



Comparative Evaluation Of Clinical Characteristics And Visual Outcomes Of Traumatic And Non-Traumatic Graft Dehiscence Following Corneal Transplantation Surgery

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Purpose: To compare patient demographics, clinical associations and visual outcomes between traumatic and non-traumatic wound dehiscence, following corneal transplantation.

Methods: Retrospective review of all patients presenting with post-keratoplasty wound dehiscence to the Royal Victorian Eye and Ear Hospital between January 2005 and December 2017. Patients with wound dehiscence following keratoplasty of any cause were included.

Results: Of 71 eyes from 71 patients included, 60 (85%) were penetrating keratoplasty patients. The mean age was 56.4 years (SD=22.7, range 17.6–97) and 62% (n = 44) of patients were male. There were 28 (39%) cases of traumatic dehiscence and 43 (61%) cases of non-traumatic dehiscence. The median time interval from keratoplasty to dehiscence was significantly less in non-traumatic patients than traumatic patients (0.2 years, IQR 0.1–2.0 vs 2.3 years, IQR 0.3–14.8, $p=0.01$). There was no significant difference in best-corrected visual acuity at 6 months between traumatic and non-traumatic dehiscence (6/60 vs 6/36, $p=0.62$), suture technique (continuous vs interrupted, $p=0.12$), or graft type (penetrating keratoplasty vs deep anterior lamellar keratoplasty) after adjusting for keratoconus ($p=0.41$).

Conclusion: Post-keratoplasty wound dehiscence is a serious complication and can cause significant loss of vision. While the risk of dehiscence is lifelong, the first 3 years post-keratoplasty carry the highest risk, with non-traumatic dehiscence tending to occur earlier than traumatic dehiscence.

Keywords: graft dehiscence, trauma, keratoplasty, cornea

Introduction

Wound dehiscence is a well-recognised complication following corneal transplantation surgery and its incidence has been known to range from 0.6% to 5.8%^{1–12} of penetrating keratoplasties (PK) and 0.5% to 3.2%^{8,13} of deep anterior lamellar keratoplasties (DALK). Occurrence of graft dehiscence remains a lifelong risk due to suboptimal wound healing and remodelling at the graft host junction^{14,15} and is associated with poor visual outcomes,^{1,8,9,12,16–19} thus making it a significant clinical concern.

Dehiscence may occur secondary to traumatic or non-traumatic causes. Human-induced injuries in young patients, or falls in the elderly, account for the majority of traumatic cases,^{8,12,20} while non-traumatic causes include suture removal, microbial keratitis or spontaneous dehiscence.^{16,19}

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A number of studies have sought to describe patient characteristics, visual outcomes and clinical associations of post-keratoplasty wound dehiscence. To date, the majority of research has focused exclusively on traumatic dehiscence and little is known about the relative differences between traumatic and non-traumatic dehiscence.^{19,20} Our study has comparatively evaluated traumatic and non-traumatic wound dehiscence following PK and DALK, presenting to our institution over a 12-year period between 2005 and 2017.

Methods

A retrospective review of patients presenting to the Royal Victorian Eye and Ear Hospital, East Melbourne, Australia, was performed, to identify patients who had wound dehiscence following corneal transplantation surgery. Patients with graft-host junction dehiscence of any cause, presenting between January 2005 and December 2017, were included by identifying unique clinical coding. Keratoplasty techniques other than PK and DALK were excluded, as were patients with insufficient clinical data. Idiopathic or spontaneous dehiscence was defined as that in which no precipitating event such as microbial keratitis, trauma, loose sutures or recent suture removal could be identified.

Patients were operated on by multiple surgeons during the study period who had either completed or were in the process of undertaking subspecialty corneal training. At our institution, sutures are usually removed 1–2 years post-PK and 6–12 months post-DALK. However, this is clinician dependent and early suture removal may be necessitated by suture-related complications. Topical steroids are typically tapered over 12–18 months following PK and 6–9 months following DALK. However, this is again guided by the preference of the treating clinician.

Collected data included; demographics, cause of dehiscence, type of graft (PK vs DALK), indication for grafting, suture technique (continuous vs interrupted), suture removal prior to graft dehiscence, protective eyewear use, highest intraocular pressure (IOP) during first the month post-dehiscence repair, and best-corrected visual acuity (BCVA) pre-keratoplasty, pre-dehiscence, and 1 week, 3 months and 6 months post-dehiscence repair. Where patients were followed up at an institution other than the Royal Victorian Eye and Ear Hospital, treating doctors were contacted for missing clinical information.

