Eye (2009) 23, 1295–1301
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www.nature.com/eye

CLINICAL STUDY

The visual and refractive outcomes of combined and sequential penetrating keratoplasty, cataract extraction, and intraocular lens insertion

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Abstract

Purpose **The aim of this study was to investigate the visual and refractive outcome of combined penetrating keratoplasty, cataract extraction, and intraocular lens insertion (triple procedure) compared with cataract surgery following penetrating keratoplasty (sequential surgery).**

Methods **Retrospective cohort study of 1256 first penetrating keratoplasty for Fuchs' dystrophy performed between April 1999 and December 2005. In all, 1202 triple and 54 sequential procedures were reviewed. At 1 year, refractive outcomes were available for 499 triple procedure and 26 sequential surgery eyes. At 2 years, data were available for 264 triple procedure and 10 sequential surgery eyes. At 1 and 2 years postoperatively, graft survival, best-corrected visual acuity (BCVA), spherical equivalent, and cylindrical error were recorded. χ^2-Tests were used to compare visual outcomes between the two groups.**

Results **At 1 year after triple procedure surgery, 61% of eyes attained BCVA of $\geqslant$6/12, with 47% of eyes within $\pm$2 D of emmetropia. After sequential surgery, 59% achieved BCVA of $\geqslant$6/12 with 67% of eyes within $\pm$2 D of emmetropia ($=0.05$). Mean spherical equivalent (MSE) at 1 and 2 years after triple procedure was $+1.20$ D (SD 5.45) and $+0.15$ D (SD 3.58), respectively. MSE following sequential surgery at 1 and 2 years was $+0.08$ D (SD 3.06) and -1.50 D (SD 3.14), respectively. Mean refractive cylinder after combined surgery was $+4.16$ D (SD 5.11) and $+3.91$ D (SD 2.79) at 1 and 2 years, respectively, compared with $+3.65$ D (SD 2.24) and $+3.70$ D (SD 2.06) after sequential surgery. In all, 29% of triple procedure and 27% sequential surgery eyes had an astigmatic error $\geqslant$5.0 D after 1 year ($P=0.64$), which increased to 34 and 30%, respectively, by the second year. The 5-year graft survival was 85% in both groups. There were no differences in graft survival, visual or refractive outcomes between triple procedure, and sequential surgery techniques.**

Conclusions **This analysis provided no evidence of improved visual or refractive outcome after sequential surgery compared with triple procedure.**

Eye (2009) **23,** 1295–1301; doi:10.1038/eye.2008.301; published online 3 October 2008

Keywords: astigmatism; intraocular lens; penetrating keratoplasty; refractive outcome; triple procedure; visual acuity

Introduction

A number of patients with corneal pathology requiring penetrating keratoplasty (PK) will also have cataracts. For such patients, the triple procedure (combined PK, cataract extraction, and intraocular lens (IOL) implantation) has been an established surgical treatment for over 30 years,[1] providing good visual outcome in patients with corneal opacity and cataracts.[2–24] Combined surgery is of particular benefit for

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Received: 25 June 2008
Accepted in revised form: 6 September 2008
Published online: 3 October 2008

This study has been previously presented at the Royal College of Ophthalmologists Congress, Liverpool, 2008
Financial interests: None

patients requiring quicker visual recovery, like the elderly patients those with poor vision in their fellow eye or who have significant health problems.

An alternative technique, sequential surgery, delays cataract surgery and IOL implantation until some time after PK with a consequential delay in visual rehabilitation and the associated risks of a second operative procedure. Whether to perform a triple procedure or sequential surgery remains a debated topic.[25,26] Small comparative studies have reported superior visual and refractive outcomes with sequential surgery owing to better IOL power calculation from stable post-PK keratometry readings.[26–30] Our aim was to compare triple procedure and sequential surgery, in terms of visual and refractive outcomes at 1 and 2 years after PK, using data collected routinely through the UK Transplant (UKT).

