Clinical Ophthalmology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

REVIEW

Cystoid Macular Edema Following Rhegmatogenous Retinal Detachment Repair Surgery: Incidence, Pathogenesis, Risk Factors and Treatment

Enrico Bernardi[1], Neil Shah[2], Lorenzo Ferro Desideri[1,3], Jelena Potic[4], Janice Roth[1,2], Rodrigo Anguita[1,2]

[1]Department of Ophthalmology, Inselspital, Bern University Hospital, University of Bern, Bern, CH-3010, Switzerland; [2]Moorfields Eye Hospital NHS Foundation Trust, London, UK; [3]Bern Photographic Reading Center, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; [4]Department of Ophthalmology, University of Lausanne, Jules-Gonin Eye Hospital, Fondation Asile des Aveugles, Lausanne, Switzerland

Correspondence: Rodrigo Anguita, Email rodrigoanguita@gmail.com

Purpose: To review the incidence, risk factors, and treatments for cystoid macular edema (CME) following rhegmatogenous retinal detachment (RRD) repair surgery.

Methods: A comprehensive literature search was conducted across multiple databases. Relevant studies published within the last 20 years were selected and reviewed.

Results: The incidence of CME following RRD repair ranges from 6% to 36%, with higher rates associated with silicone oil tamponade. Key risk factors include recurrent RRD, pre-existing proliferative vitreoretinopathy, older age, and post-RRD cataract surgery. Treatment options primarily focus on anti-inflammatory approaches, with topical NSAIDs and corticosteroids as first-line treatments. For persistent cases, intravitreal corticosteroid injections, particularly dexamethasone implants, have shown potential.

Conclusion: CME remains a significant complication following RRD repair, impacting visual recovery. While various treatment options exist, management of persistent CME remains challenging. Better understanding of the underlying mechanisms of CME is required to develop more effective treatment strategies, particularly for cases resistant to current therapies.

Plain Language Summary: Cystoid macular edema is a common complication following rhegmatogenous retinal detachment repair, affecting visual recovery. Its incidence varies widely, influenced by surgical approach and patient factors. Treatment primarily involves anti-inflammatory medications, with intravitreal corticosteroids showing promise for persistent cases. Further research is needed to improve management of this challenging complication.

Keywords: retinal detachment, cystoid macular edema, vitrectomy, scleral buckle, silicone oil, steroids, retinectomy, PVR

Introduction

Surgery for repair of rhegmatogenous retinal detachment (RRD) often achieves anatomical repair, however, functional results are suboptimal in some cases. Significant microvascular changes have been detected in superficial and deep capillary plexuses in eyes with RRD, associated with poorer post-operative visual acuity.[1,2]

Among the most frequent macular changes following rhegmatogenous retinal detachment (RRD) repair surgery, cystoid macular oedema (CME) represents a common complication.[3–6] This condition is characterized by the accumulation of intraretinal fluid, leading to a subsequent decline in visual acuity, which can persist for months following RRD repair, impeding visual rehabilitation efforts.[7] Functional recovery subsequent to RRD repair has garnered considerable attention,

Received: 2 August 2024
Accepted: 20 December 2024
Published: 21 February 2025

with CME emerging as a primary factor hampering such recovery, alongside post-operative changes such as epiretinal membrane formation (ERM), cellular and subcellular pathological processes which underlie the loss of visual function.[8–11]

The specific etiology of this post-operative complication remains debated, but several risk factors, such as age, lens status, macular status, the severity of the retinal detachment, surgical technique and especially proliferative vitreoretinopathy (PVR), have been reported in multiple papers.[12]

Conservative treatment, including steroidal and non-steroidal anti-inflammatory (NSAID) eye drops, guarantees a resolution in the vast majority of post RRD CME cases within 6 weeks after the therapy is started. There is, however, a number of eyes in which the CME becomes chronic. In these cases, more invasive treatments are usually needed.

This article presents a comprehensive overview of the incidence, risk factors, and treatments for this condition, based on the available literature on the subject.

Materials and Methods

A comprehensive literature search was done to find all published studies on these topics and the following databases were searched: Medline, PubMed, Web of Science Core Collection, and the Cochrane Library. Controlled vocabulary and keywords related to "macular edema" and "cystoid macular edema" were used in combination with terms "retinal detachment", "vitrectomy", "postoperative". Prospective and retrospective clinical studies, as well as narrative reviews, were considered. We limited our search to studies that were relevant to our subject, written in the English language, and published within the last 20 years. A comprehensive review of 112 publications by 2 authors (EB and NS) was conducted, with relevant articles being selected for an in-depth review based on their significance to the topic. Furthermore, reference lists of the eligible articles were manually scrutinized to identify additional pertinent studies. Ongoing research was also explored by examining clinical trial registries, including www.clinicaltrials.gov.

Incidence

RRD requiring surgical repair is a common condition, affecting between 6 and 18 patients per 100,000 people worldwide each year.[13] The incidence of CME is influenced by a number of factors, including the type of surgery, the presence of PVR and the tamponade. Following any of the different techniques used to repair RRD, the rate of post-operative CME incidence usually ranges from 6% to 36% (see Table 1).[14–17] More extreme numbers regarding are, however, also reported, with mere 5.5% after PPV for symptomatic floaters to 40% after complicated retinal detachment repairs.[15,18,19] Smaller studies have shown a range of 12–45% of postoperative CME following RRD repair although a majority of these eyes had PVR preoperatively which likely increased the incidence of CME.[19–22]

Merad et al reported that 34% of patients receiving multiple different tamponades (gases and silicone oil) experienced at least one episode of CME within the first year of follow-up, while the rate of CME at 12 months was 28%.[23]

The highest incidence of CME development occurs usually when silicone oil (SO) is used as tamponade. In these cases, the incidence of CME varies between studies and possibly depends on the interval between the operation and the SO removal,[28] and is reported to be between 14% and 36%.[16,21,29–32] Gharbiya et al reported an incidence of 14.95% in

