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Authors

Group, Writing Committee for the Cornea Donor Study Research
Mannis, Mark J
Holland, Edward J
[et al.](#)

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The Effect of Donor Age on Penetrating Keratoplasty for Endothelial Disease: Graft Survival after 10 Years in the Cornea Donor Study

Mark J. Mannis, MD¹, Edward J Holland, MD², Robin L. Gal, MSPH³, Mariya Dontchev, MPH³, Craig Kollman, PhD³, Dan Raghinaru, MS³, Steven P. Dunn, MD⁴, Robert L. Schultze, MD⁵, David D. Verdier, MD⁶, Jonathan H. Lass, MD⁷, Irving M. Raber, MD⁸, Joel Sugar, MD⁹, Mark S. Gorovoy, MD¹⁰, Alan Sugar, MD¹¹, R. Doyle Stulting, MD, PhD¹², Monty M. Montoya, MBA¹³, Jeffrey G. Penta, MBA¹⁴, Beth Ann Benetz⁷, Roy W. Beck, MD, PhD³, and The Writing Committee for the Cornea Donor Study Research Group*

¹University of California Davis, Sacramento, CA

²Cincinnati Eye Institute, Department of Ophthalmology and Visual Sciences, Cincinnati, OH

³Jaeb Center for Health Research, Tampa, FL

⁴Michigan Cornea Consultants, P.C., Southfield, MI

⁵Cornea Consultants of Albany, Albany, NY

⁶Verdier Eye Center, Grand Rapids, MI

⁷Case Western Reserve University and University Hospitals Eye Institute, Cleveland, OH

⁸Ophthalmic Partners of Pennsylvania, Bala Cynwyd, PA

⁹University of Illinois at Chicago, Chicago, IL

¹⁰Gorovoy Eye Specialists, Ft. Meyers, FL

¹¹W.K. Kellogg Eye Center, University of Michigan, Ann Arbor, MI

¹²Emory University (now at Woolfson Eye Institute), Atlanta, GA

¹³SightLife, Seattle, WA

¹⁴San Diego Eye Bank, San Diego, CA

Abstract

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Address for Reprints: Mark J. Mannis, M.D., c/o CDS Coordinating Center, Jaeb Center for Health Research, 15310 Amberly Drive, Suite 350, Tampa, FL 33647, Phone: (813) 975-8690; Fax: (813) 975-8761; cds@jaeb.org.

*A full listing of the Cornea Donor Study Research Group is available at <http://aojournal.org>.

Conflict of Interest: Edward J. Holland, MD is employed by the Cincinnati Eye Bank, and serves as a consultant and receives lecture fees from Bausch & Lomb. Irving M. Raber, MD receives lecture fees from Bausch & Lomb. Robert L. Schultze, MD is employed by Sight Society of Northeastern New York and receives lecture fees from Bausch & Lomb. Monty M. Montoya, MBA is employed by SightLife. Jeffrey G. Penta, MBA is employed by San Diego Eye Bank.

The following material should appear online only: Table 2, Table 5, Figure 3, and the listing of the Cornea Donor Study Research Group.

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Objective—To determine whether the 10-year success rate of penetrating keratoplasty for corneal endothelial disorders is associated with donor age.

Design—Multi-center, prospective, double-masked clinical trial

Participants—1090 participants undergoing penetrating keratoplasty at 80 sites for Fuchs' dystrophy (62%), pseudophakic/aphakic corneal edema (34%) or another corneal endothelial disorder (4%) and followed for up to 12 years.

Methods—Forty-three eye banks provided corneas from donors 12 to 75 years old, using a randomized approach to assign donor corneas to study participants, without respect to recipient factors. Surgery and postoperative care were performed according to the surgeons' usual routines.

Main Outcome Measure—Graft failure defined as a regrant or in the absence of a regrant, a cloudy cornea that was sufficiently opaque to compromise vision for 3 consecutive months.

Results—In the primary analysis, the 10-year success rate was 77% for 707 corneas from donors 12 to 65 years old compared with 71% for 383 donors 66 to 75 years old (difference = +6%, 95% confidence interval = -1% to +12%, $P=0.11$). When analyzed as a continuous variable, higher donor age was associated with lower graft success after the first 5 years ($P<0.001$). Exploring this association further, we observed that the 10-year success rate was relatively constant for donors 34 to 71 years old (75%). The success rate was higher for 80 donors 12 to 33 (96%) and lower for 130 donors 72 to 75 years old (62%). The relative drop in the success rate with donor ages 72 to 75 years was not observed until after year 6.

Conclusions—Although the primary analysis did not show a significant difference in 10-year success rates comparing donor ages 12 to 65 and 66 to 75 years, there was evidence of a donor age effect at the extremes of the age range. Since we observed a fairly constant 10-year success rate for donors age 34 to 71 years, which account for approximately 75% of corneas in the United States available for transplant, the Cornea Donor Study results indicate that donor age is not an important factor in most penetrating keratoplasties for endothelial disease.