Continuous variables were compared between traumatic and non-traumatic dehiscence patients using the Wilcoxon rank-sum test and categorical variables were compared using Fisher's exact test. Snellen acuities were

converted to logMAR prior to analysis. BCVA was heavily right-skewed and was, therefore, log-transformed to allow analysis of associations with risk factors via linear regression. Statistical analyses were conducted using Stata/SE version 15.1 (StataCorp, College Station, TX, USA).

Ethical approval for this project was granted by the Human Ethics Research Committee at the Royal Victorian Eye and Ear Hospital, East Melbourne, Australia, and the research was conducted in accordance with the Declaration of Helsinki.

Results

Seventy-two eyes, from 72 patients were identified in the study period. One patient was excluded due to insufficient data leaving 71 patients in the analysis cohort. There were 44 (62%) males and the mean age was 56.4 years (SD=22.7, range = 17.6–97).

There were 28 (39%) cases of traumatic dehiscence and 43 (61%) cases of non-traumatic dehiscence. Falls, human-induced injuries and other causes of trauma accounted for 7 (25%), 11 (39%) and 10 (36%) cases of traumatic dehiscence, respectively. The cause of non-traumatic dehiscence was unavailable for 1 patient. Loose sutures, microbial keratitis and idiopathic dehiscence accounted for 16 (37%), 9 (21%) and 17 (40%) cases of non-traumatic dehiscence, respectively. The timing of dehiscence ranged from <1 year to 41 years post-keratoplasty. No patients had documented use of protective eyewear.

A comparison of the clinical characteristics between traumatic and non-traumatic dehiscence patients is summarised in [Table 1](#). There was no significant difference between baseline demographics except age. Non-traumatic patients were older at the time of keratoplasty compared to traumatic patients (median age: 34.9 years, IQR 29.7–62.8 vs 58.8 years, IQR 36.2–77.1, $p=0.03$). The median time from keratoplasty to dehiscence was significantly less in patients suffering non-traumatic dehiscence compared to traumatic dehiscence (0.2 years, IQR 0.1–2.0 vs 2.3 years, IQR 0.3–14.8, $p=0.01$).

Keratoconus was the most common indication for corneal grafting (57%, $n=36$), followed by pseudophakic bullous keratopathy (8%, $n=6$), pellucid marginal degeneration (8%, $n=6$) and Fuchs' endothelial dystrophy (8%, $n=6$). Microbial keratitis, herpes simplex keratitis, traumatic corneal scarring, ocular cicatricial pemphigoid, corneal dystrophy, autoimmune disease, anterior segment dysgenesis and scarring following chemical eye injury accounted for the remaining keratoplasty indications. There was no difference in the indication for corneal

Table 1 Comparison Of Clinical Characteristics Between Patients With Traumatic And Non-Traumatic Graft Dehiscence

	Traumatic		Non-Traumatic		p-value ^a
	(n = 28)		(n = 43)		p-value
	n	(%)	n	(%)	
Sex					0.461
Male	19	(68%)	25	(58%)	
Female	9	(32%)	18	(42%)	
Eye					0.332
Left	11	(39%)	23	(53%)	
Right	17	(61%)	20	(47%)	
Indication for graft					0.115
Other	1	(4%)	2	(5%)	
Keratoconus	17	(61%)	19	(44%)	
Pseudophakic bullous keratopathy	3	(11%)	3	(7%)	
Microbial keratitis with perforation	0	(0%)	5	(12%)	
Herpes simplex	0	(0%)	6	(14%)	
Pellucid marginal degeneration	0	(0%)	1	(2%)	
Fuchs' endothelial dystrophy	3	(11%)	1	(2%)	
Traumatic corneal scarring	2	(7%)	4	(9%)	
Ocular cicatricial pemphigoid	0	(0%)	1	(2%)	
Corneal dystrophy	1	(4%)	1	(2%)	
Unknown	1	(4%)	0	(0%)	
Type of graft					0.508
Penetrating keratoplasty	25	(89%)	35	(81%)	
Deep anterior lamellar keratoplasty	3	(11%)	8	(19%)	
Suture type ^c					0.647
Interrupted	23	(96%)	39	(91%)	
Continuous	1	(4%)	4	(9%)	
Graft sutures removed prior to dehiscence					0.327
No	10	(36%)	21	(50%)	
Yes	18	(64%)	21	(50%)	
More than half of the sutures removed if removed					0.464
No	3	(17%)	6	(29%)	
Yes	15	(83%)	15	(71%)	
IOP >21mmHg in 1st month post-op ^c					0.545
No	21	(78%)	36	(84%)	
Yes	6	(22%)	7	(16%)	
	Median	(IQR)	Median	(IQR)	p-value ^b
Age at grafting (years)	34.9	(29.7, 62.8)	58.8	(36.2, 77.1)	0.030
Age of patient at time of dehiscence (years)	48.4	(32.9, 72.2)	62.7	(38.2, 78.6)	0.196
Age of graft at time of dehiscence (years)	2.3	(0.3, 14.8)	0.2	(0.1, 2.0)	0.010
Time to dehiscence repair (days)	0	(0, 0)	0	(0, 2)	0.059
Highest IOP 1 st month post-op (mmHg) ^c	17	(11, 22)	15	(10, 19)	0.186
BCVA pre-graft (LogMAR)	1.50	(1.00, 3.00)	2.00	(1.00, 3.00)	0.855
BCVA pre-dehiscence (LogMAR)	0.48	(0.18, 1.50)	1.00	(0.50, 2.00)	0.014
BCVA 1 week post-repair (LogMAR)	2.00	(0.54, 3.00)	1.00	(0.60, 2.00)	0.157
BCVA 3 months post-repair (LogMAR)	0.95	(0.30, 2.50)	1.00	(0.48, 2.00)	0.582
BCVA 6 months post-repair (LogMAR)	1.00	(0.44, 2.00)	0.78	(0.48, 2.00)	0.620