Table 1 Incidence of Post RRD Repair Surgery Macular Edema Development

Study	Sample Size	Type of Surgery	Tamponade Used	Incidence of ME (%)
Merad et al (2022)[23]	493	PPV +/− Phako IOL	Gas, SO	34% during 1st year, At 28% (12 months)
Yang et al (2018)[16]	58	PPV	SO	36.20%
Starr et al (2021)[24]	1466	SB, PPV or combined PPV/SB	Air, gas, SO	9.60%
Gebler et al (2022)[25]	150	SB, PPV or combined PPV/SB	Gas, SO	18.70%
Gharbiya et al (2022)[26]	107	SB or PPV	Gas	14.95%
Chatziralli et al (2019)[27]	86	PPV	Gas	16.3%

a retrospective study comparing scleral buckling (SB) versus PPV. The results showed that PPV has higher rate of post-operative occurrence of CME compared to SB.[26]

The occurrence of CME seems to be lower in eyes operated using gas tamponades. Starr et al reported a 9.6% incidence in a retrospective multicenter study examining the Primary Retinal Detachment Outcomes database, including 1466 eyes and in which gases were used in 95.3% of cases. He argued that the lower rates of incidence of CME compared to older studies were due to the primary use of vitrectomy for repair, as opposed to the primary use of scleral buckles in the previous studies.[24] However, it is important to note that older studies predominantly used fluorescein angiography for diagnosis, which could lead to an underestimation of the true incidence of CME in these cases, A recent study by Gebler et al, using OCT for diagnostic imaging, included eyes treated primarily with SB (54.2%) or a combination PPV with SB (20.6%). This study reported a higher incidence of CME at 18.7% and identified epiretinal membrane (ERM) and macula-off RRD as potential risk factors.[25]

Mechanism of Cystoid Macular Edema Development

In the normal physiologic state, free leakage of protein and fluid from macular vasculature is prevented by the blood retinal barrier (BRB).[33] This is categorised into either the inner or the outer BRB. The inner BRB is formed by the tight junctions of retinal blood vessel endothelium, whereas the outer BRB is derived from the retinal pigment epithelium (RPE).[34]

The macula is susceptible to oedema due to lax interconnecting fibres in Henle's layer[35] and relative lack of Müller cells, which support fluid absorption from retinal tissue.[36] The specific mechanism of oedema can be categorised into either vasogenic or cytotoxic. Although some retinal vascular conditions primarily cause either one or the other, usually a combination occurs, with vasogenic being the most common pathway (Table 2).

In vasogenic oedemas, the primary defect is in the BRB, resulting in an abnormal accumulation of extracellular fluid.[34] In cytotoxic oedemas, the issue is in retinal parenchymatous cells. An insult to these, whether hypoxic, ischaemic or other, causes intracellular fluid accumulation and secondary breakdown of the BRB.[37]

Both the BRB[38] and blood aqueous barrier (BAB)[39] have been shown to break down in rhegmatogenous retinal detachment (RRD). BRB breakdown itself causes the release of inflammatory mediators and pre-disposes the retina to vasogenic oedema.[40]

Furthermore, the vitreous concentration of pro-inflammatory mediators such as Vascular Endothelial Growth Factor (VEGF)[41] and multiple other cytokines[42] are raised in eyes with RRD. These cause further disruption of the inner BRB, tight junction dysfunction, permeability and leukocyte migration, resulting in vasogenic oedema.

Following surgery for RRD, CME is predominantly thought to be secondary to postoperative subclinical intraocular inflammation.[40] Studies have demonstrated the pro-inflammatory effect of vitrectomy.[43,44] SB also alters the BRB and induces inflammation.[45] Cryotherapy, a common adjunctive treatment, works by causing inflammation and BRB breakdown with consequent scarring for the necessary effect around a retinal break.[46] However, this association has not been demonstrated. On the other hand, pneumatic retinopexy (PnR) is less invasive and inflammatory than vitrectomy or scleral buckling[47] and therefore associated with less post-operative CME.[48,49]

Table 2 Mechanism of Macular Oedema Development

Mechanism	Description
Vasogenic	BRB breakdown causing extracellular fluid accumulation
Cytotoxic	Intracellular fluid accumulation due to cellular insult
Inflammation	Post-surgical inflammation causing BRB breakdown
VEGF and Cytokines	Elevated levels causing further BRB disruption

https://doi.org/10.2147/OPTH.S489859

Overall, these pro-inflammatory surgical factors compound BRB breakdown, resulting in intraretinal capillary serous exudation mainly between the outer plexiform and inner nuclear layers.[40] Elevated prostaglandin levels also likely play a major role in postoperative CME.[50,51]

The postsurgical inflammation theory is also supported by the fact treatments for post-RRD surgery CME are mainly anti-inflammatory. Commonly, either non-steroidal anti-inflammatory drugs (NSAIDs)[50] and/or steroids[52,53] are used.

Other less substantiated theories of post-RRD surgery CME are in relation to loss of cellular function from apoptosis secondary to RRD[54] or secondary to Müller cell dysfunction.[55] Changes in Müller cell morphology and pathologic damage following retinal detachment and re-attachment may cause cytotoxic oedema as they swell.[40]

Risk Factors

Many studies have identified risk factors for CME development following RRD surgery (see Table 3). Most recently, a large multi-institutional study of 1466 primary RRD surgeries found the biggest risk factors for postoperative CME were recurrent RRD, pre-existing PVR, older age and cataract surgery following RRD repair.[24] Of these surgeries, 13.1% were undertaken by primary SB, 50.6% by PPV and 36.3% with primary combined PPV/SB. Notably, this study excluded PnR. Another large study of 1042 patients treated with PPV for RRD,[23] showed similar findings in relation to identifying PVR and post-vitrectomy cataract surgery as risk factors for CME. Similarly, a recent retrospective study, including 708 eyes, found that factors such as prior intraocular surgery, presence of an ERM, number of retinal redetachment surgeries, and PPV surgery were associated with a higher risk of developing CME.[56]

Recurrent RRD

Two large studies of more than 1000 patients each found that a greater number of surgeries increase the risk of postoperative CME.[23] Single surgery leads to a lower number of post-RRD surgery CME in both phakic (OR 0.42,