Patients and methods

We retrospectively reviewed the results of all eyes that underwent triple procedure or sequential surgery (cataract extraction and IOL insertion within 16 months of PK) between April 1999 and December 2005. Data on approximately 2500 corneal grafts per annum are routinely collected by UKT through the UK Ocular Tissue Transplant Audit. Surgeons submit data at the time of surgery, including patient details, such as age, sex, indication for transplantation, type of procedure, previous grafts and other risk factors, and the best-corrected visual acuity (BCVA). Data, including Snellen VA and refractive outcomes (spherical equivalent and astigmatism) are also submitted at 1, 2, and 5 years postoperatively. For our analysis, postoperative data from 1 and 2 years were used. The acceptable range for visual outcome data was considered to be between 8 and 16 months and between 20 and 28 months for 1- and 2-year visual outcomes, respectively.. Patients without complete refractive data were excluded from the analysis of refractive outcomes. All statistical analyses were performed using SAS V9.1 software (SAS institute inc., Cary, NC, USA). Kaplan–Meier survival estimates were used to determine graft survival. Differences in recipient age between the two groups were evaluated using the Kruskal–Wallis test. χ^2-Squared tests were used to compare visual outcomes between the two groups.

Results

Patient population

The study population consisted of 1256 first PK for Fuchs' dystrophy where cataract extraction was performed either at the time of transplant or within 16 months following PK: 1202 having had a triple procedure and 54 sequential surgeries. A larger proportion of women received both triple procedure (68%) and sequential surgeries (57%). The median age for patients undergoing a combined triple procedure was 75, (IQ 68, 79) compared with 71 (IQ 63, 77) for those who had sequential surgery ($P = 0.006$). The 2-year BCVA data were available for 596 triple procedures and 32 sequential surgery eyes, where BCVA had also been reported to UKT preoperatively. The 2-year refractive data were available for 264 triple procedures and 10 sequential surgery eyes.

Visual acuity

The type of surgery made no difference to postoperative BCVA with similar proportions of patients in both groups achieving a BCVA of 6/12 or better: at 1 year, 61% of triple procedures and 59% of sequential surgeries achieved this level of vision and at 2 years, the respective figures were 71 and 75%. Table 1 shows the median BCVA and interquartile (IQ) range along with the number of lines of improvement on the Snellen chart. At 1 year, median BCVA was 6/12 for both techniques with two lines of improvement on the Snellen chart (IQ = 1 and 4). At 2 years, BCVA remained at 6/12 for

Table 1 Visual acuity of patients post-penetrating keratoplasty and IOL insertion

	N	*Preoperative acuity*		*Postoperative acuity*		*Lines of change*	
		Median	*IQ range*	*Median*	*IQ range*	*Median*	*IQ range*
One year							
Triple	858	6/36	6/18, 6/60	6/12	6/9, 6/18	2	(1, 4)
Sequential	46	6/24	6/18, 6/60	6/12	6/9, 6/18	2	(1, 4)
Two years							
Triple	596	6/36	6/18, 6/60	6/12	6/9, 6/18	3	(1, 4)
Sequential	32	6/18	6/18. 6/36	6/9	6/6, 6/12	2	(1, 4)

IOL, intraocular lens; IQ, interquartile range.

triple procedures with an improvement of three lines (IQ = 1 and 4) compared with a median acuity of 6/9 after sequential surgery with an improvement of two lines (IQ = 1 and 4) on the Snellen chart.

Refraction

Complete refractive data were available after sequential surgery for only 26 eyes at 1 year and for 10 eyes at 2 years postoperatively. One year after triple procedure, the mean spherical equivalent (MSE) was +1.20 D and +0.08 D following sequential surgery. At 2 years, the MSE was +0.15 D after triple procedure surgery and −1.50 D after sequential surgery. Forty-seven percent of eyes undergoing triple procedure were within ±2 D of emmetropia at 1 year with 55% achieving this by the second year. For sequential surgery, the equivalent data were 67% of eyes at 1 year ($P = 0.05$) and 50% at 2 years ($P = 0.80$; Table 2). Mean refractive cylinder for triple procedure and sequential surgery was 4.16 D and 3.65 D at 1 year, respectively, and 3.91 D and 3.70 D at 2 years, respectively (Table 3). There was little difference between the techniques in spherical equivalent and scalar cylinder at 2 years, although the paucity of refractive data in the sequential surgery group should be noted.

