Predictors of visual outcome and the role of early vitrectomy in Streptococcal endophthalmitis

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Short running title: Streptococcal endophthalmitis outcomes

Received 21 April 2017; accepted 18 September 2017

Conflict of interest: None

Funding sources: None

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: [10.1111/ceo.13077](https://doi.org/10.1111/ceo.13077)

Ethics approval: This study conformed to the tenets of the Declaration of Helsinki, and has been approved by the Ethics Committee of the Royal Victorian Eye and Ear Hospital, Melbourne, Australia.

ABSTRACT

Importance: *Streptococcus* endophthalmitis has devastating sequelae. This study aims to identify factors which may be targeted to optimise patient outcomes.

Background: This study investigated characteristics influencing visual outcomes, and the role of early vitrectomy.

Design: Retrospective observational case series of consecutive patients

Participants: All patients with a culture-positive diagnosis of *Streptococcal* endophthalmitis treated at a tertiary ophthalmology referral centre between July 1997 and February 2012

Method: Patient records were reviewed and data collected on their presentation, examination, microbiology results, procedures and final outcome.

Main outcome measures: Visual acuity (VA) and enucleation/evisceration

Results: Of 101 patients, 35.6% presented with a VA of hand movements (HM) and 42.6% with light perception (LP). Final VA was poor (6/60 or worse) in 77.6%, and 24.7% were enucleated/eviscerated. Presenting VA of LP or worse ($p=0.008$), no view of fundus ($p=0.001$), large number of organisms ($p<0.001$), recognition of *Streptococci* on gram stain ($p=0.010$), heavy growth on culture ($p<0.001$), and more intravitreal injections ($p=0.038$) were significantly associated with poor visual outcome (6/60 or worse). Presenting VA of LP or worse ($p=0.042$) and non-viridans *Streptococci* ($p=0.002$) were significantly associated with enucleation/evisceration. Fifteen patients (14.9%) had early vitrectomy within 48 hours which was not associated with poor final VA or removal of the eye ($p=1.000$).

Conclusions: Early vitrectomy did not influence visual outcome in this cohort. Microbiology results were useful in predicting poor outcomes, and may allow clinicians to make early treatment decisions and provide prognostic information for patients.

Keywords: infection, microbiology, treatment surgery, retina

INTRODUCTION

Streptococcus species is an important pathogen in endophthalmitis. It is the leading cause of endophthalmitis in late bleb-related endophthalmitis (30-57%), following intravitreal injections (30.8%), and is a contributor to post-traumatic endophthalmitis (21.6-26.9%).¹⁻³ It is also the second most common cause of endophthalmitis following cataract surgery (8.2-11.5%), and is an important pathogen in endogenous endophthalmitis.^{4, 5} *Streptococcal* endophthalmitis often presents with florid inflammation and poor visual acuity, and have worse visual outcomes compared to *Staphylococcal* endophthalmitis.⁶⁻¹⁰

Currently, most experts advocate intravitreal tap and injection of antibiotics as first line treatment for infective endophthalmitis. While outcomes have improved since intravitreal antibiotics were introduced, there is still controversy regarding other aspects of management such as vitrectomy. Despite this current practise, the role and timing of vitrectomy, the use of systemic antibiotics and intravitreal steroids remain unclear.¹¹⁻¹³

This study looks at the spectrum of *Streptococcal* endophthalmitis presenting to a tertiary referral centre over 15 years, from 1997 to 2012. It aims to describe the range of clinical presentation, microbiological results, management and outcomes. The study also looks into factors of presentation, investigation and management that may determine visual outcomes and the likelihood of removal of the eye, in particular the role of early vitrectomy.

METHODS

Consecutive patients who presented to a single tertiary referral centre, the Royal Victorian Eye and Ear Hospital (RVEEH, Melbourne, Australia) between July 1997 and February 2012 with culture-positive *Streptococcal* endophthalmitis were included. The Human Research and Ethics Committee of RVEEH approved the study, and the conduct of the study followed the tenets of the Declaration of Helsinki. Medical records of these patients were reviewed. Examination findings at presentation were gathered, including presenting visual acuity, presence of hypopyon, and whether the fundus was visible on examination. The putative cause was recorded and medical co-morbidities were noted, including diabetes status.

