

SCIENTIFIC REPORT

Early postoperative trabeculectomy leakage: incidence, time course, severity, and impact on surgical outcome

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Aim: To establish the incidence, time course, and severity of conjunctival wound leakage following trabeculectomy, and also to establish whether early wound leakage adversely affects the ultimate outcome of the surgery.

Method: A prospective, observational case series of sequential trabeculectomies performed in a single institution over a 12 month period. Datasets on 286 operations were analysed. A fornix based conjunctival flap was used in 254 cases and a limbus based conjunctival flap in 41 cases. At every postoperative visit trabeculectomies were assessed for four grades of leakage (none; mild; moderate; severe), and for success or failure at the 6 month follow up post surgery. Pressure was applied to the trabeculectomy bleb to record the maximum rates of leakage and improve kappa statistics. Study clinicians were validated with respect to their scoring of leaks before starting the study.

Results: 169 of the 286 trabeculectomies (59%) showed leakage at some stage postoperatively. 159 of 245 fornix based flaps (65%) leaked compared with 10 of 41 limbus based flaps (24%). Median time to leak was 3.5 (range 0–408) days. Median duration of leakage was 14 (range 2–457) days. 14 (5%) of trabeculectomies failed completely. A further 40 (14%) were a partial failure. In total, 23 of 117 (20%) without postoperative leaks partially or completely failed compared with 31 of 169 (18%) with leaks. Cross tabulation of partial and complete failure by leak shows no evidence of an adverse effect of leaking on the outcome ($\chi^2 = 1.81$, $p = 0.4$).

Conclusions: There is no evidence to support the hypothesis that early postoperative leakage of fornix based conjunctival flaps affects the outcome of trabeculectomy.

Early postoperative bleb leak is a common complication of trabeculectomy.^{1–13} There is a wide variation in the reported incidence of this complication from 0% to 30%.^{1–14} It has been reported to be more common following trabeculectomy with fornix based flaps than limbus based flaps.^{1–5, 15} For example, Batterbury and Wishart reported postoperative bleb leaks in 1 of 27 patients (4%) treated with limbus based trabeculectomy and 15 of 26 patients (56%) treated with fornix based trabeculectomy.¹

The effect of early wound leakage on the outcome of trabeculectomy is not well characterised. The most serious consequence of a bleb leak is endophthalmitis.¹⁵ A substantial leak can also cause a shallow or flat anterior chamber, and hypotony can develop. The fluorouracil filtering surgery study group reported that an early postoperative wound leak was a risk factor for trabeculectomy failure.¹²

A flat anterior chamber following surgery has been reported to be more common following trabeculectomy with a fornix based flap than a limbus based flap.¹⁵ However

studies to compare the results of limbus versus fornix based conjunctival flaps have suggested that results are equally successful in both groups independent of the type of conjunctival flap.^{2–5, 16}

A prospective study was designed to establish the incidence, time course, and severity of conjunctival wound leakage following trabeculectomy, and also to establish whether early wound leakage adversely affects the ultimate outcome of the surgery.

MATERIALS AND METHODS

A prospective, observational cohort study was performed assessing sequential trabeculectomies for leakage postoperatively. Over a period of one year, every patient who underwent trabeculectomy in the glaucoma unit of a single institution was graded during every outpatient visit into one of four categories of leak from their conjunctival wound. The assessments were recorded on sheets of paper collected at the end of each clinic. The endpoint for success or failure was at the 6 month follow up after surgery. Success was defined as an intraocular pressure (IOP) less than 20 mm Hg with no treatment. Partial failure was defined as an IOP controlled at less than 20 mm Hg with topical medication. Complete failure was defined as an IOP greater than 20 mm Hg.

Before starting the study, clinicians involved in assessing the eyes postoperatively were validated with respect to their scoring of leaks. Kappa statistics of between 0.51 and 0.85 were obtained (weighted kappas 0.88–0.96) between clinicians for four grades of leak: no leak, mild leak, moderate leak, severe leak. Where unsatisfactory kappa statistics were obtained for any particular clinician, the most common reason was lack of pressure on the bleb to record “maximum” leaks. Without this pressure their results were much less consistent. This means that the recorded prevalence of postoperative leakage is a maximum in this study. Data sets on 286 operations were analysed, 79 trabeculectomies, 183 trabeculectomies with cytotoxic application at the time of surgery, and 24 more complex procedures. Fifty four individuals underwent surgery on both eyes. A fornix based conjunctival flap was used in 245 cases and a limbus based conjunctival flap in 41 cases. iSTATA version 7.0 (StataCorp, College Station, TX, USA) was used for statistical analysis.