INTRODUCTION

In 2012, more than 46,000 cornea transplants were performed in the United States.¹ Although there is a sufficient supply of donor corneas to fulfill current domestic needs, increasing regulatory requirements pertaining to donor testing² may limit the supply of available tissue. Analysis of United States statistics from 2005–2011 confirms significant increases in the percent of recovered tissue that is excluded from transplantation due to positive donor serological test results, donor medical-social histories, and slit lamp exams.³ Moreover, there remains a significant shortage of donor tissue internationally, with just over 19,000 corneas distributed by Eye Bank Association of America (EBAA) member eye banks for international use in 2012.¹ Another potential challenge to the donor supply has been the transition from penetrating keratoplasty to endothelial keratoplasty for patients with endothelial disease, which has resulted in an increase in the number of patients having transplant surgery. EBAA statistics indicate that the number of endothelial keratoplasties in the United States increased from 1398 in 2005 to 24,277 in 2012.¹ For these reasons, there is a continued need to expand the cornea donor pool worldwide. Currently, approximately half of all cornea donors are over the age of 60¹, and this number is likely to increase as the older population in the United States continues to expand. Widespread utilization of older donor tissue could expand the donor pool.

The Cornea Donor Study (CDS) was initiated in 2000 to provide the requisite data needed by eye banks and surgeons to evaluate whether corneas from older donors would produce the same outcomes as tissue from younger donors after corneal transplantation for corneal endothelial conditions considered to be at moderate risk for failure, primarily Fuchs'

dystrophy and pseudophakic corneal edema.⁴ Although some of the factors that can limit the available donor pool differ now compared with 2000, the objective of the study with respect to donor age remains important. The CDS 5-year outcome data published in 2008 demonstrated that the 5-year cumulative probability of graft survival was 86% in both the 12 to 65 and the 66 to 75 year old donor age groups and there was no significant association between donor age and outcome.⁵ In addition, the distribution of causes of graft failure did not differ between the two donor age groups. The Specular Microscopy Ancillary Study (SMAS), which included 347 of the original cohort followed for five years without graft failure, found that there was a substantial decrease in endothelial cell density (ECD) from baseline for all donor ages.⁶ There was a weak negative association between ECD and donor age. Among eyes with a clear graft at 5 years, those in which the cornea was from a donor 12 to 65 years old experienced a median cell loss of 69%, resulting in a 5-year median ECD of 824 cells/mm², whereas eyes receiving a cornea from a donor 66 to 75 years old experienced a cell loss of 75%, resulting in a median 5-year ECD of 654 cells/mm².⁶ This finding of a slightly greater cell loss with older donors raised the question as to whether graft success would remain unassociated with donor age over longer-term follow up.

To determine whether the results obtained after 5 years, showing no meaningful effect of donor age on graft success, would be sustained, observation of the CDS cohort was continued. Herein, we report the CDS results over 11 years of follow up. ECD outcomes are reported separately.⁷

METHODS

The CDS is registered as a clinical trial through the Clinical Trials Registry of the National Institutes of Health (NCT00006411) and information is publically available (<http://www.clinicaltrials.gov>, accessed 05/16/13). The protocol was approved by institutional review boards for all investigational sites. Each participant gave written informed consent to participate in the study, which was initially planned for 5 years of follow up. Follow up was extended, and participants without a regrant were re-consented after five years to continue follow up through December 31, 2012, which allowed for potential follow up of 10 to 12 years depending on the time of penetrating keratoplasty during study enrollment. Study methods have been detailed in prior publications and are briefly described here.^{5, 8-10}

Between January 2000 and August 2002, 80 clinical sites enrolled 1,090 eligible participants whose median age at time of surgery was 72 years (interquartile range 65 to 76 years); 697 (64%) were female and 1,011 (93%) were Caucasian. The primary indication for transplant was Fuchs' dystrophy in 676 (62%), pseudophakic or aphakic corneal edema in 369 (34%) and another corneal condition in 45 (4%) eyes. 383 (35%) study eyes received a cornea from a donor 66 to 75 years old and 707 (65%) from a donor 12 to 65 years old. Participant characteristics and donor cornea slit lamp characteristics and procurement factors were similar in the older and younger donor age groups.

At 43 eye banks, donor corneas were procured and evaluated according to the standard procedures of each eye bank, including assessment of ECD by specular microscopy. Corneas were from donors 12 to 75 years old (a range investigators found acceptable given that they were masked to donor age), with a median ECD of 2666 cells/mm² (interquartile range 2462 to 2872 cells/mm²) measured by the eye banks. The donor corneas were assigned to study participants using a randomization procedure without respect to recipient age or other participant characteristics. Clinical investigators and participants were masked to all characteristics of the donor cornea including donor age and ECD while the participant was still active in the study. Preoperative management, surgical technique, and postoperative

care, including prescription of medications, were provided according to each investigator's customary routine.

Of the 765 living participants eligible for follow up after the first 5 years (no graft failure, choroidal hemorrhage, or trauma; and not withdrawn or lost to follow up), 663 (87%) consented to continuation of annual study visits through December 31, 2012. Additional visits were at the discretion of the investigator.