Table 3 Risk Factors Identified

Study	Risk Factors Identified	Significance (*P*-value)
Starr et al (2021)[24]	Single surgery success (Recurrent RRD)	*P* <0.0001
	Pre-operative PVR	*P* = 0.0400
	Cataract surgery following primary RRD surgery	*P* = 0.0001
	Older Age	*P* = 0.0038
Pole et al (2021)[57]	Recurrent RRD	*P* < 0.0001
	Pre-operative PVR	*P* = 0.09
	Macula-off RRD	*P* = 0.06
	Retinectomy	*P* = 0.009
Chatziralli et al (2019)[27]	Pre-operative PVR	*P* = 0.042
	Macula-off RRD	*P* = 0.027
	Duration of RRD >1 week	*P* = 0.012
	Pseudophakia	*P* = 0.039
Gebler et al (2022)[25]	Epiretinal membrane	*P* <0.001
	Macula-off RRD	*P* = 0.044

95% CI 0.19–0.92) and pseudophakic eyes (OR 0.22, 95% CI 0.12–0.39).[24] Another study of 99 eyes undergoing RRD surgery also found patients with CME underwent greater numbers of surgeries ($P < 0.0001$).[24,57]

Pre-Operative Proliferative Vitreoretinopathy (PVR)

In the largest study detailing risk factors for CME in this context, pre-operative PVR (OR 1.74, 95% 1.03 to 2.95, $p = 0.0400$) was significantly associated with postsurgical CME.[24] This is corroborated by other studies[20,21] assessing postoperative CME rates following PVR detachment surgery, which are much higher. Specifically, PVR-C has been implicated as a major risk factor.[23,57,58]

Cataract Surgery Following Primary RRD Surgery

In a mixed intervention study, rates of CME following RRD surgery were similar in both pseudophakic (9.0%) and phakic (9.9%) cohorts. Following primary RRD repair, 47.4% (400) of the phakic eyes that underwent cataract surgery had a significantly increased postoperative ME risk (OR 7.28, 95% CI 3.78–14.03, $p = 0.0001$).[24] In a study solely on PPV for RRD repair, post-vitrectomy cataract surgery was significantly associated with CME at 12 months (OR, 1.96; 95% CI, 1.06–3.63; $p = 0.03$).[23]

Macula-off RRD

Some studies have shown a higher rate of postsurgical ME in macula-off RRD eyes. A higher rate of postsurgical CME eyes (83%) had a macula-off retinal detachment compared with those without CME (44%) in a study of 99 eyes.[57] In a monocentric retrospective study of 62 consecutive patients, macula-off RRD increased the risk of CME by 4.3 times compared to macula-on RRD regardless of the surgical procedure ($p = 0.04$).[59] Another study of 150 patients with primary RRD undergoing surgery patients with macula-off RRD had more postsurgical ME (26.5% versus 11.1%, $p = 0.044$).[25] In relation to SB, rates of postsurgical CME were also higher in the initially macula-off cohort.[60]

Comparing two larger studies, one found no statistically significant difference in postsurgical CME dependent on pre-operative macula status.[24] In multivariate analysis of another, eyes with macula-off status were at higher risk of postsurgical CME (OR, 1.80; 95% CI, 1.02–3.28; $p = 0.048$). This also matches with the significant finding of worse initial BCVA as a risk factor for CME.[23]

Extensive RRD

In patients with more extensive RRD (defined as macular detachment plus RD of more than three clock hours before surgery), more frequent CME has been reported.[60] Other results also suggest that the greater the extent of RRD, the greater the risk of CME by 1.43 times.[23]

Silicone Oil (SO) Tamponade

In a Korean study of 58 eyes treated with PPV and SO for RRD, 36.2% of patients exhibited postsurgical CME.[16] This high rate supports SO as a risk factor for postsurgical CME. In fact, SO tamponade was found to be a statistically significant risk factor (OR, 2.84; 95% CI, 1.57–5.13; $p < 0.001$)[23] in a large study. In another study of 99 eyes, 64% of patients with postsurgical CME had SO tamponade, compared to only 5% of those without CME.[57]

Surgical Approach

Different techniques have demonstrated inconsistencies regarding incidence rates of CME. In a large subset analysis of 1466 eyes undergoing primary RRD surgery, PPV and PPV/SB had a lower odds ratio linked with postsurgical CME compared to SB, but this showed no statistic significance; Starr et al argued, however, that the lower incidence rates of CME compared to older studies were due to the primary use of vitrectomy for repair, as opposed to the primary use of scleral buckles in previous studies, where subretinal fluid may have persisted much longer.[24] The findings of Gharbiya et al, in a study comparing PPV and SB and including 107 patients, concluded the opposite, with CME higher in the PPV cohort.[26] Gebler et al did, instead, also not find any differences between surgical techniques ($p = 0.494$).[25] In another

https://doi.org/10.2147/OPTH.S489859

study of 62 eyes affected by RRD who underwent SB (20) or PPV (42), CME occurred in 33.3% of the PPV group regardless of epiretinal membrane formation; no CME cases were identified in the SB group.[59]

In relation to PnR, a study evaluating angiographic CME found presence in 11% of PnR eyes as opposed to 29% of SB eyes at 6 weeks post-operatively (p = 0.0005).[49]

Laser Retinopexy

Laser retinopexy has been reported to significantly increase the risk of postsurgical CME in pseudophakic patients undergoing surgery for RRD.[58] Another study comparing to cryotherapy also found endolaser retinopexy was associated with an increased risk of postoperative CME at 12 months (OR, 3.06; 95% CI, 1.33–7.84; $p = 0.01$).[23]

Retinectomy

Rates of retinectomy have also been reported to be significantly higher in the postsurgical CME group (36%) as opposed to those who do not have CME (5%).[57] This also ties in with macula-off detachment and PVR data.