RESULTS

Although the data on leaks were collected prospectively at the end of each clinic visit, the outcome for each subject was determined retrospectively by note recall and review. This enabled uniform review and application of outcome criteria but suffered from difficulties with note retrieval. An initial review yielded only 46% of notes for outcome determination in those eligible by virtue of complete information with respect to bleb leakage. In an attempt to assess if there was

Abbreviations: 5-FU, 5-fluorouracil; FFSS, fluorouracil filtering surgery study; MMC, mitomycin C.

bias in the sample obtained, a concentrated effort was made to review all cases performed from September to December 1993. For these months the proportion reviewed was increased to 96% of those eligible. A comparison of those missed at the first review with those seen at the first review showed no major difference in proportion of operative failures ($\chi^2 = 2.7$, $p = 0.3$) or conjunctival leaks ($\chi^2 = 0.3$, $p = 0.6$). Because substantial effort went into this further validation and as there was no suggestion of bias in the sample obtained, we analysed the dataset with a total of 286 operations. This represents 61% of eligible operations performed during the 12 month period.

Mean follow up was 353 (standard deviation, 196) days, the median was 323 days. The operations that were performed and the per cent found to have a conjunctival aqueous leak to some degree are shown in table 1.

A cross tabulation of partial and complete failure by leak shows no evidence of an adverse effect of leaking on the outcome (table 2).

For the purposes of further analysis, partial failure and complete failure were combined as failure, and logistic regression analysis performed to investigate potential risk factors for failure and determine whether confounding by other factors could be concealing an association between leakage and failure. In addition, because mild leaks were induced and may not be considered clinically in the same league as moderate or severe leaks, regression analysis was performed combining no leak with mild leak, and moderate with severe leak. Analysis was tried using all four categories of leak. In all cases the results were similar, and those for the simplest model of two categories of leak are given. Table 3 shows the crude and adjusted odds of failure of the operation according to various risk factors (leakage scored as present if moderate or severe only).

Correlation between results for two eyes of the same individual is always possible, resulting in interaction. The analysis was repeated using right eyes only of those with two eyes included in the dataset. This gave virtually identical results but with wider 95% confidence intervals. The only result of note was that for a past history of topical adrenaline use, which developed an adapted odds ratio of 3.20 (95% CI 0.78–13.2) for trabeculectomy failure. Concordance of results between right and left eyes for the 54 individuals with bilateral operations in the dataset was no different from that expected by chance for leak, but shows concordance for failure (table 4).

Table 5 shows the leakage rate according to limbus or fornix based conjunctival flaps. The median time to leak was 3.5 days with a range from the first postoperative day to 408 days postoperatively. Figure 1 illustrates the distribution

Table 1 Operations performed and the percentage found to have leak to some degree

Operation	Leak			Total
	None	Mild	Moderate/severe	
Trabeculectomy	36	26	17	79
Trabeculectomy+5-FU	32	42	49	123
Trabeculectomy +0.2 mg/ml MMC	16	3	2	21
Trabeculectomy +0.4/ml MMC	5	0	0	5
Triple procedure*+5-FU	19	12	3	34
Trabeculectomy +other procedure	9	10	5	24
Total	117 (41%)	93 (32%)	76 (27%)	286

*Cataract extraction+lens implant+trabeculectomy. 5-FU, 5-fluorouracil; MMC, mitomycin C.

Table 2 Result of trabeculectomy by presence or absence of conjunctival leakage of aqueous humour.

Leak	Result			Total
	Success	Partial failure	Failure	
Mild/moderate/severe leakage				
None	94 (80%)	15 (13%)	8 (7%)	117
Any leak	138 (82%)	25 (15%)	6 (4%)	169
Total	232 (81%)	40 (14%)	14 (5%)	286
Moderate/severe leakage				
None	171	27	12	210
Moderate/severe	61	13	2	76
Total	232	40	14	286

Pearson $\chi^2(2) = 1.73$, $p = 0.42$.