Graft Failure

The primary study outcome was graft survival, meaning that criteria were not met for graft failure. The criteria for graft failure, based on the definition used in Collaborative Corneal Transplantation Studies (CCTS)^{11, 12}, was a regrant or, in the absence of regrant, a cloudy cornea in which there was loss of central graft clarity sufficient to compromise vision for a minimum of three consecutive months. Cases also were considered to be graft failures when the cornea was cloudy at the last visit and there was no further follow up. Treatment of a graft which became cloudy and/or had signs of allograft rejection was administered according to each investigator's usual routine. The date of graft failure was the date of the first examination at which the cornea was cloudy as part of the failure event. For cases in which the cornea was not documented to be cloudy prior to regrant, the date of regrant was considered to be the failure date.

Eyes were not considered to be graft failures if there was a serious operative complication such as an expulsive choroidal hemorrhage or major postoperative trauma that required surgical intervention. The data for these eyes were censored at the time of surgery or the last completed visit prior to the trauma.

Graft rejection episodes were classified as *definite* when an endothelial rejection line was present in a previously clear graft and *probable* when there was inflammation (stromal infiltrate, keratic precipitates, cells in the anterior chamber, or ciliary injection) without an endothelial rejection line in a previously clear graft.

The primary cause of graft failure was classified as one of the following: (1) *primary donor failure* when the graft was cloudy on the first postoperative day and did not clear within two months, (2) *graft rejection* when an allograft reaction occurred that, in the investigator's judgment, was the primary reason for graft failure, (3) *refractive* when a regrant was performed for this indication in a clear cornea, and (4) *non-rejection* when not classified in either of the other three categories. The primary reason for a non-rejection failure was classified as one of the following: endothelial decompensation, infection, epithelial defect, epithelial downgrowth, wound dehiscence, hypotony, corneal thinning, glaucoma, or another cause. Glaucoma was only considered to be the primary cause when a surgical procedure was performed for glaucoma.

Statistical Methods

Analyses paralleled those reported after 5 years.⁵ Cumulative probabilities of graft survival (subsequently referred to as "graft survival rates or success rates") along with pointwise 95% confidence intervals were calculated using the Kaplan-Meier method at 10 and 11 years for the two pre-specified primary donor age groups (12 to 65 years and 66 to 75 years). The log-rank test was used to assess whether there was a difference in the graft survival rates between different donor age groups. Post-hoc analyses were replicated in three data-derived (not pre-specified) donor age groups (12 to 33, 34 to 71, and 72 to 75 years) following an inspection of graft outcomes across the entire donor age distribution, which showed relatively constant success rates within each of the three age ranges. The proportional

hazards model was used to assess the relationship between graft survival and donor age analyzed as a continuous variable. Because the proportional hazards assumption was invalid for donor age, separate hazard ratios were estimated for the first five years following surgery versus years 5–12. All reported p-values are two-sided. Statistical analyses were conducted using SAS version 9.3 software (SAS Institute Inc., Cary, NC).

RESULTS

Overall, among the 1,090 participants, 224 (21%) experienced graft failure; 207 (19%) died prior to the end of the study; 21 (2%) had data censored due to operative choroidal hemorrhage or penetrating ocular trauma; 445 (41%) completed 10 years of follow up without graft failure; and 193 (18%) without graft failure or known death completed less than 10 years of follow up (Figure 1). Compared with participants who completed the study without graft failure, the participants who died, were lost to follow up, or withdrew (including those who declined continued participation after 5 years) were older at baseline (73 years versus 67 years), more likely to be male (40% versus 34%), and similar in race (93% versus 95% white). Among the 866 participants who did not have a graft failure, the median follow-up time was 9.7 years (interquartile range = 5.0 to 11.1 years).

Graft Outcome

Among the 224 cases with graft failure, a regrant was performed in 177 (79%) cases, while the other 47 (21%) cases met the cloudy cornea failure criteria without a regrant as of the study closure date (8 of the 47 had a cloudy cornea at the last examination without 3 months of documented cloudiness). The overall 10-year cumulative probability of graft success was 75%. While at 5 years there was no difference in graft success rates comparing the 66 to 75 and 12 to 65 year old donor age groups (N= 383 and 707, respectively), with longer follow up the survival curves of these two donor age groups separated slightly (Figure 2) although they were not significantly different (P=0.26). The 10-year cumulative probability of success was 77% for donors 12 to 65 years old compared with 71% for donors 66 to 75 years old (difference = +6%, 95% confidence interval = -1% to +12%, P=0.11). At 11 years post-transplant, the group difference was similar (difference = +5%, 95% confidence interval = -2% to +12%, P=0.18).