Other Potential Risk Factors

Age

Some studies have found increasing age to be a risk factor. Controlling for surgical modality (PPV/SB), older age was a statistically significant factor in the development of post-RRD surgery CME (OR 1.03 per year, 95% CI 1.01 to 1.05, $p = 0.0038$).[24] A study of 130 eyes undergoing SB also found increasing risk with increasing age.[60] However, another large study focussed on PPV and a smaller retrospective series[57] did not find any association between development of postsurgical CME with age.[23]

Epiretinal Membrane

In a study of 150 patients with primary RRD undergoing surgery, the risk of postsurgical ME was significantly elevated in patients with ERM (42.9%) versus those without (6.9%).[25] However, another large study found no association between ERM and CME.[24]

Diabetes

Diabetes mellitus was not found to be a risk factor in 2 large studies.[23,24] In a study of 1466 eyes,[30] 172 (11.8%) patients were diabetic (type 1 or 2). The risk of postsurgical CME was not found to be significant (OR, 0.83; 95% CI, 0.47–1.48; $p = 0.5258$).

Treatments

The treatment of CME linked to PPV ranges from waiting to several different agents, mostly with an anti-inflammatory effect (Table 4). These treatment options aim to limit the presence of inflammatory components, which are released from the disruption of the BRB. These mediators cause dilation of vessels, elevated permeability of the capillaries, leukocyte attraction, and finally CME.[40,61] Post-PPV CME is believed to be more resistant to treatment than post-cataract surgery CME, with around 69% of eyes not responding to medical treatment alone in a recent study.[7] A distinction can be made for post-RD repair eyes which received SO, as resolution of most cases, which developed after an SO tamponade often occurs spontaneously after SO removal, possibly due to the relieving of both inflammatory and mechanical insults.[30,62] In case of a chronicization of the edema, more invasive treatment is usually needed.[7]

NSAIDs

The most widespread class of drugs used to treat post-operatory CME is Nonsteroidal anti-inflammatory drugs (NSAIDs). Their topical form is considered as a first line. NSAIDs block cyclooxygenase-1 and cyclooxygenase-2 and, thus, prostaglandin. As a result, the ocular tissue penetrance of topical NSAIDs is a treatment of choice when dealing with CME, and they are effective even for chronic postoperative cases.[70,71] Only a few articles in the literature are centered around CME after RRD, with none reporting about the use of topical NSAID alone. Most of the evidence does, in fact, derive from post-cataract surgery studies. A small retrospective case–control series including 25 cases of

Table 4 Treatment Approaches and Efficacy

Treatment Type	Study	Sample Size	Success Rate (%) (N)	Comments
Topical NSAIDs	Pole et al (2021)[57]	25	25% (5)	Limited efficacy
Intravitreal Triamcinolone	Gao et al (2012)[63]	2	100% (2)	SO filled eyes Recurrence after 2 months in both patients
	Alam et al (2016)[64]	39	Unknown % Significant decrease in mean CFT at 3, 6 and 12 months	VA gain noted at 1 month but not sustained
Dexamethasone Implant 0.7mg (DEX-I)	Thanos et al (2018)[65]	17	100% (17)	All patients developed recurrence of ME at 3 months requiring retreatment
	Chatziralli et al (2021)[27]	14	93% (13)	12 month follow up
	Pole et al (2021)[57]	4	0% (0)	Small sample size. No significant change in CST ($P = 0.125$)
	Freissinger et al (2020)[66]	15	46% (7)	CDVA gain > 1 line
	Banerjee et al (2017)[67]	69	57.3% (40)	The proportion of eyes with ME in the adjunct group was 42.7%, compared with 67.2% in the control group ($P = 0.004$)
Fluocinolone Acetonide (0.19 mg) Implant	Alfaqawi et al (2018)[68]	1	100% (1)	Case report, ME-free for 13 months
	Motloch et al (2024)[69]	49	71.4% (35)	All eyes had received DEX implants beforehand

CME developing post-RRD-repair surgery showed a resolution of only 25% of cases with a combined topical treatment of NSAID and corticosteroids.[57] For eyes that have been vitrectomized, the efficacy of topical treatment seems to be usually limited.[24,57,72] More studies are therefore needed to assess the efficacy of topical NSAID in eyes developing CME after RD repair surgery.

Corticosteroids

Corticosteroids are the most reported treatment in the literature for post-PPV CME and seem to be the most frequently used as well. They effectively minimize inflammation and cellular proliferation, as they also block prostaglandin and leukotriene production, and therefore increase the tightness of the BRB.[73]

Topical application is not very present in the literature, as no study reported about its use for repaired RRD and CME. It has been, however, demonstrated that, in eyes developing CME after cataract surgery, topical Prednisolone acetate, when used in combination with topical NSAIDs (such as Ketorolac), seems to be more effective than the use of single agents for acute CME.[40,74]

Periocular and intravitreal injections seem to be more effective for CME treatment compared to systemic steroids but are mostly reserved for cases of CME that do not respond to topical therapy.[75] Among the intravitreal options, triamcinolone has been considered as possible treatment. Gao et al studied its use in eyes filled with SO as an option for post-operative CME but showed a recurrence of the CME 2 months after administration. In one instance a repeated injection was administered with good result, but the sample was limited to 2 patients.[63] Alam et al evaluated the outcomes of intravitreal triamcinolone acetonide for chronic ME after PPV in a retrospective study, and found that it was

effective in reducing CME, with, however, only a short-term VA improvement reported.[64] Some experimental studies have, however, shown a decrease in the vitreous half-life of different drugs after PPV, and intravitreal triamcinolone acetonide is more rapidly cleared in vitrectomized eyes.[76,77]

Another major option is the intravitreal injection of a dexamethasone implant (DEX-I) which has a 25-fold higher anti-inflammatory potency than cortisol.[76,78] Dexamethasone has a short half-life and its utility has previously been limited by this, hence the need for a slow-release implant such as DEX-I.[79] The efficacy of dexamethasone is furthermore enhanced by its high hydrophilicity, allowing for higher vitreous concentrations compared to other corticosteroids.[80] It is considered to have similar results between non-vitrectomized and vitrectomized eyes in decreasing central retinal thickness and improving visual acuity.[81] The implant slowly releases dexamethasone, gradually degrading into water and carbon dioxide, up to a complete degradation at almost six months post-insertion. This has also shown to be effective in chronic post RD repair surgery CME.[65] A recent retrospective study including 86 eyes post-vitrectomy for RD repair, of which 14 experiencing postoperative CME and been treated with DEX-I, showed that these achieved a 71% resolution rate with a single injection, and showed a significant improvement in best-corrected visual acuity (BCVA) after one year.[27] Its long-term efficacy has also been proven despite recurrence, indicating that repeated intravitreal injections may be necessary.[57,66]

Two large retrospective multicenter studies (EPISODIC 1 and 2) with 150 patients in total and assessing the effectiveness of intravitreal dexamethasone implants for treating postsurgical CME demonstrated functional and anatomical improvements, but reported poorer outcomes in the postoperative CME group due to RRD compared to the post-cataract surgery group.[82,83] They postulated that in cases of vitrectomy for RD or ERM peeling, the presence of an underlying macular disease represented a poor prognosis factor of functional effectiveness. The studies did, however, mostly include eyes, which developed CME after cataract surgery (82% and 58% of all eyes) and included only 9 patients who developed CME after an RD repair surgery.