All cases of clinically suspected endophthalmitis underwent a strict protocol of aqueous and vitreous taps, followed by immediate standard intravitreal antibiotic administration (Ceftazidime 2mg/0.1ml, Vancomycin 1mg/0.1ml) – known as a “tap and inject”. Under sterile technique and local anaesthetic, 0.05-0.10ml of aqueous humour was aspirated using a 30-gauge needle mounted on a 1ml syringe. Vitreous tap was performed using a 25-gauge needle, entering the vitreous cavity at the pars plana (4mm from the limbus if phakic and 3.5mm if pseudophakic), to obtain 0.3ml of vitreous humour. All ocular samples were sent to a single pathology department in a tertiary centre (St. Vincent’s Hospital, East Melbourne).

Microscopy results were noted for gram stain results (positive or negative), amount of organisms (graded as 1+, 2+ or 3+), morphology (*cocci*, *bacilli* or *coccobacilli*), and whether or not organisms resembled *Streptococci* (yes or no). Grading for amount of organisms was performed on high-power oil immersion field (x1000) as follows: 0 (<1 per 10 oil immersion fields), 1+ (<1 per oil immersion field), 2+ (1-10 per oil immersion field), or 3+ (>10 per oil immersion field).

Culture results were confirmed for presence of *Streptococci*, and noted for species of *Streptococci*, amount of growth on culture (light, moderate, heavy), and presence of other microorganisms. The amount of growth on culture plate was graded as follows: none (no growth on culture plate), light (organisms grown in primary inoculum only), moderate (organisms grown in primary and secondary inoculums), or heavy (organisms grown in three or more inoculums).

The management and progress of each case of endophthalmitis were noted in detail. Data was collected on the number and timing of each intravitreal injection, use of intravitreal steroid, vitrectomy and timing of vitrectomy, the use of systemic antibiotics, and if any other procedures (enucleation/evisceration) were performed.

Main outcome measure was the final visual outcome, at least six months after presentation or when vision became stable. The secondary outcome measure was removal of the eye, either by enucleation or evisceration. If follow-up data was not available in patient records, information was obtained through correspondence with treating ophthalmologists.

All statistical analysis was performed on SPSS version 15 (SPSS Inc, Chicago, IL, USA). Categorical data was analysed using the chi-squared test and Fisher's exact test. Where applicable, the Yates' correction was used. Continuous data was stratified into appropriate categorical groups for analysis, unless otherwise noted. Binary logistic regression models were used to analyse the association between patient characteristics and study endpoints.

RESULTS

Out of 856 patients diagnosed with endophthalmitis in this centre over the 15-year period, 101 (11.8%) were culture-positive for *Streptococcus*. Most of these cases occurred postoperatively (87.1%). Cataract surgery accounted for 51 (50.5%), followed by glaucoma surgery (24, 23.8%), corneal surgery (5, 5.0%), intravitreal injection (6, 6.0%), and vitreoretinal surgery (2, 2.0%). Among the other causes, seven (6.9%) occurred following corneal ulceration, five (5.0%) following trauma, and one (1.0%) was from endogenous spread.

The presenting VA was *count fingers* (CF) or better in only 10 (9.9%) of cases. Most patients presented with *hand motion* (HM) (36, 35.6%) or *light perception* (LP) vision (43, 42.6%), eight (7.9%) had *no light perception* (NLP), **Table 1**. At initial examination, the fundus was not visible in 91 cases (90.1%). Hypopyon was seen in 76 of 90 patients (84.4%). 20 patients (19.8%) had a history of diabetes mellitus.

On microscopy gram stain, type of organisms was reported in 80 cases (79.8%). The majority were gram-positive cocci, and further identification of gram-positive cocci resembling *Streptococci* was made in 48 cases (47.5%). The number of organisms was reported as 1+ in 12 cases (11.9%), 2+ in 18 cases (17.8%), and 3+ in 50 cases (49.5%). On culture, the most common species was *S. pneumoniae* (23 cases, 22.8%); viridans group *Streptococci* such as *S. oralis* and *S. mitis* accounted for 63 cases (62.4%), which included cases of mixed growth. Growth on culture, regardless of identification of organism, was noted as either light (26 cases, 25.7%), moderate (16 cases, 15.8%) or heavy (52 cases, 51.5%). Antibiotic sensitivity testing was routinely performed. 100% of strains cultured were susceptible to Vancomycin, 98.7% to Chloramphenicol, 89.7% to Cefazolin, 88.1% to Ofloxacin, 86.5% to Penicillin, and 4.0% to Neomycin.