When donor age was analyzed as a continuous variable using the exact donor age in the analysis, there was not a significant association with graft success during the first 5 years (P=0.15). However, for cases still in follow up at 5 years without prior graft failure, higher donor age was associated with lower graft success after the first 5 years (P<0.001). Results were similar after adjusting for baseline ECD. In exploring this association further across the entire donor age distribution (Figure 3, available at <http://aaojournal.org>), relatively constant 10-year success rates were observed within three data-derived (not pre-specified) groupings according to donor age (Table 1): 96% (95% confidence interval 89% to 99%) among the 80 study eyes (7% of the 1,090 eyes) that received a cornea from a donor 12 to 33 years old, 75% (95% confidence interval 71% to 78%) among the 880 eyes (81% of the 1,090 eyes) that received a cornea from a donor 34 to 71 years old, and 62% (95% confidence interval 51% to 72%) among the 130 eyes (12% of the 1090 eyes) that received a cornea from a donor 72 to 75 years old. The consistency of success rates from donors age 34 to 71 years can be seen in Figure 4 where this wide age range is stratified into two groupings (34 to 52 and 53 to 71 years). Baseline characteristics were similar in these three donor age groups (Table 2, available at <http://aaojournal.org>).

Among those with a graft that survived for at least 5 years, the conditional probability of success in the next 5 years was 88% (95% confidence interval = 85% to 91%) in the 12 to 65 years donor age group and 82% (95% confidence interval = 76% to 87%) in the 66 to 75

years donor age group. After surviving for 5 years, a graft from a donor 34 to 71 years old had a 86% (95% confidence interval 83% to 89%) probability of success in the next 5 years, while a graft from a donor 72 to 75 years had a 75% (95% confidence interval 62% to 84%) probability of success. In Figure 4, it can be seen that the survival curves appear virtually identical for the first 2 years across the entire donor age range, indicative of a lack of association of donor age with failures during the first 2 years. None of the 74 successful grafts at 2 years from a donor 12 to 33 years failed after the first 2 years. The relative decrease in the success rate with donors 72 to 75 years old relative to the younger donor ages was not observed until after year 6 (Figure 4).

As was observed at 5 years, the success rate when Fuchs' dystrophy was the indication for transplant was substantially higher than when pseudophakic/aphakic corneal edema was the indication (80% versus 63% at 10 years, $P < 0.001$). Within each of the two diagnostic groups, a similar association between graft success and donor age was seen with a higher success rate with donors 12 to 33 years old and a lower rate with donors 72 to 75 years old (Table 3). The association observed between donor age and graft success was similar across the recipient age range (P value for interaction = 0.86).

Causes of Graft Failure

Causes of graft failure were similar in the 12 to 65 and 66 to 75 years old donor age groups (Table 4). Among 224 eyes with graft failure, 100 (45%) were due to endothelial decompensation, 77 (34%) were due to rejection, 11 (5%) were due to uncorrectable refractive error, 3 (1%) were due to primary donor failure and 33 (15%) were due to other causes listed in Table 4. At least one probable or definite graft rejection episode preceded graft failure in 30 (30%) of the 100 failures attributed to endothelial decompensation. Among the 135 graft failures in the first 5 years, 46 (34%) were due to endothelial decompensation compared with 54 (61%) of the 89 graft failures after 5 years (Table 4 and Table 5, available at <http://aojournal.org>). After 5 years, all except 6 of the 89 graft failures (93%) were due to either endothelial decompensation or graft rejection.

DISCUSSION

The CDS was designed to evaluate the effect of donor age on the success of penetrating keratoplasty for corneal disorders due to endothelial disease, mainly Fuchs' dystrophy and pseudophakic corneal edema. Five-year graft survival data demonstrated identical graft survival rates among recipients who received corneas from donors 66 to 75 years of age compared with those receiving corneas from donors 12 to 65 years of age and an analysis using donor age as a continuous variable did not show a significant association with 5-year graft success. The study was extended to determine whether similar outcomes would be sustained for at least 10 years. As at 5 years, there was not a significant difference comparing the 10-year survival curves of the 12 to 65 and 66 to 75 years old donor age groups. However, in contrast with 5 years, donor age was significantly associated with graft success when exact donor age was analyzed as a continuous variable. Further exploration of the relationship between donor age and graft survival showed that the 10-year success rate was fairly constant over a wide range of donor ages, and differences in success rates were only observed at the lower and upper extremes of the donor age range. Inspection of the data suggested inflection points for differences in success rates at a donor age of 33 years, below which the 10-year success rate was higher and at a donor age of 72 years, above which the 10-year success rate was lower. The lower success rate with donors 72 to 75 years of age relative to the younger donor ages was not apparent until after 6 years of follow up. With the survival curves for all donor ages virtually identical for the first two years, the data demonstrate that there was no association of donor age with early graft failures. As expected, endothelial decompensation was more likely to be the cause of graft failure after 5

years than before 5 years, with prior graft rejection episodes likely contributing in about a third of such cases. The lower graft survival seen at 5 years for pseudophakic corneal edema compared with Fuchs' dystrophy, irrespective of donor age, was retained in the 10-year data. There was no indication of an interaction between donor age and recipient age on graft survival, meaning that the donor age-graft survival relationship was comparable across the recipient age range. Analysis of the 11-year data provided similar findings to the 10-year data.