The efficacy of DEX-I in post-RD repair eyes was further corroborated by a 2-year, large, multicenter, prospective, randomized, clinical trial investigating the clinical efficacy of DEX-I in cases of RRD with PVR grade C, showing a greater reduction in CME in patients treated with DEX-I at 6 months compared to the placebo group, although no difference in primary anatomic success rate was observed.[67]

Finally, The ILUvien study investigated the safety and efficacy of an additional corticosteroid, namely a long-acting 0.19 mg fluocinolone acetonide implant, in treating patients with refractory CME post-RD repair surgery. This included 49 patients and demonstrated that the implant improved BCVA and reduced the CRT of the eyes involved.[69] This was corroborated by a case report, in which a patient, unresponsive to prior interventions with intravitreal triamcinolone and DEX-I, was shown to be CME-free for a duration of 13-month follow-up after receiving the fluocinolone acetonide implant.[68]

Others

Agents such as carbonic anhydrase inhibitors and intravitreal anti-VEGF have been tested and considered for the treatment of post-operative pseudophakic CME. However, there is no evidence to support the effective use of these treatments for the treatment of CME following retinal RRD surgery.

Conclusions

CME is a significant complication following RRD repair surgery, affecting visual recovery and overall patient outcome. With a complex pathogenesis and factors involved in its development, it remains a challenge for vitreoretinal surgeons.

Treatment approaches include topical NSAIDs and corticosteroids, but this evidence is extrapolated from CME after cataract surgery and we lack strong evidence of their role in CME after RRD repair. Periocular and intravitreal corticosteroids, such as triamcinolone and dexamethasone implants, have shown more promise in the treatment of persistent CME. Recently, also Fluocinolone Acetonide implants demonstrated encouraging results, as pointed out in the Iluvien study. However, the management of persistent CME remains challenging and often requires repeated interventions.

Further studies are essential to better understand the mechanisms underlying CME and to develop more effective treatment strategies. For example, looking into other biomarkers of subclinical postoperative inflammation and their association with CME. Inconsistencies in findings highlight the need for more research on the etiology of post-operative CME.

Evaluating current therapies is crucial for assessing their efficacy, especially where there remain large gaps in the literature (eg fluocinolone). Clinical trials for therapies targeting novel pathways such as IL-6 in relation to other inflammatory causes of macular oedema are underway and their application to patients with CME after RRD repair surgery may significantly improve patient outcomes.[84]

Disclosure

The authors report no conflicts of interest in this work.