An initial intravitreal '*tap and inject*' was performed in 94 of 101 patients (93.1%) on the day of admission. Of the seven patients who did not have any intravitreal injections, six proceeded directly to surgery: one had a vitrectomy and lensectomy, four had an evisceration, and one had an enucleation. A single patient received only topical and systemic antibiotics. In total, 15 (14.9%) patients had a vitrectomy within 48 hours of admission. Overall, 30 (29.7%) patients received one set of intravitreal therapy, 42 (41.6%) patients received two sets, 21 (20.8%) received three sets, and one (1.0%) received four. Intravitreal dexamethasone (400µg in 0.1ml) was used in 83 of 94 cases (88.3%). Systemic antibiotics were used only in 51 cases (50.5%), mostly oral ciprofloxacin.

At final follow-up, 31 patients (30.7%) had at least one vitrectomy. Data on final visual outcome was not available in 15 cases (14.9%), due to loss to follow-up. Of 86 remaining cases, visual outcome was 6/36 or better in only 20 cases (23.3%). The majority of patients had poor visual outcomes. There were 17 patients (19.8%) who were NLP, 12 (14.0%) had an evisceration and nine (10.5%) had an enucleation.

Final visual outcomes were stratified as either good (defined as a VA of 6/36 or better) or poor (VA of 6/60 or worse), following categories used in the Endophthalmitis Vitrectomy Study (EVS).⁵ On univariate analysis, **Table 2**, patients with a presenting VA of LP or worse were more likely to have poor visual outcomes than those presenting with HM or better (90.2% vs. 64.3%, $p=0.008$). Patients with no view of the fundus at presentation were also more likely to end up with a VA of 6/60 or worse (82.7% vs. 30.0%, $p=0.001$). The presence of hypopyon and a history of diabetes were not significant predictors of poor visual outcome.

On gram stain, a larger number of organisms seen (3+ vs. 2+ vs. 0-1+) was associated with poor final VA (92.9% vs. 73.3% vs. 51.9%, $p<0.001$). This factor remained significant on multivariate analysis ($p=0.032$), **Table 3**. In addition, when *Streptococci* were readily identified on gram stain, cases had worse visual outcomes (89.7% vs. 65.2%, $p=0.010$). On culture, heavy microbial growth was more likely to be associated with poor visual outcome than moderate or light/no growth (93.3% vs. 75.0% vs. 39.1%, $p<0.001$). However, the species of *Streptococcus* involved and the presence of a second microorganism did not correlate with final VA.

Snellen visual acuity	Number of cases (n=101)
6/9	1
6/18	2
6/24	1
6/36	2
6/60	1
Counting Fingers (CF)	3
Hand Movements (HM)	36
Light Perception (LP)	43
No Light Perception (NLP)	8

† Data not available for 4 cases

Table 1: Number of cases by presenting visual acuity

Characteristic	N	VA 6/36 or better (%)	VA 6/60 or worse (%)	p value
Presenting visual acuity				0.008
LP or worse	41	4 (9.8)	37 (90.2)	
HM or better	42	15 (35.7)	27 (64.3)	
Fundus visible at presentation	10	7 (70.0)	3 (30.0)	0.001

