suffered permanent foveal damage with resultant visual consequences, thus limiting the urgency of repair.[12] However, this meta-analysis found that final BCVA was better when macula-off RRDs were treated in 0-3 days. This conclusion is in line with a large sample study of 847 eyes with RRD by Williamson and associates, who noted better postoperative visual acuity following surgery in 1-3 days relative to 4-6 days ($P = .013$).[36] A longer duration to macula-off repair was associated with worse visual outcomes when considering the 7-day and 10-day thresholds; however, this was not different at the 15-day threshold. We found that macula-on RRDs were associated with better final BCVA when treated in 0-24 hours vs >24 hours; however, the difference was small.

Heterogeneity was high for analyses of final BCVA after macula-off RRD repair in 0-7 vs >7 days and was moderate for ΔBCVA after macula-off RRD repair in 0-7 vs >7 days and for RR of final BCVA <0.4 logMAR after macula-off RRD repair in 0-3 vs 4-7 days. Given the heterogeneity, a random effects model was used, and subgroup analysis did not decrease heterogeneity in these outcomes. This was expected given our inclusion of studies with heterogeneous populations with respect to geographic region, age, ethnicity, and presence of medical and ocular comorbidities. The high heterogeneity for the analyses of final BCVA after macula-off RRD repair in 0-15 days vs >15 days (high) and RR of final BCVA <0.4 logMAR after macula-on RRD repair in 0-24 hours vs >24 hours was attributable to low sample size (n=2 studies) and a heterogeneous patient population.

Leave-1-out analyses identified several studies that had a significant influence on the observed results. Liu and associates[27] found that macula-off RRD repair in 0-3 days from symptom onset was superior to 4-7 days for final BCVA and that macula-off RRD repair in 0-7 days was superior to >7 days for RR of final BCVA <0.4 logMAR: this study included only patients receiving SB. Geiger and associates[22] found that macula-off RRD repair in 0-3 and 4-7 days from

symptom onset had similar RR of final BCVA <0.4 logMAR. This study had the largest sample size of the included studies; however, the authors found that preoperative BCVA was significantly better in patients who had a final BCVA <0.4 logMAR, and did not adjust for this in the analysis of time to surgery.

Lai and associates[16] found that macula-on RRD in 0-24 hours from presentation was superior to ≥24 hours for ΔBCVA with a narrow confidence interval. Yang and associates[30] found that macula-off RRD repair in 0-7 days from symptom onset had an increased RR of final BCVA <0.4 logMAR compared with >7 days, but only included patients receiving SB and excluded patients with partial macular involvement.

Two studies conducted statistical adjustment for confounding,[15,16,22,26,30] whereas most included studies controlled for potential confounders through strict inclusion and exclusion criteria.[11,13–16,21,23,27–31,33–35] Doyle and associates[26] conducted univariable then multivariable logistic regression assessing age, time to repair, preoperative BCVA, number of involved quadrants, surgeon experience, lens status, and presence of proliferative vitreoretinopathy on anatomic and visual outcomes. The authors found an association between time to repair and final BCVA in the univariable model though no significant association ($P = .052$) in the multivariable model.[26] Geiger and associates[22] conducted a multivariable regression including only the factors that showed statistical significance in univariable regression. Because there was no significant association between time to RRD repair and visual outcomes, time to RRD repair was not included in multivariable analysis.

This analysis found better final BCVA when macula-off RRDs were treated in 0-3 days from symptom onset and macula-on RRDs in 0-24 hours from presentation; however, we did not identify a difference in ΔBCVA. Post hoc analysis of variance of preoperative BCVA was done for analysis of final BCVA and ΔBCVA in macula-on RRD in 0-24 vs >24 hours from presentation, which demonstrated high between-study variance in preoperative BCVA (0-24 hours: $F = 8.62$, $P < .001$; >24 hours: $F = 12.94$, $P < .0001$) but similar mean preoperative BCVA between groups for individual studies and pooled data (combined mean [SD]: 0.22 [0.4] (0-24 hours), 0.21 [0.29] (>24 hours), $P > .05$). The differences in means and variances across studies limit the quality of conclusions derived. It is possible that there was a higher probability of progression to macula-off RRD when repair occurred after 24 hours for macula-on RRDs; however, this was not specifically reported by individual studies.