Table 2 Refractive outcome (±2 D and ±5 D emmetropia) post-keratoplasty and IOL insertion

	N	*MSE*	*±2 D*	*±5 D*
One year				
Triple	499	+1.20 (±5.45)	47%	13%
Sequential	26	+0.08 (±3.06)	67%	7%
P-value			0.05	0.41
Two years				
Triple	264	+0.15 (±3.58)	55%	12%
Sequential	10	−1.50 (±3.14)	50%	10%
P-value			0.80	0.87

D, diopters; IOL, intraocular lens; MSE, mean spherical equivalent.

Table 3 Refractive outcome (⩽2 D and ⩾5 D cylinder) post-keratoplasty and IOL insertion

	N	*Mean cylinder*	*⩽2 D*	*⩾5 D*
One year				
Triple	499	+4.16 (±5.11)	29%	29%
Sequential	26	+3.65 (±2.24)	35%	27%
P-value			0.64	0.64
Two years				
Triple	264	+3.91 (±2.79)	35%	34%
Sequential	10	+3.70 (±2.06)	20%	30%
P-value			0.89	0.89

D, diopters; IOL, intraocular lens.

Large ametropic errors

Thirteen percent of triple procedure and 7% of sequential surgery eyes had a spherical equivalent greater than ±5 D at 1 year ($P = 0.41$). At 2 years, 12% of triple procedures and 10% of sequential surgery eyes had a spherical equivalent greater than ±5 D ($P = 0.87$). Similar proportions in both groups had a postoperative astigmatic error ⩾5.0 D (Table 3).

Graft survival

Graft survival was 97% at 1 year in the triple group, decreasing to 93% at 2 years. The 5-year survival was 85% for both the triple procedure (95% CI: 80–89%) and sequential surgery (95% CI: 51–95%) with follow-up reported for 33% of triple procedures and 38% of sequential cataract after PK group.

Discussion

Surgical management of patients with coexisting corneal pathology and cataract is commonly approached by performing combined penetrating keratoplasty, cataract extraction, and IOL insertion (triple procedure); or performing PK alone followed by cataract extraction and IOL implantation at a later operation (sequential surgery). Debate continues as to which procedure is most appropriate for patients and offers the best visual and refractive outcomes. Performing a single combined operation reduces the risks to the patients and the costs of surgery with more rapid visual rehabilitation. This is advantageous for elderly patients, those with other health problems; and patients in urgent need for improved functional vision.

BCVA

The majority of previous studies have reported similar outcomes to our results with BCVA ⩾6/12 in 64–85% of eyes;[3–5,7,11,18,21–23,31,32] a few studies managed this acuity in only 38–46% of their patients.[8,10,16,17,29,33] Serdarevic *et al*[15] reported that all of their patients achieved BCVA ⩾6/12. They hypothesised a correlation existed between the preoperative dioptric power of peripheral recipient corneas and the postoperative central power of grafted donor corneas and used videokeratoscopic analysis of peripheral recipient corneas to determine IOL power.