There are few previous prospective long-term studies of the effect of donor age on penetrating keratoplasty success. Ing et al¹³ reported a 40% increased risk of graft failure for every 25 years of increasing donor age in a cohort of 394 eyes which included high, intermediate, and low risk cases, with up to 10 years of follow up available for 119 eyes. The Australian Corneal Graft Registry, which includes the full spectrum of high, intermediate, and low risk cases, reported no significant association of donor age with graft failure with follow up ranging from <1 year to 22 years in a 2008 report¹⁴ although an earlier report did indicate a significant though weak association.¹⁵

How will the CDS results impact eye banking and distribution of tissue for corneal transplantation? Available tissue from the extremes of donor age represents a small percentage of the donor pool. In the present study, only 7% of the 1,090 donors were under the age of 34 and only 12% were 72 or older. Most (81%) transplants were performed with a cornea from a donor 34 to 71 years of age, a range over which the graft survival rate was fairly constant. Current Eye Bank Association of America data are fairly similar, in that only 7.9% of corneas procured for transplantation in the U.S. are from donors under the age of 31 and 12.8% are from donors 71 to 80 years of age.¹ The limited availability of tissue from young donors (<40 years old), for transplantation for endothelial disease, raises the question for corneal surgeons and eye banks as to whether age-matching of donors and recipients is appropriate at the extremes of recipient age, reserving the very youngest donors for the youngest recipients with the greatest life expectancy. With respect to the oldest donors, it is important to note that compared with transplants from donors 34 to 71 years old, transplants from donors 72 to 75 years old had similar survival through 6 years of follow up, and even after 10 years of follow up the difference in survival was modest.

The CDS investigated patients with diagnoses of corneal endothelial disease that placed them at moderate risk for graft failure. Therefore, the results may not apply to patients with a higher likelihood of graft survival such as those with keratoconus or a lower likelihood of survival such as those with failed grafts, chemical burns or densely vascularized corneas. As corneal transplantation has recently shifted to lamellar techniques targeting the diseased stromal or endothelial layer, most of the patients who underwent a penetrating keratoplasty in the CDS likely would undergo some type of endothelial keratoplasty instead today.¹⁶ Without a prospective clinical trial, one cannot be certain that the findings of this study of penetrating keratoplasty would be the same as those of a study of endothelial keratoplasty. Until such a study is performed, the current study will provide the most useful data to guide eye banks and surgeons in their selection of appropriate corneal tissue for endothelial keratoplasty. Although its primary objective is to evaluate donor cornea preservation time in endothelial keratoplasty, the ongoing Cornea Preservation Time Study funded by the National Eye Institute should provide important data on the effect of donor age on endothelial keratoplasty outcomes.

In summary, the CDS evaluated the effect of donor age on the success of penetrating keratoplasty performed principally for Fuchs' dystrophy or pseudophakic corneal edema. Although the primary analysis did not show a significant difference in 10-year success rates comparing donor ages 12 to 65 and 66 to 75, there was evidence of a donor age effect at the

very extremes of the age range. Since we observed a fairly constant 10-year success rate for donor ages 34 to 71 years, which account for approximately 75% of corneas in the United States available for transplantation, the CDS results indicate that donor age should not be an important factor in most transplants for endothelial disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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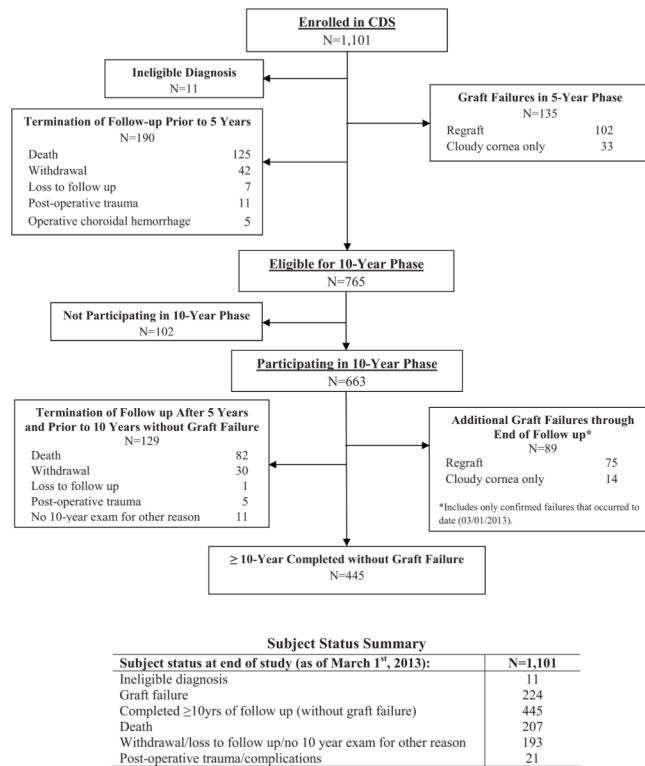
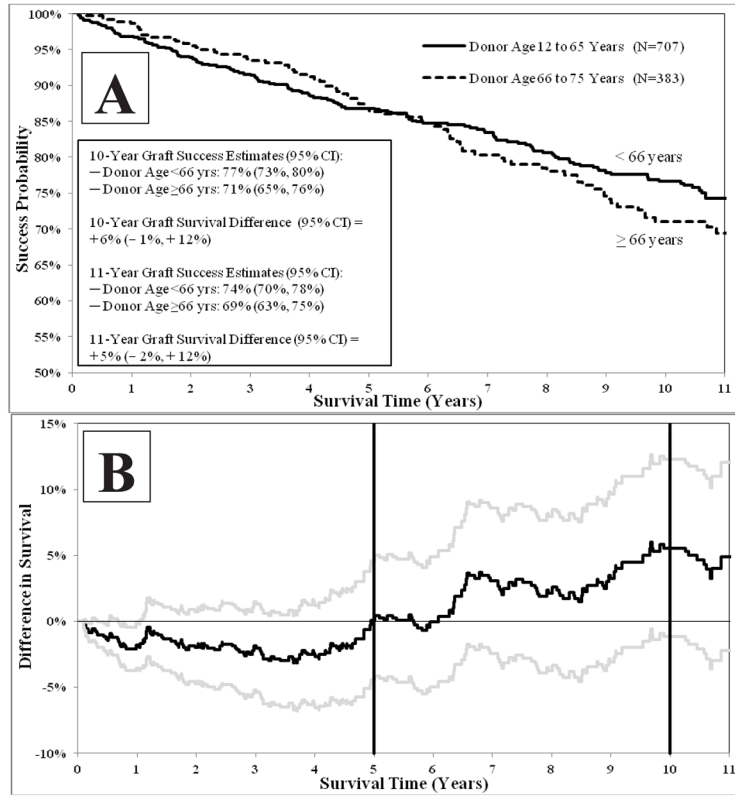