Notes: ^aP-value derived using Fisher's exact test. ^bP-value derived using Wilcoxon the rank-sum test. ^cMissing value for IOP in first month (n = 1) and suture type (n = 4).

Abbreviations: BCVA, best-corrected visual acuity; IOP, intraocular pressure; IQR, interquartile range.

grafting between traumatic and non-traumatic patients ($p=0.12$).

Sixty (85%) and 11 (15%) patients underwent PK and DALK, respectively. Interrupted and continuous sutures were used in 62 (87%) and 5 (7%) patients, respectively. Suture technique data were unavailable for 4 (6%) patients. Sutures were removed prior to dehiscence in 39 (55%) patients, of which 30 (77%) had more than half their sutures removed. There was no difference in the type of graft ($p=0.51$), suturing technique ($p=0.65$), removal of sutures prior to dehiscence ($p=0.33$) or extent of suture removal prior to dehiscence ($p=0.46$) between traumatic or non-traumatic patients.

The median pre-dehiscence BCVA was better in patients who suffered traumatic dehiscence compared to those who suffered non-traumatic dehiscence (LogMAR: 0.48, IQR 0.18–1.50 vs 1.00, IQR 0.50–2.00. Snellen: 6/18, IQR 6/9 - <6/60 vs 6/60, IQR 6/19 – count fingers, $p=0.01$). At 6 months post-dehiscence repair, traumatic patients had worse median BCVA compared to non-traumatic patients (LogMAR: 1.00 vs 0.78, Snellen: 6/60 vs 6/36) however this did not reach statistical significance ($p=0.62$).

Variables associated with visual acuity outcomes at 1 week, 3 months and 6 months post-dehiscence repair, derived from univariate linear regression analysis, are summarised in Table 2. Patients who were grafted for keratoconus had favourable visual outcomes at 6 months compared to those who were not ($p<0.001$). This remained significant in multivariate analysis ($p<0.001$). Similarly, patients who underwent DALK, had better visual acuity outcomes at 6 months compared to those who underwent PK ($p=0.04$). However, this was not statistically significant after adjusting for keratoconus status ($p=0.41$). Advanced age at the time of grafting and dehiscence was associated with poorer visual outcomes at 1 week, 3 months and 6 months in univariate analysis. However, after adjusting for age at the time of dehiscence, advanced age at the time of grafting was associated with improved visual acuity at 1 week ($p=0.003$) and 3 months ($p=0.02$), with no statistically significant association observed at 6 months ($p=0.11$). Time to dehiscence repair, gender, elevated IOP in the first month post-dehiscence repair and suture technique were not associated with a change in visual outcome at 6 months.

Discussion

Anterior and full-thickness corneal transplantation surgeries entail the formation of a circular 360-degree wound that heals by scarring, inadvertently resulting in a site of life

long weakness. While this complication has been well reported in the literature, ours is the first to comparatively evaluate the clinical associations and risk factors for poor visual outcomes between traumatic and non-traumatic dehiscence. Additionally, this report contains the largest number of post-keratoplasty wound dehiscence cases of any cause and the largest number of non-traumatic cases.