Table 3 Crude and adjusted odds of the operation according to various risk factors (leakage scored as present if moderate or severe only)

Risk factor	Crude odds (95% CI)	Adjusted odds (95% CI)
Any leak	1.08 (0.56–2.09)	0.98 (0.44–2.15)
Maximum leak grade 2	0.85 (0.42–1.72)	
Maximum leak grade 3	0.76 (0.31–1.84)	
Maximum leak grade 4	1.59 (0.52–4.26)	
Asian	2.74 (1.08–6.94)	2.11 (0.71–6.22)
African Caribbean	1.61 (0.73–3.56)	2.12 (0.80–5.66)
Previous trabeculectomy	2.22 (0.01–4.86)	2.04 (0.73–5.70)
Chronic open angle glaucoma	2.17 (0.91–5.22)	1.84 (0.62–5.48)
Other glaucoma	0.93 (0.44–1.97)	0.57 (0.22–1.46)
Limbus base conj. flap	1.11 (0.48–2.58)	0.46 (0.12–1.87)
Previous cataract surgery	2.51 (1.19–5.29)	2.33 (0.82–6.67)
Other previous surgery	2.45 (1.32–4.54)	1.87 (0.86–4.07)
Trabeculectomy+5FU	1.11 (0.52–2.35)	0.68 (0.29–1.63)
Trabeculectomy+0.2 mg/ml MMC	1.59 (0.49–5.10)	1.47 (0.25–8.75)
Trabeculectomy+0.4 mg/ml MMC	1.27 (0.13–12.3)	0.37 (0.02–5.69)
Triple procedure*+5FU	1.55 (0.55–4.35)	2.07 (0.62–6.91)
Other complex procedure	1.69 (0.56–5.08)	0.74 (0.19–2.80)
Age (per year older)	0.99 (0.97–1.01)	0.97 (0.95–1.00)
Pilocarpine drops use in past	1.07 (0.52–2.23)	1.20 (0.53–2.73)
Adrenalin drops use in past	1.78 (0.54–5.89)	3.20 (0.78–13.2)
Betablocker drops use in past	1.12 (0.36–3.42)	1.37(0.35–5.43)
Systemic acetazolamide use in past	1.25 (0.69–2.27)	1.43 (0.73–2.80)

*Cataract extraction+lens implant+trabeculectomy. MMC, mitomycin C.

of time to leak (defined as occurring halfway between a review with no leak and the first review with a leak observed). Figure 2 illustrates the duration of leakage calculated from halfway between the onset of leak as defined above, and the stop of leakage halfway between the last review with a leak and the next review without a leak. The median duration of leak was 14 (range 2–457) days. Seven eyes had leaks lasting longer than 100 days. Of these one was a limbus based flap; the leak eventually sealed spontaneously

Table 4 Concordance of results for leak and trabeculectomy failure in 54 individuals who underwent surgery to both eyes

	Leak/no leak	Pass/failure
Concordance between eyes	30	47
Discordance between eyes	24	7

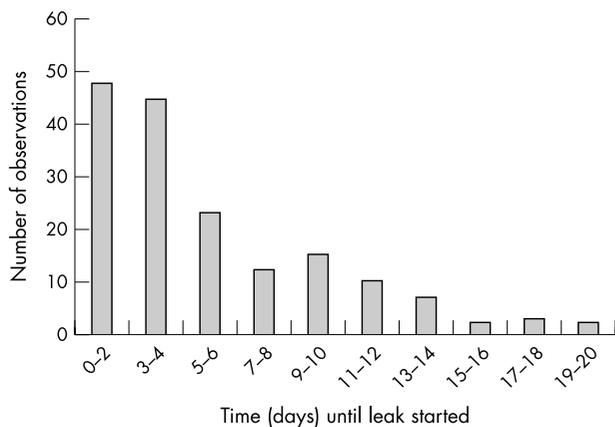


Figure 1 Histogram of time until leak in eyes which leaked.

however this operation failed. Four of the remaining six fornix based conjunctival flap operations with prolonged leaks sealed spontaneously. The remaining two were taken back to theatre after more than a year of leakage and underwent successful bleb reconstruction.