Figure 1. Flow-diagram of Subject Participation and Outcome Status for 5- and 10-Year Phases of the Cornea Donor Study (CDS)

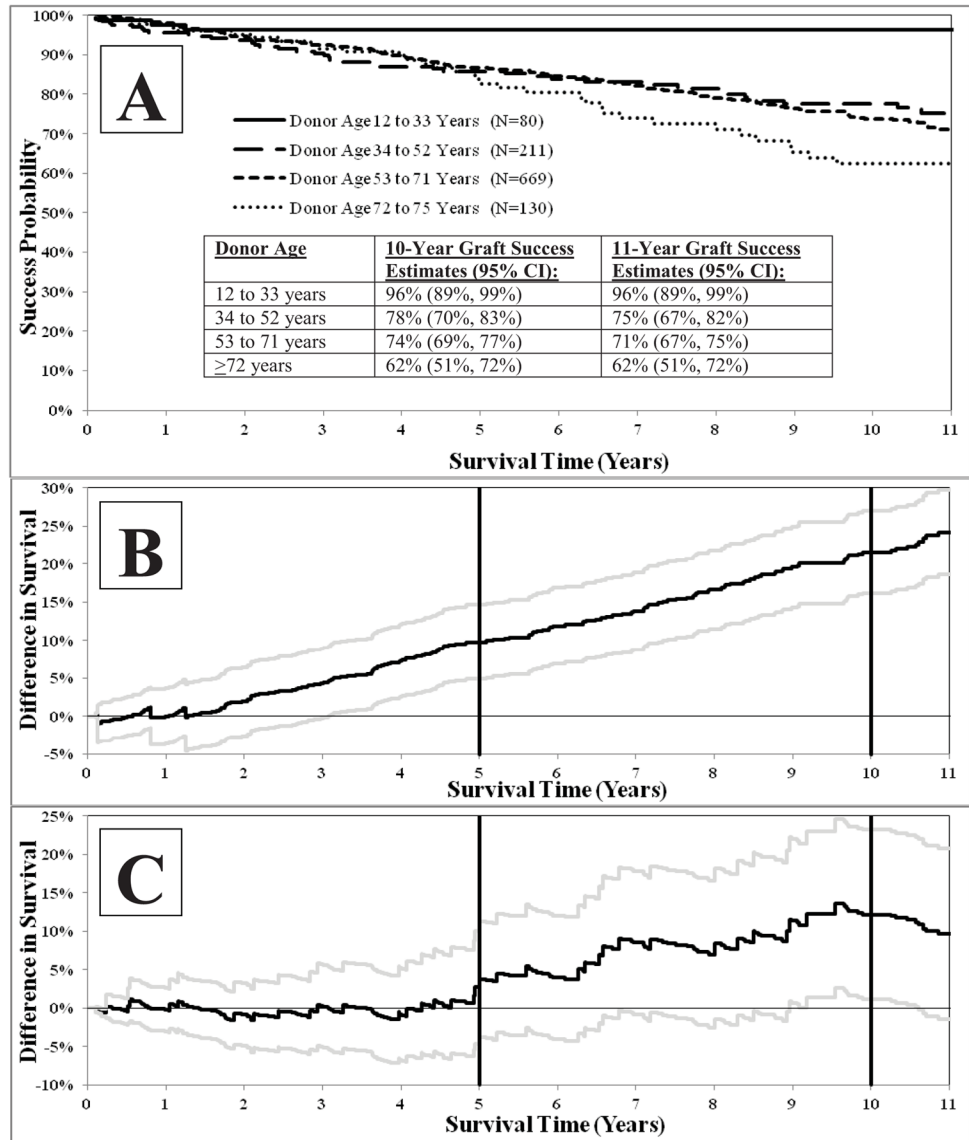


<i>Donor Age 12 to 65 years</i>												
# at risk at beginning of interval	707	664	620	581	544	493	418	395	364	328	292	164
# graft failures during interval	22	20	15	18	11	11	6	13	12	5	7	2
# deaths during interval	14	15	19	13	10	15	14	10	18	3	0	0
# lost to follow up/ study withdrawal during interval	3	6	5	6	29	47	2	4	2	2	0	0
# censored during interval	4	3	0	0	1	2	1	4	4	26	121	162
<i>Donor Age 66 to 75 years</i>												
# at risk at beginning of interval	383	360	326	300	281	238	196	176	164	151	130	70
# graft failures during interval	5	10	8	7	13	5	10	4	8	7	2	3
# deaths during interval	14	15	11	8	12	7	6	6	5	0	0	0
# lost to follow up/ study withdrawal during interval	1	7	5	3	16	30	4	1	0	1	0	0
# censored during interval	3	2	2	1	2	0	0	1	0	13	58	67

Figure 2. Graft Success in Main Donor Age Groups over Time

In panel A, Kaplan-Meier cumulative probabilities of graft survival are shown for the 12 to 65 and 66 to 75 donor age groups. With a log-rank test, the p value comparing the two donor age groups was 0.26. In panel B, the difference in survival probabilities between the 2 donor age groups are shown, with the middle (solid) curve showing the estimated survival difference and the lighter gray curves denoting the lower and upper bounds of the pointwise 95% confidence interval. A positive difference denotes better graft survival with the younger donor age group and vice versa. At 10-years, the difference in survival probabilities between the 2 donor age groups was +6% (95% confidence interval=-1% to +12%). The table beneath panel B presents the number of subjects at risk in the beginning of each year along with the number of graft failures, deaths, lost to follow up and censored subjects during the year.