The visual outcomes we found after sequential surgery are comparable with previous studies of sequential surgery.[13,29,31,34,35] An advantage of sequential surgery is the ability to perform additional refractive surgery before and during the second operation. Hsiao *et al*[13] and Geggel[34] reported BCVA ⩾6/12 in 81 and 86% from their

series of eyes, with relaxing corneal incisions performed in 23 and 59% of patients, respectively. The potential for wide variations in refractive outcome highlights the challenge faced by the surgeon in determining the appropriate IOL power for triple procedures. To predict accurately the postoperative refractive error, reliable axial length and keratometry (*K*) readings are essential. This can become complicated when corneal oedema or irregular corneal scarring presents abnormal *K*-values, increasing the risk of unanticipated ametropic errors and significant anisometropia.[6] The use of *K* readings from the fellow eye does not provide reliable measurements.[3] As post-PK corneal curvature cannot be accurately predicted in advance,[5] use of multiple regression analysis with surgeon-specific values, such as average post-keratoplasty *K* values, individualised A-constants, or fixed values for the anterior chamber depth has been advocated.[4–6,8,12,18–21,36–38] However, there remains no universally accepted formula that will reliably predict an IOL power to produce emmetropia.

Emmetropia

The number of eyes achieving ±2 D emmetropia may be a more accurate reflection of visual outcome than BCVA. Our results reveal 47% of eyes undergoing triple procedure surgery were within ±2 D of emmetropia at 1 year, with 55% achieving this by the second year. This compares favourably with other studies where 39–47% of eyes attained ±2 D of emmetropia.[27–31] The majority of studies evaluating triple surgery alone have shown approximately 50% of eyes achieve ±2 D of emmetropia, although the range of 26–95% within ±2 D of emmetropia is rather wide.[3–5,9,10,13,15–22,24,32,36] Supporters of sequential surgery highlight the potential for large ametropic errors with triple procedure surgery, arguing that IOL power can be calculated with greater accuracy when biometry is performed on a stable graft.[26,34] Sixty-seven percent of eyes that underwent sequential surgery in our study were within ±2 D of emmetropia at 1 year. Only 50% of eyes recorded this at the second year, but this may have been influenced by the low numbers of eyes with complete follow-up data. Other comparative studies (Table 4) have demonstrated 48–96% of eyes to be within ±2 D of emmetropia.[27–31] Geggel[34] reported 95% of eyes within ±2 D of emmetropia; but 59% of eyes in this series received astigmatic correction at the time of secondary surgery, and all graft corneal sutures had been removed in 86% of eyes. Corneal curvature has been shown to change in an unpredictable manner after suture removal,[39] and, if possible, it is preferable to remove all graft sutures before IOL power calculation for sequential surgery. Other factors that could potentially influence the refractive outcome after surgery includes the size of the graft and recipient corneal bed, trephination, and suturing technique.[38,40,41]

Astigmatic error

In our study, a scalar cylinder of ⩾5.0 D was found in 29% of triple procedures and 27% of sequential surgery eyes after 1 year ($P=0.64$) increasing to 34 and 30% of eyes, respectively, at the second year ($P=0.89$). The increase in the scalar cylinder (astigmatism) may have resulted from the overall lower number of keratoplasties reported at the second year. Other studies have reported refractive astigmatism ⩾5 D occurring in 29–44% of eyes after triple procedure[9,10,42] and 12% of eyes after

Table 4 Previous comparative studies of triple procedure and sequential surgery

Study design	*Design*	*Number of eyes*	*Mean follow-up (monthss)*	*Eyes ±2 D of target/ emmetropia (%)*	*MSE (D)*	*Mean cylinder*	*BCVA ⩾6/12 (%)*	*Graft survival (%)*
Nguyen and colleagues[24]	Retrospective	T—499	12	47	1.20	4.16	61	97
		S—26		67	0.08	3.65	71	100
		T—264	24	55	0.15	3.91	71	93
		S—10		50	−1.50	3.70	75	100
Hayashi and Hayashi[27]	Prospective	T—29		39				
		S—23		70				
Gruenauer *et al*[30]	Retrospective	T—53	20.5	47	−2.06	−4.00		100
		S—29		96	0.70	−3.50		100
Parmar *et al*[29]	Retrospective	T—28	9.4	55			39	79
		S—30	8.5	42			47	90
Shimmura *et al*[28]	Prospective	T—22		45		3.40		
		S—11		91		2.40		
Pineros *et al*[31]	Retrospective	T—93		42%		3.90	65	
		S—23		48		4.10	66	

D, diopters; BCVA, best-corrected visual acuity; MSE, mean spherical equivalent; S, sequential surgery; T, triple procedure surgery.

sequential surgery.[13] The comparative studies of Pineros *et al*[31] revealed an astigmatic error $\geqslant 5$ D in 38% triple procedure and 42% sequential surgery eyes. In contrast, Parmar *et al*[29] reported an astigmatic error >5 D in 23% after triple procedure surgery, but in only 9% of eyes after sequential surgery.

