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Impact of the Cornea Donor Study (CDS) on Acceptance of Corneas from Older Donors

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Abstract

Purpose—Evaluate retrospectively whether findings from the Cornea Donor Study (CDS) led to changes in the transplantation of corneas from older donors.

Methods—United States eye banks provided complete data on donor age and placement (domestic or international) for 86,273 corneas from 1998 to 2009. The data were analyzed by 3 time periods: preceding CDS (1998–1999), during CDS (2000–2007) and after publication of CDS 5 year results (2008–2009), and separately for corneas placed within vs. outside the United States.

Results—For corneal tissues transplanted in the United States, the percentage of donors 66 years old increased from 19% before CDS to 21% during CDS and 25% after CDS ($p < 0.001$). Corresponding median (25th–75th percentile) donor ages were 53 (39–63), 54 (41–64) and 57 (46–66), respectively ($p < 0.001$). The opposite trend was observed for corneas distributed outside the United States with the percentage of donors 66 years old decreasing from 56% to 42% to 34%, respectively. Donor age trends over time varied by eye bank.

Conclusions—There was a modest overall increase in the donor age of corneas transplanted in the United States from 1998 to 2009, but the retrospective nature of the study limits our ability to attribute this change to the CDS. The modest increases in the donor age of corneas transplanted is a positive finding, but wider acceptance of older corneal donor tissue should be encouraged based on the five-year evidence generated by the CDS.

Keywords

cornea transplantation; donor age; eye bank

Introduction

The Cornea Donor Study (CDS) was designed to determine the effect of corneal donor age on corneal graft survival in moderate risk cases over a five-year follow-up period. The study found that the outcomes for grafts from donors 66 to 75 years old were comparable to those from donors 65 years old or less.¹ The rationale for the CDS was that the practice of only transplanting donors up to age 65, which was prevalent at the onset of the study in 1999, limited the potential pool of donors.² The present study was designed to determine whether the CDS and its findings have led to changes in eye banking practices and transplantation of corneas from older donors.

Materials and Methods

In June 2009, a survey was sent to 35 United States (US) eye banks requesting data on donor age, type of transplant (penetrating keratoplasty vs. endothelial keratoplasty) and placement in the US vs. internationally. Fifteen eye banks provided data for analyses. Two of the 15 eye banks that contributed data, did not participate in CDS (Lions Eye Bank of Texas at Baylor College of Medicine and Watson Gailey Eye Bank). The eye banks are listed and a summary of the donor age data they provided are shown in Table 1.

Seven of the 15 responding eye banks (47%) provided a full set of data for the survey period from 1998 to 2009. The data from these eye banks were analyzed by 3 time intervals relative to the duration of CDS: preceding CDS (1998-1999), during CDS (2000-2007) and post-CDS 5 year results publications (2008-2009). The other 8 eye banks provided data for various periods of time from 2000 to 2009, which limited the analysis of the data from these eye banks to the last 2 intervals (2000-2007 and 2008-2009).

Corneas used as part of the CDS were excluded from this analysis. Results were similar when analysis was adjusted for eye bank (data not shown). Adjustments were made by applying weights corresponding to the percent of data each eye bank contributed in each of the three time periods. Due to the large sample size in this dataset, even differences in donor age too small to be clinically relevant may still be statistically significant. Statistical comparisons of median donor age were performed by Spearman rank correlation tests for time, rank-sum tests for location and percentage of donors 66 years or older by logistic regression models. All statistical analyses were conducted using SAS version 9.2 software (SAS Institute Inc., Cary, NC).

Results

For the 7 eye banks that provided complete data, the percentage of donors 66 years old for tissues distributed within the US increased from 19% before CDS (1998-1999) to 21% during CDS (2000-2007) and 25% after CDS results publication (2008-2009) with a

corresponding increase in the median (25th - 75th percentile) age from 53 (39 – 63) to 54 (41 – 64) and to 57 (46 – 66), respectively (all $p < 0.001$). Conversely, the opposite trend was observed for tissues distributed internationally over the same time periods with the percentage of donors 66 years old falling from 56% to 42% to 34%. The median age declined from 67 (58 – 72) to 63 (54 – 70) to 61 (53 – 68; Table 2) during the three time periods (all $p < 0.001$). These data are shown by individual year in Figure 1.