CI = confidence interval.



Number at risk at beginning of interval:

Donor 12 to 33 years	80	77	74	69	65	61	53	49	45	44	39	20
Donor 34 to 52 years	211	192	178	164	153	137	116	112	107	95	89	44
Donor 53 to 71 years	669	633	583	549	515	452	382	354	325	295	252	149
Donor 72 to 75 years	130	122	111	99	92	81	63	56	51	45	42	21

Figure 4. Graft Success by 4 Donor Age Groups over Time

In panel A, Kaplan-Meier cumulative probabilities of graft survival are shown for 4 donor age groupings. With a log-rank test, the p value comparing the four donor age groups was <0.001. In panel B, the difference in survival probabilities between eyes receiving a cornea from a donor 12 to 33 years old (N=80) and from a donor 34 to 71 year old (N=880) are shown, with the middle (solid) curve showing the estimated survival difference and the lighter gray curves denoting the lower and upper bounds of the pointwise 95% confidence interval. A positive difference denotes better graft survival with the younger donor age grouping and vice versa. At 10 years, the difference was +22% (95% confidence interval= +16% to +27%). In panel C, the difference in survival probabilities between the eyes receiving a cornea from a donor 34 to 71 years old (N=880) and from 72 to 75 years old

(N=130) are shown, with the middle (solid) curve showing the estimated survival difference and the lighter gray curves denoting the lower and upper bounds of the pointwise 95% confidence interval. A positive difference denotes better graft survival with the younger donor age grouping and vice versa. At 10 years, the difference was +12% (95% confidence interval=+1% to +23%). The table under panel C presents the number of subjects at risk in the beginning of each interval.
CI = confidence interval.