References

1. Tandias R, Garg I, Duich MJ, et al. Assessment of microvascular changes after rhegmatogenous retinal detachment repair using wide-field swept-source optical coherence tomography angiography. *Ophthalmic Surg Lasers Imaging Retina*. 2024;55:310–317. doi:10.3928/23258160-20240130-01
2. McKay KM, Vingopoulos F, Wang JC, et al. Retinal microvasculature changes after repair of macula-off retinal detachment assessed with optical coherence tomography angiography. *Clin Ophthalmol*. 2020;14:1759–1767. doi:10.2147/OPTH.S214623
3. Spaide RF. Retinal vascular cystoid macular edema: review and new theory. *Retina*. 2016;36:1823–1842. doi:10.1097/IAE.0000000000001158
4. Mitry D, Charteris DG, Fleck BW, Campbell H, Singh J. The epidemiology of rhegmatogenous retinal detachment: geographical variation and clinical associations. *Br J Ophthalmol*. 2010;94:678–684. doi:10.1136/bjo.2009.157727
5. Bonnet M. Prognosis of cystoid macular edema after retinal detachment repair. *Graefes Arch Clin Exp Ophthalmol*. 1986;224:13–17. doi:10.1007/BF02144125
6. Sabates NR, Sabates FN, Sabates R, Lee KY, Ziemianski MC. Macular changes after retinal detachment surgery. *Am J Ophthalmol*. 1989;108:22–29. doi:10.1016/S0002-9394(14)73255-6
7. Souissi S, Allou V, Trucchi L, et al. Macular oedema secondary to rhegmatogenous retinal detachment repair: risk factors for resistance to first-line therapy and long-term response to dexamethasone intravitreal implant. *Eye*. 2024;38:1155–1161. doi:10.1038/s41433-023-02852-x
8. Soares RR, Mahmoudzadeh R, Salabati M, et al. Epiretinal membrane surgery after retinal detachment repair: visual acuity outcomes and OCT analysis. *Ophthalmol Retina*. 2022;6:49–57. doi:10.1016/j.oret.2021.03.013
9. Hassan A, Abdel-Radi M, Aly MOM, Alattar S. Correlation between multifocal electroretinogram and optical coherence tomography findings with visual acuity after vitrectomy surgery for retinal detachment: an observational study. *Int J Retina Vitr*. 2024;10:10. doi:10.1186/s40942-024-00527-7
10. Quarta A, Gironi M, Ruggeri ML, et al. Baseline imaging characteristics and early structural changes in macula on rhegmatogenous retinal detachment. *Sci Rep*. 2024;14:1370. doi:10.1038/s41598-024-51183-8
11. Anguita R, Charteris D. Visual loss in surgical retinal disease: retinal imaging and photoreceptor cell counts. *Br J Ophthalmol*. 2023;107:1583–1589. doi:10.1136/bjo-2022-321845
12. Shah YS, Abidi M, Ahmed I, et al. Risk factors associated with cystoid macular edema among patients undergoing primary repair of rhegmatogenous retinal detachment. *Ophthalmol Retina*. 2023;2023:1.
13. Steel D, Fraser S. Retinal detachment. *BMJ Clin Evid*. 2008;2008.
14. Delolme MP, Dugas B, Nicot F, et al. Anatomical and functional macular changes after rhegmatogenous retinal detachment with macula off. *Am J Ophthalmol*. 2012;153:128–136. doi:10.1016/j.ajo.2011.06.010
15. Meredith TA, Reeser FH, Topping TM, Aaberg TM. Cystoid macular edema after retinal detachment surgery. *Ophthalmology*. 1980;87:1090–1095. doi:10.1016/S0161-6420(80)35114-2
16. Yang JY, Kim HK, Kim SH, Kim SS. Incidence and risk factors of cystoid macular edema after vitrectomy with silicone oil tamponade for retinal detachment. *Korean J Ophthalmol*. 2018;32:204–210. doi:10.3341/kjo.2017.0050
17. Ahmadieh H, Moradian S, Faghihi H, et al. Anatomic and visual outcomes of scleral buckling versus primary vitrectomy in pseudophakic and aphakic retinal detachment: six-month follow-up results of a single operation--report no. 1. *Ophthalmology*. 2005;112:1421–1429. doi:10.1016/j.ophtha.2005.02.018
18. de Nie KF, Crama N, Tilanus MA, Klevering BJ, Boon CJ. Pars plana vitrectomy for disturbing primary vitreous floaters: clinical outcome and patient satisfaction. *Graefes Arch Clin Exp Ophthalmol*. 2013;251:1373–1382. doi:10.1007/s00417-012-2205-3
19. Miyake K, Miyake Y, Maekubo K, Asakura M, Manabe R. Incidence of cystoid macular edema after retinal detachment surgery and the use of topical indomethacin. *Am J Ophthalmol*. 1983;95:451–456. doi:10.1016/0002-9394(83)90264-7
20. Odrobina DC, Michalewska Z, Michalewski J, Nawrocki J. High-speed, high-resolution spectral optical coherence tomography in patients after vitrectomy with internal limiting membrane peeling for proliferative vitreoretinopathy retinal detachment. *Retina*. 2010;30:881–886. doi:10.1097/IAE.0b013e3181c96952
21. Kiss CG, Richter-Müksch S, Sacu S, Benesch T, Velikay-Parel M. Anatomy and function of the macula after surgery for retinal detachment complicated by proliferative vitreoretinopathy. *Am J Ophthalmol*. 2007;144:872–877. doi:10.1016/j.ajo.2007.08.001
22. Schocket LS, Witkin AJ, Fujimoto JG, et al. Ultrahigh-resolution optical coherence tomography in patients with decreased visual acuity after retinal detachment repair. *Ophthalmology*. 2006;113:666–672. doi:10.1016/j.ophtha.2006.01.003
23. Merad M, Vérité F, Baudin F, et al. Cystoid macular edema after rhegmatogenous retinal detachment repair with pars plana vitrectomy: rate, risk factors, and outcomes. *J Clin Med*. 2022;11:4914. doi:10.3390/jcm11164914
24. Starr MR, Cai L, Obeid A, et al. Risk factors for presence of cystoid macular edema following rhegmatogenous retinal detachment surgery. *Curr Eye Res*. 2021;46:1867–1875. doi:10.1080/02713683.2021.1929330