Yes	75	13 (17.3)	62 (82.7)	0.492
No				
Presence of hypopyon	66	16 (24.2)	50 (75.8)	0.542
Yes	12	4 (33.3)	8 (66.7)	
No				
History of diabetes	19	3 (15.8)	16 (84.2)	<0.001
Yes	66	17 (25.8)	49 (74.2)	
No				
Organisms on gram stain	27	13 (48.1)	14 (51.9)	0.010
0-1+	15	4 (26.7)	11 (73.3)	
2+	42	3 (7.1)	39 (92.9)	
3+				
Strep identified on gram stain	39	4 (10.3)	35 (89.7)	<0.001
Yes	46	16 (34.8)	30 (65.2)	
No				
Growth on culture	23	14 (60.9)	9 (39.1)	0.251
Light or none	12	3 (25.0)	9 (75.0)	
Moderate	45	3 (6.7)	42 (93.3)	
Heavy				
Strep species on culture	20	4 (20.0)	16 (80.0)	1.000
Pneumococcal	52	15 (28.8)	37 (71.2)	
Viridans	13	1 (7.7)	12 (92.3)	
Other				
Presence of second organism	9	2 (22.2)	7 (77.8)	0.315
Yes	76	18 (23.7)	58 (76.3)	
No				
Systemic antibiotics	47	9 (19.1)	38 (80.9)	1.000
Yes	38	11 (28.9)	27 (71.1)	
No				
Vitrectomy within 48 hours †	13	3 (23.1)	10 (76.9)	0.038
Yes	66	16 (24.2)	50 (75.8)	
No				

No. of intravitreal injections	24	10 (41.7)	14 (58.3)	1.000
†	35	7 (20.0)	28 (80.0)	
1	20	2 (10.0)	18 (90.0)	
2				
3 or more	71	17 (23.9)	54 (76.1)	
	8	2 (25.0)	6 (75.0)	
Intravitreal dexamethasone †				
Yes				
No				

† Excludes patients who proceeded directly to enucleation or evisceration

N.B where n≠86, data was not available in patient records

Table 2: Characteristics associated with final visual outcome

Characteristic	p value	Odds ratio (95% CI)
Presenting visual acuity of LP or worse	0.367	2.056 (0.429-9.859)
Fundus not visible at presentation	0.044	8.958 (1.056-75.962)
History of diabetes	0.241	
Large (3+) number of organisms on gram stain ‡	0.021	3.198 (0.458-22.311)
Streptococci identified on gram stain	0.923	
Non-viridans Streptococcal species on culture	0.403	9.072 (1.403-58.638)
Presence of second organism	0.584	
Use of systemic antibiotics	0.867	1.084 (0.211-5.574)
Vitrectomy within 48 hours	0.846	2.183 (0.350-13.616)
Use of intravitreal dexamethasone	0.992	0.550 (0.065-4.667)
		1.144 (0.239-5.470)
		0.803 (0.088-7.368)
		1.012 (0.102-10.041)

‡ Adjusted for presenting visual acuity, visibility of fundus, history of diabetes, number of organisms on gram stain, type of organism identified, presence of second organism on culture, use of systemic antibiotics, vitrectomy within 48 hours, and use of intravitreal dexamethasone.

‡ Grading for amount of single organism seen on high-power oil immersion field (x1000) as described in methods.

N.B. Streptococcal groups divided into two – viridans vs. non-viridans Streptococci

Table 3: Multivariate analysis of predictors of poor visual outcome

The decision to perform early vitrectomy, within 48 hours of presentation, had no correlation with visual outcome (76.9% vs. 75.8%, $p=1.000$). The use of systemic antibiotic therapy and intravitreal dexamethasone also did not significantly affect the visual outcome. The need for a higher number of intravitreal injections performed was significantly associated with a poor final VA ($p=0.038$).

For the secondary endpoint, patients were separated into groups who had removal of the eye (enucleation or evisceration, 21 patients) and no removal of the eye (65 patients). As illustrated in **Table 4**, patients with a presenting VA of LP or worse were more likely to lose the affected eye than patients with vision of HM or better (34.1% vs. 14.3%, $p=0.042$). In addition, patients who were infected with *viridans* group *Streptococci* were less likely to undergo enucleation or evisceration (11.5% vs. 45.0% and 46.2%, $p=0.002$), and this association remained significant on multivariate analysis ($p=0.005$), **Table 5**.

