Published in final edited form as:
Am J Ophthalmol. 2011 March ; 151(3): 397–398. doi:10.1016/j.ajo.2010.10.006.

GRAFT SURVIVAL AFTER PENETRATING KERATOPLASTY

Sanjay V. Patel
Department of Ophthalmology, Mayo Clinic, Rochester, Minnesota

Corneal transplantation has evolved toward selective tissue transplantation over the last decade, with many corneal diseases being treated by a variety of anterior and posterior lamellar graft procedures. Surgeons have rapidly adopted these new techniques because of distinct advantages over penetrating keratoplasty (PK).[1] Simultaneously, the quest for a tissue-engineered corneal substitute has made rapid progress, and implantation of corneal substitutes might become the future of corneal surgery.[2] Despite the exciting progress in corneal surgery, PK remains the commonest form of corneal transplantation in the world at present, and although PK might diminish in importance in the future, it will remain the default or procedure of choice for some eyes.

The success of PK has generally been measured by the longevity of graft survival, which is the time to graft failure. A wealth of graft survival and outcomes data have been amassed over the last three decades from sources such as individual surgeon series,[3–5] randomized clinical trials,[6] and corneal graft registries.[7–9] The Singapore Corneal Transplant Study (SCTS) is one such source of data, and is unique because it reflects the indications for and outcomes of PK in an Asian population.[10] Since 1991, all corneal transplant procedures at the Singapore National Eye Center, which performs 80–90% of all transplants in Singapore, have been entered into the SCTS, and postoperative outcomes have been recorded annually. During the first 13 years of the study, there were 1130 PKs, and the initial outcomes of 901 PKs in 901 eyes were reported.[10] Of these, 87% were for optical (visual rehabilitation) indications, whereas 13% were for therapeutic (surgical treatment of infectious disease) and tectonic (preservation of globe integrity) indications. The graft survival rate was highest for optical indications (64% at 5 years and 52% at 10 years) and was lower for therapeutic (37% at 5 years) and tectonic (42% at 3 years) indications. At the time of the first report of the SCTS,[10] 31% of penetrating grafts were known to have failed, and half of these were because of endothelial graft rejection and late endothelial failure. The initial results of optical PK in the SCTS are comparable to those of other large series outside of Asia (there are limited data for outcomes of PK in Asia[11]), and are a testament to successful corneal transplantation and eye banking in Asia. Not surprisingly, the proportion of therapeutic and tectonic PKs in Asia, accounting for 12–13% of all PKs,[10,11] is much higher than outside of Asia.

In this issue, Anshu et al. report the postoperative factors that influenced graft survival after PK in the SCTS.[12] Graft survival was excellent (85% at 10 years) in the absence of any postoperative risk factor, but the presence of one postoperative risk factor, including infection, rejection, disease recurrence, eyelid or glaucoma surgery, or a repeat graft, resulted in lower graft survival (34% at 10 years). Anshu et al. also performed a multivariate analysis of preoperative, intraoperative, and postoperative risk factors in the SCTS and found that the postoperative factors listed above were indeed independent risk factors for graft failure, and identified recipient diagnosis, recipient gender, preoperative inflammation,

Corresponding Author: Sanjay V. Patel, MD 200 First Street SW Rochester, MN 55905 Tel: (507) 284-4572 Fax: (507) 284-8566 patel.sanjay@mayo.edu.

and donor diameter, as additional independent risk factors. Thus, while the preoperative risk factors for graft failure cannot be modified, the prevention or early detection of postoperative risk factors for graft failure might be important for prolonging graft survival.

Many of the risk factors for graft survival in the SCTS agree with those identified in other large series. After considering the data from the SCTS and from the other series, several common risk factors become apparent, and can be divided into recipient, donor, and postoperative risk factors. Recipient diagnosis is the most important preoperative risk factor, with grafts for keratoconus having the best survival rate, and grafts for endothelial disease, corneal opacity, and ipsilateral graft failure having a worse survival rate.[3–5,8,10,13] Recipients in their first decade of life have poor graft survival,[8] and survival is also worsened by active or previous intraocular inflammation or ocular hypertension.[7,10,13] With the exception of donor diameter,[10,13] donor and preservation factors appear to have little influence on graft survival,[5,10] presumably because donors are screened and selected by eye banks for tissue quality. Postoperatively, allograft rejection has consistently been found to be a leading cause of graft failure[3–5,8,10,13]; disease recurrence and infection are also significant postoperative risk factors, and they may have more importance in Asia because of the indications for PK in Asia. There have been conflicting results for corneal neovascularization, glaucoma, donor age, and preoperative donor endothelial cell density, as risk factors for graft survival. Discrepancies between studies may arise because of differences in study design, data collection methods, and definitions of outcomes, and because of variations in the populations, inclusion criteria, and postoperative immunosuppression regimens. In addition, studies could be biased by loss to follow-up, which is inevitable with all long-term graft survival studies.[5] In the SCTS the number grafts analyzed at each follow-up examination was not reported, although, attempts were made to recall as many patients as possible.