With the exception of age at the time of grafting and dehiscence, the time interval from keratoplasty to dehiscence, and pre-dehiscence visual acuity, there was no significant difference in the clinical history or patient demographics associated with either type of graft dehiscence. This poses a clinical challenge as it does not immediately indicate a clinical risk factor or predisposition that can easily be addressed. Rather, it suggests that with the exception of patient age, the risk of traumatic and non-traumatic dehiscence is equivalent for all grafts, irrespective of the specific clinical context.

Male sex is known to be associated with traumatic injury and this relationship is reflected in our results, with almost 70% of traumatic cases affecting men. However, no statistically significant association was observed between sex and the type of dehiscence in our series, potentially indicating that male sex may also be a risk factor for non-traumatic dehiscence. Whilst this is a significant finding, the sample size in this study may be insufficient to detect a significant difference and therefore further investigation is warranted to delineate this relationship. In the interim, ophthalmologists should be particularly mindful of this patient cohort and take particular care to emphasise the importance of medication compliance and postoperative follow-up in order to improve outcomes for this demographic.

The lack of association between the nature of graft dehiscence and graft indication, type of graft, and suture type is reassuring, given that it does not suggest that the type of dehiscence is predisposed to by surgical technique. Similarly, suture technique and graft type (PK or DALK) were not associated with the nature of graft dehiscence. This suggests that the theoretical benefit of DALK of increased structural integrity was not realised in our series, and can be considered in clinical decision-making for risk profiles when deciding on grafting type. This may be due to the structural nature of DALKs, where the wound profile is similar to a full-thickness corneal transplantation except for a thin barrier of Descemet's membrane.

It is well established that traumatic wound dehiscence can occur many years after surgery.^{1,8,11,12,16–18,21} The

Table 2 Factors Associated With Visual Acuity Outcomes Derived From Univariable Linear Regression Analysis

	LogMAR Visual Acuity											
	1 Week Post-Dehiscence				3 Months Post-Dehiscence				6 Months Post-Dehiscence			
	% ^a	95% CI		p-value	% ^a	95% CI		p-value	% ^a	95% CI		p-value
Age at grafting (years)	0.7	0.2	1.2	0.003	0.6	0.1	1.1	0.019	0.5	0.1	1.0	0.031
Age of patient at time of dehiscence (years)	1.0	0.6	1.4	<0.001	0.8	0.4	1.3	0.001	0.7	0.2	1.2	0.004
Age of graft at time of dehiscence (years)	2.2	0.9	3.6	0.001	1.9	0.5	3.3	0.007	1.4	0.0	2.9	0.047
Time to dehiscence repair (days)	-1.5	-3.9	1.0	0.238	-1.9	-4.4	0.7	0.140	-1.1	-3.7	1.5	0.393
Highest IOP 1st month post-op (mmHg)	-0.6	-1.9	0.8	0.388	-0.5	-1.9	0.9	0.456	-0.2	-1.6	1.2	0.757
Log transformed BCVA pre-graft	48.4	9.8	100.5	0.011	34.5	-2.1	84.7	0.067	19.7	-13.3	65.3	0.269
Log transformed BCVA pre-dehiscence	65.1	30.7	108.5	<0.001	69.6	33.5	115.5	<0.001	51.2	17.5	94.5	0.002
Sex												
Male	Reference				Reference				Reference			
Female	34.2	7.7	67.2	0.010	18.6	-6.2	50.0	0.151	13.1	-10.7	43.3	0.301
Cause												
Traumatic	Reference				Reference				Reference			
Non-traumatic	-15.9	-32.9	5.4	0.132	2.7	-19.0	30.1	0.826	-5.6	-25.5	19.5	0.628
Keratoconus												
No	Reference				Reference				Reference			
Yes	-29.8	-43.0	-13.6	0.001	-33.0	-45.7	-17.3	<0.001	-37.3	-48.8	-23.2	<0.001
Graft type												
Penetrating keratoplasty	Reference				Reference				Reference			
Deep anterior lamellar keratoplasty	-34.9	-51.4	-12.8	0.005	-30.1	-48.6	-4.9	0.023	-28.2	-47.3	-2.1	0.036
Sutures												
Interrupted	Reference				Reference				Reference			
Continuous	23.2	-19.6	88.7	0.332	39.3	-9.6	114.7	0.130	41.2	-8.3	117.3	0.115
Suture removal												
No	Reference				Reference				Reference			
Yes	29.9	4.4	61.7	0.020	28.0	1.8	60.8	0.035	14.7	-9.2	44.9	0.245

Notes: ^aValues indicate the percentage difference in logMAR BCVA per unit increase in the predictor. Positive values indicate worse vision.