Characteristic	N	No removal of eye (%)	Removal of eye (%)	p value
Presenting visual acuity				0.042
LP or worse	41	27 (65.9)	14 (34.1)	
HM or better	42	36 (85.7)	6 (14.3)	
Fundus visible at presentation				0.439
Yes	10	9 (90.0)	1 (10.0)	
No	75	55 (73.3)	20 (26.7)	

Presence of hypopyon				0.152
Yes	66	52 (78.8)	14 (21.2)	
No	12	7 (58.3)	5 (41.7)	
History of diabetes				0.379
Yes	19	16 (84.2)	3 (15.8)	
No	66	48 (72.7)	18 (27.3)	
Organisms on gram stain				0.967
0-1+	27	20 (74.1)	7 (25.9)	
2+	15	11(73.3)	4 (26.7)	
3+	42	32 (76.2)	10 (23.8)	
Strep identified on gram stain				0.458
Yes	39	31 (79.5)	8 (20.5)	
No	46	33 (71.7)	13 (28.3)	
Growth on culture				0.064
Light or none	23	21 (91.3)	2 (8.7)	
Moderate	12	10 (83.3)	2 (16.7)	
Heavy	45	30 (66.7)	15 (33.3)	
Strep species on culture				0.002
Pneumococcal	20	11 (55.0)	9 (45.0)	
Viridans	52	46 (88.5)	6 (11.5)	
Other	13	7 (53.8)	6 (46.2)	
Presence of second organism				0.441
Yes	9	8 (88.9)	1 (11.1)	
No	76	56 (73.7)	20 (26.3)	
Systemic antibiotics				0.129
Yes	47	32 (68.1)	15 (31.9)	
No	38	32 (84.2)	6 (15.8)	
Vitrectomy within 48 hours §				1.000
Yes	13	11 (84.6)	2 (15.4)	
No	66	52 (78.8)	14 (21.2)	
No. of intravitreal injections §				0.050
1	24	18 (75.0)	6 (25.0)	

2	35	32 (91.4)	3 (8.6)	0.661
3 or more	20	13 (65.0)	7 (35.0)	
Intravitreal dexamethasone §				
Yes	71	57 (80.3)	14 (19.7)	
No	8	6 (75.0)	2 (25.0)	

§ Excludes patients who proceeded directly to enucleation or evisceration

N.B where n≠86, data was not available in patient records

Table 4: Characteristics associated with removal of the eye

Characteristic	p value	Odds ratio (95% CI)
Presenting visual acuity of LP or worse	0.124	3.534 (0.708-17.644)
Fundus not visible at presentation	0.348	4.492 (0.194-
History of diabetes	0.217	103.864)
Large (3+) number of organisms on gram stain ‡	0.887	0.291 (0.041-2.063)
Streptococci identified on gram stain	0.336	0.865 (0.117-6.379)
Non-viridans Streptococcal species on culture	0.001	0.345 (0.040-3.009)
Presence of second organism	0.999	27.547 (3.721-
Use of systemic antibiotics	0.903	203.925)
Vitrectomy within 48 hours	0.647	0.000 (N/A)
Use of intravitreal dexamethasone	0.765	1.106 (0.220-5.568)
		1.801 (0.145-22.344)
		0.692 (0.062-7.764)

¶ Adjusted for presenting visual acuity, visibility of fundus, history of diabetes, number of organisms on gram stain, type of organism identified, presence of second organism on culture, use of systemic antibiotics, vitrectomy within 48 hours, and use of intravitreal dexamethasone

‡ Grading for amount of single organism seen on high-power oil immersion field (x1000) as described in methods.

N.B. Streptococcal groups divided into two – viridans vs. non-viridans Streptococci

Table 5: Multivariate analysis of predictors of removal of the eye

Early vitrectomy did not increase the likelihood of retaining the eye: 84.6% of patients with early vitrectomy retained their eye, compared to 78.8% of patients who initially received intravitreal injections only ($p=1.000$). The use of systemic antibiotics or intravitreal dexamethasone was not associated with removal of the eye.