DISCUSSION

This study shows a high rate of postoperative trabeculectomy leaks; 169 of the 286 trabeculectomies showed leakage at some stage postoperatively (59%). Of the 245 fornix based flaps 159 (65%) and 10 of the 41 limbus based flaps (24%) leaked at some stage postoperatively.

Ng *et al* observed that the harder one looks for a leakage site, the more likely one is to find it.⁸ In this study, when assessing the trabeculectomy bleb for leak, the clinicians applied pressure to the conjunctiva in order to increase the consistency of results and increase kappa statistics for assessment. As a result the rates of leakage are a maximum. The rates of moderate or severe leakage are lower: 27% of all trabeculectomies, 29% of fornix based trabeculectomies, and 12% of limbus based trabeculectomies. This is more in line with other studies.

Cross tabulation of partial and complete failure by leak showed no evidence of an adverse effect of leaking on the outcome. Because mild leaks were often induced by the clinicians, analysis was tried using all four categories of leak, and combining no leak with mild lead and moderate leak with severe leak. In all cases the results were similar. Although studies of limbus versus fornix based conjunctival flap in trabeculectomy have shown both groups to be equally successful,^{2-5 16} there has been concern over the increased rates of early postoperative bleb leak associated with fornix based flaps.⁸⁻¹⁵ This has been a reason for advocating the use

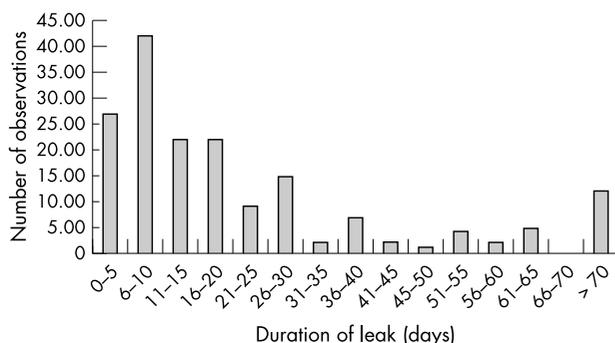


Figure 2 Histogram of duration of leak in eyes which leaked.

Table 5 Leakage rate according to limbus or fornix based conjunctival flaps

Leakage	Flap type		Total
	Fornix based	Limbus based	
No leak	86 (35%)	31 (76%)	117 (41%)
Any leak	159 (65%)	10 (24%)	169 (59%)
Total	245	41	286
No leak	74 (71%)	36 (88%)	210 (73%)
Moderate/severe leak	71 (29%)	5 (12%)	76 (27%)
Total	245	41	286

χ^2 23.8, $p < 0.001$.
 χ^2 5.1, $p = 0.025$.

of limbus based flaps in preference to fornix based flaps in trabeculectomy surgery. However the fornix based flap has the advantage of producing a better bleb morphology: it is more likely than the limbus based flap to give rise to a diffuse bleb with a normal vascular pattern rather than a cystic bleb.¹⁷ Wells *et al* have shown that in paediatric and young adult trabeculectomy with high doses of MMC, limbus based flaps may be more likely to develop serious bleb related complications such as late hypotony and bleb related infection, and may develop these earlier than fornix based flaps.¹⁸ They postulated that the higher rates of complications could be attributable to an increased risk of blebs from limbus based flaps developing cystic based morphology.

The results of this study differ from those of the fluorouracil filtering surgery study (FFSS) in which early postoperative leakage was a risk factor for trabeculectomy failure.¹² Several reasons may account for this. Firstly, the patients in the FFSS all underwent trabeculectomy with a limbal based conjunctival flap. Secondly, systematic bias is possible in the FFSS; the clinicians involved in assessing the eyes postoperatively were not validated with respect to their scoring of leaks. Thirdly, in the FFSS wound leak was not an independent significant predictor of trabeculectomy failure—when the number of previous procedures with conjunctival incisions entered into the statistical model, wound leak was no longer significant.

CONCLUSION

The results of this study show that there is no adverse effect of early postoperative bleb leak on surgical outcome. Although limited to a single institution, the results of this study have general applicability because of the large numbers of surgeons involved and the lack of case selection. Clearly the study relates to early bleb leak only: a separate study would be required to address the impact of late bleb leaks.

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