Abbreviations: BCVA, best-corrected visual acuity; IOP, intraocular pressure.

long-term risk of non-traumatic dehiscence is less well known. The longest interval from keratoplasty to dehiscence observed in this series was 41 years and represents the largest reported value in the literature. This occurred in a patient who had suffered non-traumatic dehiscence following PK and confirms that the risk of dehiscence is lifelong and patients should be counselled regarding this.

Non-traumatic dehiscence tended to occur significantly earlier than traumatic dehiscence (0.2 vs 2.3 years post-keratoplasty), a finding that is consistent with the limited available literature.^{16,19} There are a number of possible explanations for

this observation. Firstly, the immediate post-operative period is high-risk for the development of microbial keratitis, with up to 80% of cases occurring in the first year.^{22,23} Similarly, the graft-host junction is most reliant on sutures for its structural integrity during the early post-operative period, before wound healing has occurred, leaving it vulnerable to suture related complications during this time. This is in contrast to trauma, which is more likely to occur randomly throughout life. Furthermore, the immediate period following suture removal, which typically occurs between 18 months and 2 years post-operatively, is high risk for traumatic dehiscence; contributing

to the relatively delayed presentation of this complication. Lastly, it has been postulated that patients may initially be very cautious following surgery, reducing their risk of trauma initially, and with time, become more confident and engage in behaviours that put them at risk of trauma.²⁰ Patients should be advised of the bimodal distribution of risk of dehiscence and advised to be extra cautious, especially following suture removal.

The finding that patients with non-traumatic dehiscence had worse pre-dehiscence visual acuity is likely multifactorial. The younger age of traumatic patients makes them less likely to have ocular co-morbidities affecting their visual acuity. Additionally, visual recovery following penetrating keratoplasty occurs over months, and therefore grafts affected by non-traumatic dehiscence would not have reached their final visual potential even without wound dehiscence complicating their post-operative recovery. Conversely, traumatic dehiscence occurred at a median interval of 2.3 years post-keratoplasty and as such, these grafts would be much more likely to have reached their visual potential. Traumatic dehiscence is also more likely to occur in a manner that is independent of underlying graft health compared to non-traumatic dehiscence. For example, dehiscence secondary to assault does not reflect underlying graft health. This is in contrast to non-traumatic dehiscence, where poor graft health may simultaneously produce poor visual acuity and predispose to the development of microbial keratitis or suture related complications.

The 6-month visual outcomes for the cohort were poor, emphasising the clinical significance and poor prognosis of post-keratoplasty graft dehiscence. Amongst those who suffered traumatic dehiscence, the median BCVA was 6/60 whilst for those for suffered non-traumatic dehiscence the median BCVA visual acuity was 6/36. This is likely due to the associated injuries that occur with a traumatic injury such as lens expulsion and retinal detachment.⁷ Although, it is also possible that with longer follow-up, a statistically significant difference between these groups may arise, due to the propensity for endothelial cell failure to develop following traumatic injuries.¹⁸

This study is subject to limitations common to all retrospective reviews. Given the possibility that cases may have been managed at other institutions with an ophthalmology service, the study population may not be representative of the broader population. Conversely, this study contains a large number of patients, in particular non-traumatic patients, and is therefore sufficiently powered to compare the differences between traumatic and non-traumatic dehiscence.

In conclusion, post-keratoplasty wound dehiscence remains a significant and serious complication following PK and DALK, with poor visual outcomes observed across the cohort regardless of the underlying cause of dehiscence. While the risk of dehiscence is lifelong, patients should be informed that the greatest risk exists within the first 3 years post-operative, and particularly after suture removal. Patients should be informed about the use of protective eyewear to prevent traumatic dehiscence and be advised to present immediately if they develop any symptoms suggestive of suture complications.

Statement Of Human Rights

This research was conducted in accordance with the ethical standards of the institution and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethics approval was granted by the Royal Victorian Eye and Ear Hospital Human Research Ethics Committee – reference number 19/1413HQ.

Declaration Of Informed Consent

Informed consent was not obtained as this is a retrospective review and contains no identifying patient information.

Disclosure

The authors declare they have no conflicts of interest.

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