25. Gebler M, Pfeiffer S, Callizo J, et al. Incidence and risk factors for macular oedema after primary rhegmatogenous retinal detachment surgery: a prospective single-centre study. *Acta Ophthalmol*. 2022;100:295–301. doi:10.1111/aos.14940
26. Gharbiya M, Visioli G, Iannetti L, et al. Comparison between scleral buckling and vitrectomy in the onset of cystoid macular edema and epiretinal membrane after rhegmatogenous retinal detachment repair. *Retina*. 2022;42:1268–1276. doi:10.1097/IAE.0000000000003475
27. Chatziralli I, Theodossiadis G, Dimitriou E, Kazantzis D, Theodossiadis P. Macular edema after successful pars plana vitrectomy for rhegmatogenous retinal detachment: factors affecting edema development and considerations for treatment. *Ocul Immunol Inflamm*. 2021;29:187–192. doi:10.1080/09273948.2019.1652330
28. Choudhary MM, Choudhary MM, Saeed MU, Ali A. Removal of silicone oil: prognostic factors and incidence of retinal redetachment. *Retina*. 2012;32:2034–2038. doi:10.1097/IAE.0b013e3182562045
29. Bae SH, Hwang JS, Yu HG. Comparative analysis of macular microstructure by spectral-domain optical coherence tomography before and after silicone oil removal. *Retina*. 2012;32:1874–1883. doi:10.1097/IAE.0b013e318246907c
30. Karahan E, Tuncer I, Zengin MO, Kucukerdonmez C, Kaynak S. Spontaneous resolution of macular edema after silicone oil removal. *Int J Ophthalmol*. 2014;7:1005–1009. doi:10.3980/j.issn.2222-3959.2014.06.17
31. Rashad MA, Mohamed AA, Ahmed AI. Value of optical coherence tomography in the detection of macular pathology before the removal of silicone oil. *Clin Ophthalmol*. 2016;10:121–135. doi:10.2147/OPTH.S90449
32. Lo DM, Flaxel CJ, Fawzi AA. Macular effects of silicone oil tamponade: optical coherence tomography findings during and after silicone oil removal. *Curr Eye Res*. 2017;42:98–103. doi:10.3109/02713683.2016.1146776
33. Scholl S, Kirchhof J, Augustin AJ. Pathophysiology of macular edema. *Ophthalmologica*. 2010;224(Suppl 1):8–15. doi:10.1159/000315155
34. Cunha-Vaz J. The blood-retinal barrier in the management of retinal disease: EURETINA award lecture. *Ophthalmologica*. 2017;237:1–10. doi:10.1159/000455809
35. Tranos PG, Wickremasinghe S, Stangos N, et al. Macular edema. *Surv Ophthalmol*. 2004;49:470–490. doi:10.1016/S0039-6257(04)00109-2
36. Reichenbach A, Wurm A, Pannicke T, et al. Müller cells as players in retinal degeneration and edema. *Graefes Arch Clin Exp Ophthalmol*. 2007;245:627–636. doi:10.1007/s00417-006-0516-y
37. Parikh VS, Modi YS, Au A, et al. Nonleaking cystoid macular edema as a presentation of hydroxychloroquine retinal toxicity. *Ophthalmology*. 2016;123:664–666. doi:10.1016/j.ophtha.2015.09.011
38. Tsuboi S, Pederson JE. Permeability of the blood-retinal barrier to carboxyfluorescein in eyes with rhegmatogenous retinal detachment. *Invest Ophthalmol Visual Sci*. 1987;28:96–100.
39. Little BC, Ambrose VM. Blood-aqueous barrier breakdown associated with rhegmatogenous retinal detachment. *Eye*. 1991;5(Pt 1):56–62. doi:10.1038/eye.1991.11
40. Romano V, Angi M, Scotti F, et al. Inflammation and macular oedema after pars plana vitrectomy. *Mediators Inflamm*. 2013;2013:971758. doi:10.1155/2013/971758
41. Hasanpour H, Kenney MC, Kuppermann BD, et al. Vitreal concentrations of vascular endothelial growth factor in patients with rhegmatogenous retinal detachment. *J Clin Med*. 2023;12:1259. doi:10.3390/jcm12041259
42. Conart JB, Augustin S, Remen T, et al. Vitreous cytokine expression profiles in patients with retinal detachment. *J Fr Ophtalmol*. 2021;44:1349–1357. doi:10.1016/j.jfo.2021.04.007
43. Kawai K, Onouchi H, Yageta H, et al. The simple vitrectomy caused intraocular inflammation in the rabbit. *Invest Ophthalmol Visual Sci*. 2007;48:2214.
44. Inoue Y, Kadonosono K, Yamakawa T, et al. Surgically-induced inflammation with 20-, 23-, and 25-gauge vitrectomy systems: an experimental study. *Retina*. 2009;29:477–480. doi:10.1097/IAE.0b013e31819a6004
45. Sebag J. *Vitreous Anatomy, Aging, and Anomalous Posterior Vitreous Detachment*. Vol. 4. Elsevier; 2010:307–315.
46. Cryopexy FK. *Vitreoretinal Surgery: Strategies and Tactics*. Springer; 2016:259–262.
47. Wong S, Ramkissoon Y, Charteris D. *Rhegmatogenous Retinal Detachment. Encyclopedia of the Eye*. Amsterdam: Elsevier Academic Press; 2010.
48. Lisle C, Mortensen KK, Sjølie AK. Pneumatic retinopexy. A long term follow-up study. *Acta Ophthalmol Scand*. 1998;76:486–490. doi:10.1034/j.1600-0420.1998.760418.x
49. Tunc M, Lahey JM, Kearney JJ, Lewis JM, Francis R. Cystoid macular oedema following pneumatic retinopexy vs scleral buckling. *Eye*. 2007;21:831–834. doi:10.1038/sj.eye.6702431
50. Miyake K. Indomethacin in the treatment of postoperative cystoid macular edema. *Surv Ophthalmol*. 1984;28:554–568. doi:10.1016/0039-6257(84)90239-X
51. Miyake K, Ibaraki N. Prostaglandins and cystoid macular edema. *Surv Ophthalmol*. 2002;47(Suppl 1):S203–218. doi:10.1016/S0039-6257(02)00294-1
52. Valldeperas X, Romano MR, Wong D. Resolution of cystoid macular oedema after retinal detachment repair: is intravitreal triamcinolone useful? *Eye*. 2006;20:1321–1322. doi:10.1038/sj.eye.6702188
53. Bonfiglio V, Fallico MR, Russo A, et al. Intravitreal dexamethasone implant for cystoid macular edema and inflammation after scleral buckling. *Eur J Ophthalmol*. 2015;25:e98–e100. doi:10.5301/ejo.5000599
54. Berglin L, Algvere PV, Seregard S. Photoreceptor decay over time and apoptosis in experimental retinal detachment. *Graefes Arch Clin Exp Ophthalmol*. 1997;235:306–312. doi:10.1007/BF01739640
55. Fisher SK, Lewis GP. Müller cell and neuronal remodeling in retinal detachment and reattachment and their potential consequences for visual recovery: a review and reconsideration of recent data. *Vision Res*. 2003;43:887–897. doi:10.1016/S0042-6989(02)00680-6
56. Shah YS, Abidi M, Ahmed I, et al. Risk factors associated with cystoid macular edema among patients undergoing primary repair of rhegmatogenous retinal detachment. *Ophthalmol Retina*. 2024;8:456–464. doi:10.1016/j.oret.2023.11.013
57. Pole C, Chehaibou I, Govetto A, et al. Macular edema after rhegmatogenous retinal detachment repair: risk factors, OCT analysis, and treatment responses. *Int J Retina Vitr*. 2021;7:9. doi:10.1186/s40942-020-00254-9
58. Bernabei F, Marcireau I, Frongia F, et al. Risk factors of cystoid macular edema after pars plana vitrectomy for pseudophakic retinal detachment. *Ophthalmol Ther*. 2023;12:1737–1745. doi:10.1007/s40123-023-00705-0
59. Motta L, Frisina R, Ripa M, et al. Postoperative complications after successful primary rhegmatogenous retinal detachment repair. *BMC Ophthalmol*. 2023;23:77. doi:10.1186/s12886-023-02824-5