Mowatt and associates[8] found no association between time from presentation and final BCVA after macula-off RRD repair in univariable regression analysis ($P = .44$); however, the authors did not report data for this outcome. Our literature search did not identify any other studies that reported on the impact of time from presentation to macula-off RRD repair on visual outcomes, which should be addressed in future studies.

Our findings are consistent with the meta-analysis conducted by van Bussel and associates,[17] which assessed SB repair of macula-off RRDs and found that RR of final BCVA <0.4 logMAR was highest when duration of macular detachment was 0-3 days (number needed to treat = 4). The authors were criticized about their exclusion of studies including multiple retinal breaks, unclear definition of duration of macular detachment, inconsistency in results across time points, and highly certain reporting of their conclusions.[37] Our meta-analysis included a larger number of studies with multiple procedure types and endotamponade agents and found no significant relationship between time to surgery and the proportion of patients reaching BCVA <0.4 logMAR in this setting ($P = .06$). We did not exclude studies based on number of retinal breaks.

Fourteen of 16 studies included in our analysis of macula-off RRD repair reported on the time from symptom onset to repair. Of these, 10 studies defined symptom onset based on timing of central vision loss,[13,21,22,24,26,27,29,30,34,35] whereas 4 studies did not provide further specification.[11,31–33] Two macula-off RRD studies did not define whether the duration of macular detachment was from symptom onset or presentation.[24,29] Our results were consistent between time points, finding a difference in effect on final BCVA at the 3-, 7-, and 10-day time point thresholds. Exclusion of studies that did not specify the definition of duration of symptom onset did not significantly alter the results of the meta-analysis. Our findings were supported by a low-moderate quality of evidence, which limits the certainty of our conclusions.

Our results are limited by the observational design of included studies: all were nonrandomized with relatively small sample sizes, and most collected data retrospectively. Most included studies controlled for potential confounders through strict inclusion and exclusion criteria but did not conduct statistical adjustments: it is therefore unclear whether confounding was adequately controlled across studies. All studies included in macula-off RRD analyses assessed visual outcomes according to time from symptom onset, which is less reliable than time from presentation and cannot be controlled by the surgeon.

Our primary end point was final BCVA, which may be affected by baseline differences and variability in measurements. Final BCVA also may not adequately account for differential follow-up, because of inconsistent reporting of BCVA outcomes at specific time points. However, subgroup analysis based on follow-up duration did not identify any significant differences. We were unable to adjust for baseline BCVA in this study, which may have affected the reported estimates for ΔBCVA and limits the conclusions that can be drawn. Given a scarcity of data, it is important to note that our results are based on time point thresholds (eg, 0-24 hours vs >24 hours) instead of the actual duration before surgical intervention. Furthermore, we were unable

to assess whether the intervention type, lens status, or endotamponade used affected the observed relationship because of inconsistencies in reporting across studies.

In conclusion, modern retinal reattachment techniques are associated with excellent BCVA outcomes in most eyes. Macula-off RRD repair within 3 days of symptom onset may have a 0.06 logMAR (~3 Snellen letters) superior final VA compared to repair in 4-7 days. Macula-on RRD repaired within 24 hours of presentation may provide superior VA outcomes (0.02 logMAR, ~1 Snellen letter) compared with repair in >24 hours. These results were supported by evidence of moderate and low quality, respectively, and may have been influenced by differences in baseline BCVA. Future prospective studies with large sample sizes that investigate the relationship between time to RRD repair and visual outcomes are warranted.

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