DISCUSSION

Patients with culture-positive *Streptococci* endophthalmitis and a presenting VA of LP or worse, or with no view of the fundus at presentation, are more likely to have a poor visual outcome and/or more likely to lose their eye, regardless of their aetiology. This finding agrees with the outcomes in previous studies including the EVS.⁵ Poor VA and poor view of fundus are surrogate markers for worse intraocular inflammation. They may also indicate underlying complications of endophthalmitis, such as retinal or choroidal detachment, which may lead to poorer outcomes.¹⁴

In this population of culture-positive *Streptococci*, most were readily visible on gram stain as gram-positive cocci, and were identifiable as resembling *Streptococci* in nearly half of cases. This study showed that early identification of *Streptococci* on gram stain significantly predicted poorer visual outcome. Our reporting laboratory finalises gram stain results within 24 hours, and results are often available within 6 hours. Therefore, early identification of *Streptococcal* endophthalmitis, known for its virulence, may allow early prognostication of outcome and more aggressive management. Although not previously reported in endophthalmitis, the utility of gram stain identification of *Streptococci* has been extensively investigated in community-acquired pneumonia and pharyngitis.^{15, 16} Most studies show close

concordance between gram stain and eventual culture results, suggesting that gram stain results can be used for early diagnosis and tailoring of suitable therapy.

In this cohort, a large number of organisms on microscopy and heavy growth on culture were associated with worse visual outcomes. *Streptococci* are fast growing organisms, and the vitreous is a nutritive and immune-privileged environment that can allow *Streptococci* to multiply quickly. Large numbers of organisms suggest a more virulent *Streptococcal* infection leading to worse outcomes.¹⁷

The spectrum of *Streptococcal* species is similar to the prevalence of various species in the normal respiratory flora of healthy subjects.^{18, 19} This observation supports the finding that endophthalmitis are often caused by nasopharyngeal commensals, particularly a patient's own nasal flora.^{20, 21} *Viridans* group *Streptococci*, in particular, are rarely found in normal conjunctival flora, and some authors suggest that contamination may occur through aerosolisation when the patient, surgeon or staff are talking.^{2, 22} The species of *Streptococcus* did not significantly influence the visual outcome, although patients who had *viridans Streptococci* fared best compared to others. This finding mirrors previous studies, where *S. pneumoniae* or β -haemolytic *Streptococci* were associated with worse visual outcomes, compared to *viridans* group *Streptococci*.^{6, 7} Although the trend for VA is not significant, patients with *viridans Streptococci* endophthalmitis were significantly less likely to lose their eye. *Viridans Streptococci* are relatively lower in virulence compared to other *Streptococci*, due to lack of virulence factors such as streptolysins and exotoxins, and may therefore be less damaging to ocular tissues.²³

As expected, the final visual outcome is poor: 44.2% have no remaining vision, a percentage that is comparable to existing literature on *Streptococcal* endophthalmitis (28.6-58.3%).^{6-8, 10} Nearly one-quarter of patients undergo enucleation or

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evisceration, emphasising the poor outcome of this patient cohort; in contrast, only 1% of patients in the EVS study lose their infected eye.⁵ In this cohort, only 15.3% recovered vision of at least 6/18, slightly better than reported in previous studies (8.3-14.3%).^{6-8, 10}

In our institution, pars plana vitrectomy is performed if there is lack of improvement or clinical worsening at 24-48 hours, despite intravitreal antibiotics. Our data shows that early vitrectomy within 48 hours does not improve visual outcome. Vitrectomy aims to remove inflammatory debris and prevent further damage, and although few reports suggest improvement in outcomes in some endophthalmitis,¹¹ this study does not show any benefit in *Streptococcal* endophthalmitis. One other study on *Streptococcal* endophthalmitis reported a non-significant trend of worse outcomes in patients who underwent vitrectomy, compared to intravitreal tap and injection alone (80% vs. 60%, $p=0.402$).⁸ There are several possible reasons for these findings. Firstly, Streptococci are virulent bacteria capable of producing severe inflammation, and damage to ocular tissues may occur early in the course of infection, leaving minimal chance for any improvement even with early vitrectomy. Experimental studies of gram-positive endophthalmitis showed that intraocular inflammation was observed as early as 3 hours post-inoculation, with maximal inflammation from 12 hours onwards.²⁴ Early vitrectomy at our institution was within a practical 48 hours, while the EVS protocol mandated that all vitrectomies were performed within six hours. Secondly, vitrectomy in inflamed eyes is riskier due to poorer visibility and friable tissues, increasing the likelihood of iatrogenic complications such as retinal detachment.¹¹ Thirdly, this study is observational and non-randomised. Patients were chosen for vitrectomy at the treating surgeon's discretion. Therefore, it is possible that patients were chosen for vitrectomy because of worse clinical presentation or lack of response to intravitreal therapy. If patients in the early

vitrectomy group had worse disease and worse outcomes, any benefit of vitrectomy may be masked.