60. Lai TT, Huang JS, Yeh PT. Incidence and risk factors for cystoid macular edema following scleral buckling. *Eye*. 2017;31:566–571. doi:10.1038/eye.2016.264
61. Yilmaz T, Cordero-Coma M, Gallagher MJ. Ketorolac therapy for the prevention of acute pseudophakic cystoid macular edema: a systematic review. *Eye*. 2012;26:252–258. doi:10.1038/eye.2011.296
62. Kontou EP, Karakosta C, Kounas K, et al. Macular edema following silicone oil tamponade for retinal detachment: a literature review. *Cureus*. 2023;15:e51233. doi:10.7759/cureus.51233
63. Gao H, Ryu C. Intravitreal triamcinolone injection in eyes filled with silicone oil for treatment of cystoid macular edema. *Invest Ophthalmol Visual Sci*. 2012;53:907.
64. Alam MR, Arcinue CA, Mendoza NB, Freeman WR. Recalcitrant cystoid macular edema after pars plana vitrectomy. *Retina*. 2016;36:1244–1251. doi:10.1097/IAE.0000000000000892
65. Thanos A, Todorich B, Yonekawa Y, et al. Dexamethasone intravitreal implant for the treatment of recalcitrant macular edema after rhegmatogenous retinal detachment repair. *Retina*. 2018;38:1084–1090. doi:10.1097/IAE.0000000000001720
66. Freissinger S, Vounotrypidis E, Wolf A, et al. Evaluation of functional outcomes and OCT-biomarkers after intravitreal dexamethasone implant for postoperative cystoid macular edema in vitrectomized eyes. *J Ophthalmol*. 2020;2020:3946531. doi:10.1155/2020/3946531
67. Banerjee PJ, Quartilho A, Bunce C, et al. Slow-release dexamethasone in proliferative vitreoretinopathy: a prospective, randomized controlled clinical trial. *Ophthalmology*. 2017;124:757–767. doi:10.1016/j.ophtha.2017.01.021
68. Alfaqawi F, Sarmad A, Ayesh K, Mitra A, Sharma A. Intravitreal Fluocinolone Acetonide (ILUVIEN) implant for the treatment of refractory cystoid macular oedema after retinal detachment repair. *Turk J Ophthalmol*. 2018;48:155–157. doi:10.4274/tjo.34966
69. Motloch K, Soler V, Delyfer M-N, et al. Efficacy and safety of 0.19-mg fluocinolone acetonide implant in postoperative cystoid macular edema after pars plana vitrectomy: the ILUvien in postoperative CYstoid macular eDema study. *Ophthalmol Retina*. 2024;8:1181–1191. doi:10.1016/j.oret.2024.07.004
70. Flach AJ, Dolan BJ, Irvine AR. Effectiveness of ketorolac tromethamine 0.5% ophthalmic solution for chronic aphakic and pseudophakic cystoid macular edema. *Am J Ophthalmol*. 1987;103:479–486. doi:10.1016/S0002-9394(14)74268-0
71. Flach AJ, Kraff MC, Sanders DR, Tanenbaum L. The quantitative effect of 0.5% ketorolac tromethamine solution and 0.1% dexamethasone sodium phosphate solution on postsurgical blood-aqueous barrier. *Arch Ophthalmol*. 1988;106:480–483. doi:10.1001/archopht.1988.01060130526028
72. Kohli P, Mishra C. Commentary: treatment of postoperative cystoid macular edema in vitrectomized eyes: an enigma. *Indian J Ophthalmol*. 2023;71:179–181. doi:10.4103/ijo.IJO_1956_22
73. Ahuja M, Dhake AS, Sharma SK, Majumdar DK. Topical ocular delivery of NSAIDs. *AAPS J*. 2008;10:229–241. doi:10.1208/s12248-008-9024-9
74. Heier JS, Topping TM, Baumann W, Dirks MS, Chern S. Ketorolac versus prednisolone versus combination therapy in the treatment of acute pseudophakic cystoid macular edema. *Ophthalmology*. 2000;107:2034–2038; discussion 2039. doi:10.1016/S0161-6420(00)00365-1
75. Ritter M, Sacu S, Matt G, et al. Use of systemic steroid after successful macular surgery in eyes with epiretinal membrane: a randomized, controlled clinical study. *Eye*. 2011;25:1284–1293. doi:10.1038/eye.2011.190
76. Chawan-Saad J, Wu M, Wu A, Wu L. Corticosteroids for Diabetic Macular Edema. *Taiwan J Ophthalmol*. 2019;9:233–242. doi:10.4103/tjo.tjo_68_19
77. Chin HS, Park TS, Moon YS, Oh JH. Difference in clearance of intravitreal triamcinolone acetonide between vitrectomized and nonvitrectomized eyes. *Retina*. 2005;25:556–560. doi:10.1097/00006982-200507000-00002
78. Pignatelli F, Nacucchi A, Niro A, et al. Intravitreal dexamethasone implant at the time of silicon oil removal to treat persistent macular edema after rhegmatogenous retinal detachment repair. *J Clin Med*. 2023;12:1697. doi:10.3390/jcm12041697
79. Graham RO, Peyman GA. Intravitreal injection of dexamethasone: treatment of experimentally induced endophthalmitis. *Archives of Ophthalmology*. 1974;92:149–154. doi:10.1001/archopht.1974.01010010155016
80. Kwak HW, D'Amico DJ. Evaluation of the retinal toxicity and pharmacokinetics of dexamethasone after intravitreal injection. *Archives of Ophthalmology*. 1992;110:259–266. doi:10.1001/archopht.1992.01080140115038
81. Chang-Lin JE, Burke JA, Peng Q, et al. Pharmacokinetics of a sustained-release dexamethasone intravitreal implant in vitrectomized and nonvitrectomized eyes. *Invest Ophthalmol Vis Sci*. 2011;52:4605–4609. doi:10.1167/iovs.10-6387
82. Bellocq D, Pierre-Kahn V, Matonti F, et al. Effectiveness and safety of dexamethasone implants for postsurgical macular oedema including Irvine-Gass syndrome: the EPISODIC-2 study. *Br J Ophthalmol*. 2017;101:333–341. doi:10.1136/bjophthalmol-2016-308544
83. Bellocq D, Korobelnik J-F, Burillon C, et al. Effectiveness and safety of dexamethasone implants for post-surgical macular oedema including Irvine-Gass syndrome: the EPISODIC study. *Br J Ophthalmol*. 2015;99:979–983. doi:10.1136/bjophthalmol-2014-306159
84. Suhler EB, Steeples L, Elze MC, et al. IL-6 inhibition with vamikibart in patients with uveitic macular edema: Phase 3 MEERKAT and SANDCAT trials. *Invest Ophthalmol Visual Sci*. 2024;65:2609.