With all the data accumulated for PK outcomes from numerous studies over the last three decades, graft survival has remained the primary outcome measure of success. However, for several reasons, graft survival should be interpreted with caution when comparing different studies, and interpreted in the context of the study goals when assessing the success of corneal transplantation. First, there is no consensus for the definition of graft failure; some studies define this as the loss of optical clarity,[5,7,10] whereas other studies specify the loss of optical clarity in terms of a variably defined effect on vision.[3,4,6] Second, although loss of optical clarity is often considered to be a well-defined end-point,[14] there might be subjective variability in studies with multiple observers, and the gradual loss of clarity with late endothelial failure,[15] which is a leading cause of graft failure,[4,5,13] could give an uncertain end-point. Third, loss of optical clarity does not always convey success, depending on the broad indication (optical, therapeutic, or tectonic) for transplantation. For example, a cloudy graft after a therapeutic PK could be considered successful if all active infection were eradicated; in the SCTS, 13% of PKs were for therapeutic or tectonic indications, yet outcomes other than the time to loss of graft clarity were not reported to indicate whether these grafts served their initial purpose or not. Similarly, the optical clarity of grafts for optical indications does not directly convey success at restoring functional vision, or perhaps more broadly, quality of life, to the patient. While visual outcomes after corneal transplantation are important, they can be confounded by other causes of decreased vision and, after PK, are subject to the ability to provide the best refractive correction.[14] Nevertheless, as corneal transplantation techniques continue to evolve, especially for selective endothelial replacement, vision and quality of life outcomes might become more useful determinants of graft success.

Anshu et al. are to be congratulated for their valuable contribution of the risk factors for PK graft survival in an Asian population, which are pertinent to the treatment of corneal

blindness in the developing world. As the Singapore Corneal Transplant Study continues to mature, we can anticipate additional relevant outcomes data for various forms of corneal transplantation.

Acknowledgments

a. *Funding/Support:* Dr. Patel receives support from the National Institutes of Health, Bethesda, MD (EY 19339); Research to Prevent Blindness, New York, NY (Olga Keith Wiess Special Scholar); the Minnesota Partnership for Biotechnology and Medical Genomics; and Mayo Foundation, Rochester, MN.

b. *Financial Disclosures:* None.

References

1. Tan DT, Mehta JS. Future directions in lamellar corneal transplantation. Cornea. 2007; 26(9 Suppl 1):S21–28. [PubMed: 17881911]
2. Fagerholm P, Lagali NS, Merrett K, et al. A Biosynthetic Alternative to Human Donor Tissue for Inducing Corneal Regeneration: 24-Month Follow-Up of a Phase 1 Clinical Study. Sci Transl Med. 2010; 2(46):ra61.
3. Sit M, Weisbrod DJ, Naor J, Slomovic AR. Corneal graft outcome study. Cornea. 2001; 20(2):129–133. [PubMed: 11248813]
4. Thompson J, Robert W, Price MO, Bowers PJ, Price J, Francis W. Long-term graft survival after penetrating keratoplasty. Ophthalmology. 2003; 110(7):1396–1402. [PubMed: 12867398]
5. Patel SV, Diehl NN, Hodge DO, Bourne WM. Donor risk factors for graft failure in a 20-year study of penetrating keratoplasty. Arch Ophthalmol. 2010; 128(4):418–425. [PubMed: 20385937]
6. Cornea Donor Study Investigator Group. Gal RL, Dontchev M, et al. The effect of donor age on corneal transplantation outcome results of the cornea donor study. Ophthalmology. 2008; 115(4): 620–626.e626. [PubMed: 18387407]
7. Williams KA, Roder D, Esterman A, Muehlberg SM, Coster DJ. Factors predictive of corneal graft survival. Report from the Australian Corneal Graft Registry. Ophthalmology. 1992; 99(3):403–414. [PubMed: 1565452]
8. Vail A, Gore SM, Bradley BA, Easty DL, Rogers CA. Corneal graft survival and visual outcome. A multicenter study. Ophthalmology. 1994; 101(1):120–127. [PubMed: 8302544]
9. Claesson M, Armitage WJ, Fagerholm P, Stenevi U. Visual outcome in corneal grafts: a preliminary analysis of the Swedish Corneal Transplant Register. Br J Ophthalmol. 2002; 86(2):174–180. [PubMed: 11815343]
10. Tan DT, Janardhanan P, Zhou H, et al. Penetrating keratoplasty in Asian eyes: The Singapore Corneal Transplant Study. Ophthalmology. 2008; (115):975–982. [PubMed: 18061267]
11. Dandona L, Naduvilath TJ, Janarthanan M, Ragu K, Rao GN. Survival analysis and visual outcome in a large series of corneal transplants in India. Br J Ophthalmol. 1997; 81(9):726–731. [PubMed: 9422922]
12. Anshu, A.; Lim, LS.; Htoon, HM.; Tan, DT. In this Issue. Postoperative risk factors influencing corneal graft survival in the Singapore Corneal Transplant Study.
13. Williams KA, Lowe M, Bartlett C, Kelly TL, Coster DJ. Risk factors for human corneal graft failure within the Australian Corneal Graft Registry. Transplantation. 2008; 86(12):1720–1724. [PubMed: 19104411]
14. Coster DJ, Williams KA. The impact of corneal allograft rejection on the long-term outcome of corneal transplantation. Am J Ophthalmol. 2005; 140(6):1112–1122. [PubMed: 16376660]
15. Patel SV, McLaren JW, Hodge DO, Bourne WM. The effect of corneal light scatter on vision after penetrating keratoplasty. Am J Ophthalmol. 2008; 146(6):913–919. Epub 2008 Sep. [PubMed: 18774549]