The 8 eye banks, that provided partial data for the period from 2000 to 2009, demonstrated a minimal change in the percent of corneas from donors 66 years old distributed within the US during CDS and post-CDS (23% and 24% respectively, Table 2). For the same two periods, the percentage of donors 66 years old used internationally dropped from 44% during CDS to 38% after CDS.

Donor age trends over time varied substantially by eye bank (Table 3). Results were comparable for corneas used in penetrating keratoplasty and endothelial keratoplasty, when analysis was adjusted for recipient location (data not shown).

Discussion

Validation that the use of older donor corneas does not affect 5-year outcome following transplantation, as determined by the CDS, is only of public health importance if this information leads to a change in corneal surgical and eye banking practices. This survey of eye banks was undertaken to evaluate the potential impact of the CDS before and after the 5-year primary outcomes of the study were published in 2008.¹ The survey found that there was a slight increase in the placement of tissue from older donors (>65 years old) during CDS prior to the 5-year results being published and a greater increase after the publication of the results. While the impact of most clinical trials is not realized until well after results are publicized, the CDS had the potential to exert an earlier influence on clinical practice because the participation of 80 leading corneal transplant centers and 43 eye banks in the US mandated a change in the utilization of older donor corneas by many of the 105 participating surgeons for the 1101 enrolled patients, who prior to CDS were reluctant to use tissue from older donors. Such widespread acceptance of the use of older donor corneas in study participants could have influenced the use of corneas from older donors by these surgeons in non-study transplants during the time period of CDS even before the results were known.

Attributing the increase in donor age from 1998 to 2009 to the CDS cannot be confirmed by this retrospective survey, as other factors may have played a role. CDS enrollment began in 2000 and a small increase in donor age occurred among eye banks participating in CDS in the period during CDS as compared with the period preceding CDS. There also was an increase, though, in the donor age of corneas distributed by the two eye banks that participated in this survey, but that did not participate in the CDS. This could possibly be attributed to the impact of CDS as awareness of the acceptance of older corneas by the study surgeons became more widespread among non-participating eye banks and surgeons.

Another potential cause of increased donor age could be increased demand for corneas for transplantation. Data from the Eye Bank Association of America (EBAA) show a relatively

stable number of transplants in the US from 1998 (35,861) through 2006 (33,962).³ A sharp increase in the number of transplants in 2007 (39,391) and 2008 (41,652) was brought about by the rapid increase in the performance of endothelial keratoplasty. The decrease in the age of internationally exported donor corneas may merely reflect the increased availability of younger corneas as older corneas are increasingly accepted in the US, but the cause is uncertain.

Increasing the acceptable upper donor age limit increases the donor supply available to eye banks and surgeons. This increase in the donor age is important as demand for corneal tissue increases, pushed by widespread success of endothelial keratoplasty and several other new surgical innovations. There are also factors which could impact eye bank supply in the future, such as emerging diseases, increasing regulations, and the increasing number of required donor serological tests. Increasing age limits without compromising graft outcomes should benefit patients with corneal disease worldwide.

There are limitations to this study that should be considered when interpreting these results. This analysis was retrospective and dependent on the limited availability of data, which were collected in various ways and for various purposes. It is not known whether the 15 eye banks providing data for this study reflect the overall practice, but they do appear to be representative in terms of their geographic and volume diversity. Changes in eye bank procurement age limits during the period of data collection could also have impacted the data. Increased upper age limits may have been instituted by some eye banks for reasons unrelated to CDS. We were unable to separately analyze data from surgeons who did not participate in the CDS, which may have been a more accurate reflection of the influence of published data on wider clinical practice. The changes in donor age found in this study cannot necessarily be attributed to the CDS. Repeating the survey of eye bank donor distribution data for a longer period after the publication of the 5-year CDS outcomes would appear to be advisable.

It should also be noted that CDS donor criteria, in addition to age, were likely more restrictive than those in general use. The CDS only used donors with endothelial cell densities of at least 2300 cells/mm² with specific requirements for other tissue quality parameters as well.^{1, 4} It is probable that donors, of all ages, during the survey period did not meet the CDS criteria. Due to existing bias, it is possible that older donors not meeting CDS criteria may not have been used for transplant. Data to assess this factor were not available. The use of older donors with less than 2300 cells/mm², however, is not disparaged by the CDS findings.