Sequential surgery may not be appropriate for all patients undergoing surgery, when combined surgery may allow faster visual rehabilitation compared with sequential surgery.[5–8,12,18,21,43] The latter technique may not be acceptable for patients who are elderly and have other health problems, or cannot tolerate a second procedure. Newer triple procedure surgery involving endothelial keratoplasty[44,45] combined with phacoemulsification and IOL implantation have demonstrated good predictability in postoperative refractive error.

Graft survival

All sequential surgery grafts remained clear at 2 years with only two failures after 5 years. The 5-year graft survival was 85% for both groups, which compares well with published triple procedure survival rates of 69–100% over variable follow-up periods.[5,8–11,16,18,22,23,29–33,42,46] The 2007 Australian Corneal Graft Registry[47] reported 1- and 5-year graft survivals of 89 and 78%, respectively, for triple procedure. Sequential surgery has been associated with increased graft endothelial cell count loss, and graft failure as high as 13–21%.[34,35,45,48–51] However, improved surgical techniques and the use of intraocular viscoelastic agents may mean that secondary surgery can be performed with greater safety as suggested by a lower failure rate of 0–16% in more recent studies.[13,29,30,34,35,43,49–52] Other authors have found no higher risk of graft failure from sequential surgery over triple procedure surgery,[13,28,35,46] with no significant difference in the percentage of endothelial cell loss[27,28] or increase in graft rejection episodes.[31]

Limitations

The numbers of patients involved in studies of triple procedure and sequential surgery have been generally small with study methodology differing in their inclusion or exclusion criteria, with non-uniform operating and suturing techniques with single or multiple surgeons. Consequently, any confounding factors can potentially greatly influence results and subsequent conclusions. In previous studies, reporting of postoperative results can be biased depending on whether patients with posterior segment disease were excluded from the analysis with significant impacts on BCVA outcomes. We did not exclude patients with other ocular comorbidities from our study and feel that our results of spherical and cylindrical error provide a more complete picture. Registry studies can suffer from limitations in retrospective design, with less reliable methods of data collection and the inability to control all potential variables and biases. Important long-term outcome data, however, can be obtained from registries, such as UKT, where data from a large numbers of cases can be collected and used as a quality control. These results indicate that in the United Kingdom, triple procedure surgery is much more commonly performed than sequential surgery. This consequentially limits the numbers of eyes having undergone sequential surgery and makes comparisons between the two techniques difficult. The preference for triple procedure surgery reflected in our study is supported by a survey where 92% of surgeons replied that they would perform combined surgery if a patient had coexisting corneal disease and cataract.[53]

Conclusion

The majority of comparative studies suggest sequential surgery results in more reliable visual and refractive outcomes over triple procedure surgery; however, sequential surgery may not be appropriate for all patients. Our study failed to show a difference in visual and refractive outcomes between triple procedure and sequential surgery, which adds value for the current clinical practice adopted by most surgeons in the United Kingdom to perform a triple procedure when a patient possesses visually symptomatic corneal disease and cataract. One of the most important considerations for both patient and surgeon is the patient's ability to regain useful vision. The faster visual rehabilitation from a single operative procedure is an advantage of triple procedure, whereas the presumed benefit of more accurate IOL selection and better visual outcome in sequential surgery was not borne out by our study.

Acknowledgements

We thank all the ophthalmic surgeons who contributed to the UK Transplant for their continued support and active participation.

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