This study has a number of strengths. Data were collected over fifteen years at a single centre, and there was minimal variability in data collection, treatment protocols and equipment. Samples were sent to a single microbiology laboratory, allowing standardisation of testing and reporting. A minimum of six months of follow-up was imposed for final visual acuity data. Several limitations should also be noted. Due to the observational nature of the study, the possibility of selection bias could not be excluded. There are also limitations arising from incomplete data, particularly missing data points for final visual acuity, as some patients were lost to follow-up (15%). In addition, due to the small sample size, statistical significance could not be determined from subgroup analyses, particularly based on aetiology. Further to that, an observed finding in our study was that some factors, upon univariate analysis (Table 2), were statistically significant however upon multivariate analysis (Table 4) were no longer statistically significant. This implicates confounders contributing to several of the findings seen in Table 2 and should be considered in the interpretation of the results. Another consideration is that with our retrospective study design, it is difficult to interpret the relationship between treatment options and outcomes. This is because in practicality, disease severity (determined through patient symptoms and examination findings) influences treatment decisions with respect to need for vitrectomy, number of injections, use of steroids and antibiotics, confounding our interpretation. Lastly, vitrectomy technology evolved considerably over the duration of the study, with later years incorporating technologies and techniques to improve safety. These include moving from 20-gauge to 25-gauge valved pars plana ports, the use of wide-field non-contact viewing systems and utilisation of smaller aperture ocutomes with faster cut rates and valved cannulae. Unfortunately the numbers in our study are too small to perform meaningful analysis

into the significance of these improvements in vitrectomy technique. Despite this, improvements in outcomes are expected and expert opinion has noted improvements in the safety of vitrectomy with the technological advancements leading to less iatrogenic retinal breaks, an important complication to avoid in the setting of endophthalmitis due to the high risk of development of proliferative vitreoretinopathy (PVR).^{25, 26} Continued data collection may further clarify the role of modern vitrectomy in virulent endophthalmitis.

Our findings confirm that, disappointingly, *Streptococcal* endophthalmitis has devastating sequelae in our cohort, with florid inflammation leading to poor visual outcomes. The prime focus for treating clinicians should be early detection and early treatment to minimize disease impact. Patient education and regular re-education following intraocular procedures is a vital process. Following dissemination of our findings in our department, consideration of early vitrectomy in the management of endophthalmitis is being sought. With recent advances in vitrectomy techniques, we feel that for research clinicians there can only be one recommendation, that a multi-centred, multi-regional prospective randomized clinical control trial that includes an arm for immediate vitrectomy (within 4-6 hours of presentation). This protocol should include close collaboration with microbiologists.

Clinical presentation and microbiological results can provide useful information on visual outcome in *Streptococcal* endophthalmitis. In the right setting, microscopy results can be available within hours of specimen collection, and culture results shortly after. In fact, polymerase chain reaction (PCR) testing of *Streptococci* now allows even faster identification of pathogens using known genes like pneumolysin and autolysin.²⁷ Given the ability to identify this devastating pathogen early, clinicians can make earlier treatment decisions to attempt to improve visual

outcomes. Rapid diagnosis also better prepares the treating physician to counsel patients on their prognosis.

Acknowledgements

The authors would like to thank all staff involved in this study.

Contributors: All authors (EDK, JRR, SSS, PJA) contributed to design, collection, analysis and interpretation of data, and review of manuscript.

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Title:

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Date:

2018-05-01

Citation:

Kurniawan, E. D., Rocke, J. R., Sandhu, S. S. & Allen, P. J. (2018). Predictors of visual outcome and the role of early vitrectomy in streptococcal endophthalmitis. CLINICAL AND EXPERIMENTAL OPHTHALMOLOGY, 46 (4), pp.424-431. <https://doi.org/10.1111/ceo.13077>.

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