Impact of residual retinal fluid after anti-VEGF therapy for DME and ME secondary to RVO: a systematic review

Andrew Mihalache BMSc(C)[1], Nikhil S. Patil MD(C)[2], Arjan S. Dhoot BMSc MD(C)[3], Marko M. Popovic MD MPH(C)[4], Rajeev H. Muni MD MSc FRCSC[4,5], Peter J. Kertes MD CM FRCSC[4,6]

[1]Faculty of Science, University of Western Ontario; [2]Michael DeGroote School of Medicine, McMaster University; [3]Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada; [4]Department of Ophthalmology and Vision Sciences, University of Toronto; [5]Department of Ophthalmology, St. Michael's Hospital/Unity Health Toronto; [6]John and Liz Tory Eye Centre, Sunnybrook Health Sciences Centre

Purpose

- While anti-vascular endothelial growth factor (VEGF) treatment regimens typically aim for complete resolution of retinal fluid, recent findings in neovascular age-related macular degeneration have suggested that residual subretinal fluid may not hinder visual acuity.
- The association between residual retinal fluid and visual acuity for diabetic macular edema (DME) and macular edema (ME) secondary to retinal vein occlusion (RVO) is not well established.

Methods

- We conducted a systematic literature search on Cochrane Library, Ovid MEDLINE, and EMBASE for peer-reviewed articles reporting on visual acuity outcomes stratified by SRF, IRF, or any retinal fluid at final follow-up after intravitreal anti-VEGF injection for the treatment of DME or ME secondary to RVO.

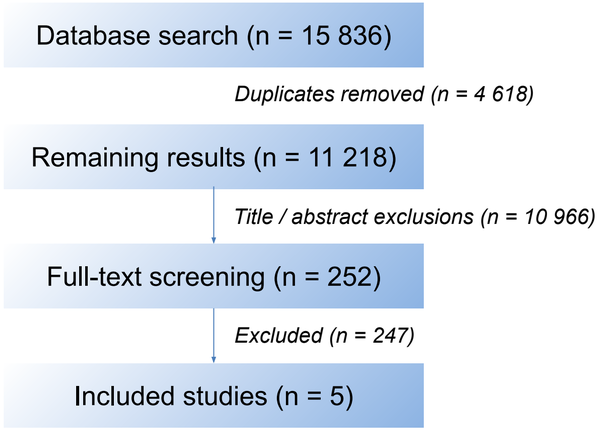

Table 1. Final Outcomes of Included Studies

Author, Year	Study Arm	Final BCVA (ETDRS) (mean, SD)	Change in BCVA (ETDRS) (mean, SD)	Final Retinal Thickness (μm) (mean, SD)	Change in RT (μm) (mean, SD)	Final Follow-up (Months) (mean, SD)
Tomita 2019	Fluid	77.5, 7	NA	230, 27.9	NA	1
	No Fluid	73, 17	NA	215, 37.2	NA	
Kida 2019	Fluid	62.26, 20.09	NA	NA	NA	35.6, 14.0
	No Fluid	62.75, 22.89	NA	NA	NA	35.1, 13.8
Busch 2019	Fluid	74.5, 12.35	0.008, 0.09 LogMAR	348, 61	NA	8.5, 5.6
	No Fluid	78.4, 10.4	0.169, 0.188 LogMAR	249, 38	NA	
Gurudas 2022	Fluid	63.2, 17.8	6.4, 21.2	471.6, 146.3	−218.0, 238.2	23
	Recurrent ME	65.8, 17.6	13.1, 19.6	331.3, 124.2	−401.0, 247.1	
	No Fluid	73.3, 15.3	16.8, 16.2	248.9, 32.9	−370.2, 179.0	
Halim 2021	Fluid	NA	8.6, 9.5	NA	−184.9, 142.1	12
	Rebound	NA	5.6, 8.2	NA	−139.1, 105.0	
	No Fluid	NA	11.0, 8.4	NA	−210.6, 116.7	

Results

- Five studies reporting on 613 eyes were included.
- Two observational studies on ME secondary to RVO and one on DME found no significant differences between eyes with and without residual retinal fluid for final BCVA after anti-VEGF treatment.
- One RCT found that eyes with residual retinal fluid had significantly worse final BCVA in ME secondary to RVO (n=161, $p<0.001$).
- Another RCT found similar changes in BCVA from baseline between eyes with and without residual retinal fluid for DME (n=123, $p=0.18$).
- No studies stratified outcomes based on the presence of subretinal or intraretinal fluid.

Conclusion

- There is a paucity of evidence examining the impact of residual retinal fluid on visual acuity in DME and ME secondary to RVO.
- The limited evidence suggests that aggressive fluid resolution is worthwhile in these patients, however, further RCT evidence is needed for more nuanced treatments.

Conflicts of Interest

A.M: None Declared, A.H: None Declared, N.P: None Declared, M.P Conflict with PSI Foundation, P.K Conflict with Bayer, Roche, Novartis; Equity owner – ArcticDx, R.M Conflict with Bayer, Novartis