Table 1

Graft Survival Rates According to Donor Age

Donor Age (years)	N	Graft Failure (N)	10 Year Graft Survival* (Pointwise 95% Confidence Interval)	11 Year Graft Survival* (Pointwise 95% Confidence Interval)	5 Year Graft Survival* (Pointwise 95% Confidence Interval)
Overall	1,090	224	75% (72%, 78%)	73% (69%, 76%)	86% (84%, 88%)
12 to 65	707	142	77% (73%, 80%)	74% (70%, 78%)	86% (83%, 89%)
66 to 75	383	82	71% (65%, 76%)	69% (63%, 75%)	86% (82%, 90%)
12 to 30	69	3	96% (87%, 99%)	96% (87%, 99%)	96% (91%, 100%)
31 to 40	58	11	78% (63%, 88%)	75% (58%, 85%)	91% (83%, 98%)
41 to 45	63	11	80% (67%, 89%)	80% (67%, 89%)	80% (70%, 91%)
46 to 50	68	11	81% (68%, 90%)	78% (62%, 87%)	92% (86%, 99%)
51 to 55	126	34	72% (62%, 80%)	65% (54%, 74%)	80% (73%, 87%)
56 to 60	152	29	76% (67%, 83%)	76% (67%, 83%)	87% (82%, 93%)
61 to 65	171	43	70% (62%, 77%)	69% (60%, 76%)	84% (79%, 90%)
66 to 70	217	40	75% (67%, 81%)	75% (67%, 81%)	87% (82%, 92%)
71 to 75	166	42	66% (56%, 74%)	62% (51%, 71%)	85% (79%, 91%)
12 to 33	80	3	96% (89%, 99%)	96% (89%, 99%)	96% (92%, 100%)
34 to 71	880	185	75% (71%, 78%)	72% (68%, 76%)	86% (83%, 88%)
72 to 75	130	36	62% (51%, 72%)	62% (51%, 72%)	82% (74%, 89%)

* Kaplan-Meier estimates

Table 3

Graft Survival at 5, 10, and 11 Years by Baseline Diagnosis and Donor Age Groups

	Fuchs Dystrophy		Pseudophakic/Aphakic Corneal Edema	
	<i>N</i>	<i>Graft Survival Estimates* (95% Confidence Interval)</i>		
5 Years	676	93% (91%, 95%)	369	73% (68%, 78%)
Donor age 12 to 33 years	51	100%	27	89% (77%, >99%)
Donor age 34 to 71 years	542	93% (90%, 95%)	300	73% (67%, 78%)
Donor age 72 to 75 years	83	88% (81%, 95%)	42	64% (47%, 82%)
10 Years	676	80% (77%, 84%)	369	63% (57%, 69%)
Donor age 12 to 33 years	51	100%	27	89% (69%, 96%)
Donor age 34 to 71 years	542	80% (76%, 84%)	300	63% (56%, 69%)
Donor age 72 to 75 years	83	68% (55%, 78%)	42	43% (21%, 65%)
11 Years	676	78% (74%, 82%)	369	61% (54%, 68%)
Donor age 12 to 33 years	51	100%	27	89% (69%, 96%)
Donor age 34 to 71 years	542	78% (73%, 82%)	300	61% (53%, 68%)
Donor age 72 to 75 years	83	68% (55%, 78%)	42	43% (21%, 65%)

* Kaplan-Meier estimates and pointwise 95% confidence interval

Table 4

Causes of Graft Failure

	Total Graft Failures (N=224)						Graft Failures 0–5 years after surgery (N=135)			Graft failures >5 years to end of study (N=89)		
	Donor Age Group			Donor Age Group			Donor Age Group			Donor Age Group		
	12 to 65	66 to 75	707	12 to 65	66 to 75	707	12 to 65	66 to 75	447*	12 to 65	66 to 75	216*
Number of Patients	707	383		707	383		447*	383		447*	216*	
Total Graft Failures:	142	82		90	45		52	45		52	37	
Primary Donor Failure	3 (2%)	0		3 (3%)	0		0	0		0	0	
Refractive	7 (5%)	4 (5%)		5 (6%)	3 (7%)		2 (4%)	3 (7%)		2 (4%)	1 (3%)	
Graft Rejection	50 (35%)	27 (33%)		32 (36%)	16 (36%)		18 (35%)	16 (36%)		18 (35%)	11 (30%)	
Non-rejection	82 (58%)	51 (62%)		50 (56%)	26 (58%)		32 (62%)	26 (58%)		32 (62%)	25 (68%)	
Causes of Non-rejection Graft Failure:												
Endothelial decompensation	61 (43%)	39 (48%)		30 (33%)	16 (36%)		31 (60%)	16 (36%)		31 (60%)	23 (62%)	
Signs of definite/probable rejection prior to failure	17	13		6	6		11	6		11	7	
No signs of definite/probable rejection prior to failure	44	26		24	10		20	10		20	16	
Infection	12 (8%)	5 (6%)		11 (12%)	4 (9%)		1 (2%)	4 (9%)		1 (2%)	1 (3%)	
Epithelial defects	3 (2%)	3 (4%)		3 (3%)	3 (7%)		0	3 (7%)		0	0	
Glaucoma	2 (1%)	2 (2%)		2 (2%)	1 (2%)		0	1 (2%)		0	1 (3%)	
Epithelial downgrowth	2 (1%)	0		2 (2%)	0		0	0		0	0	
Graft failure following retinal detachment repair	0	1 (1%)		0	1 (2%)		0	1 (2%)		0	0	
Corneal thinning	1 (<1%)	0		1 (1%)	0		0	0		0	0	
Hypotony	1 (<1%)	0		1 (1%)	0		0	0		0	0	
Wound dehiscence	0	1 (1%)		0	1 (2%)		0	1 (2%)		0	0	

* Number in follow up after 5 years without graft failure in the first 5 years