A recommendation for increased acceptance by surgeons and eye banks of the use of older donor corneas is supported by the published outcomes of the CDS, which show that graft outcome five years after transplant is not associated with donor age.¹ The impact of evidence based medicine on changes in clinical practice involves a complex process⁵ that appears to be happening in corneal transplantation. We see the obvious role for continued education related to the suitability of older tissue for use. With continued education, the prior prejudice toward use of younger tissue should disappear.

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Appendix

A listing of the Cornea Donor Study Investigator Group, including clinical site investigators, eye bank staff, coordinating center staff, specular microscopy reading center staff, and committees, has been previously published online.

The following CDS Publications Committee members independently reviewed and approved this manuscript for submission: Christopher R. Croasdale, MD, Richard A. Eiferman, MD, Christopher J. Rapuano, MD.

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Figure 1. Donor Age of Corneal Tissues Placed in US and Internationally

Includes data from 15 US eye banks on donor tissues placed in the US (n=110,139, **A**), and internationally (n=38,379, **B**) during the period from 1998 to 2009. Corneas used in the CDS were excluded. For 1394 tissues the recipient location is unknown. Black dots indicate mean values; horizontal lines in the boxes, medians; the bottom and top of the boxes, the 25th and 75th percentiles, respectively; and the horizontal lines outside of the boxes, the range of donor age. Horizontal line across the graph corresponds to donor age of 66 years. The percentage figure above each box is the percentage of donors 66 or older.

Table 1
Distribution of Donor Age by Eye Bank in the Period from 1998 to 2009*

Eye Bank Name	N (%)	Time Interval	Donor Age	
			Median	25 th – 75 th Percentiles
Sight Life	26,397 (18%)	2000-2009	61	51 – 69
Heartland Lions Eye Bank	23,086 (15%)	1998-2009	60	49 – 68
Michigan Eye Bank, Midwest Eye Banks	17,433 (12%)	1998-2009	57	45 – 66
Illinois Eye Bank, Midwest Eye-Banks	14,822 (10%)	1998-2009	56	45 – 65
Minnesota Lions Eye Bank	12,248 (8%)	1998-2009	57	45 – 66
Texas (Lions Eye Bank of Texas at Baylor College of Medicine)	11,255 (8%)	1998-2009	50	31 – 62
Oregon (Lions Eye Banks of Oregon – Vision Share)	10,476 (7%)	2001-2009	60	51 – 67
Georgia Eye Bank, Inc.	8,413 (6%)	2002-2009	57	46 – 66
Watson Gailey, Midwest Eye Banks	4,546 (3%)	1998-2009	57	45 – 65
Utah Lions Eye Bank at the John A. Moran Eye Center – Vision Share	4,092 (3%)	2003-2009	51	32 – 61
One Legacy	4,035 (3%)	2006-2009	56	43 – 64
West Virginia (Medical Eye Bank of Western Virginia – Vision Share)	3,793 (3%)	1998-2009	54	42 – 63
Cleveland Eye Bank – Vision Share	3,622 (2%)	2004-2009	57	47 – 65
Eastern Virginia (Lions Medical Eye Bank & Research Center of Eastern Virginia, Inc. – Vision Share)	3,362 (2%)	2005-2009	57	45 – 66
Rochester Eye & Human Parts Bank	2,332 (2%)	2001-2009	59	48 – 67
Total	149,912 (100%)	1998-2009	58	46 – 66
				27%

* Excludes corneas used in the CDS.

Table 2
Donor Age by Eye Banks and Time Periods Relative to CDS Beginning and Release of 5 Year CDS Results*

Eye Bank Name	Period Before CDS (1998-1999)			Period During CDS (2000-2007)			Period After CDS (2008-2009)		
	N	Median (25 th -75 th percentile)	66 %	N	Median (25 th -75 th percentile)	66 %	N	Median (25 th -75 th percentile)	66 %
<i>Eye Banks with Complete Data for Period 1998-2009</i>									
Heartland Lions Eye Bank	3,804	61 (49 – 69)	37%	14,274	60 (50 – 68)	34%	5,008	59 (49 – 67)	28%
Michigan Eye Bank, Midwest Eye Banks	2,803	53 (39 – 63)	20%	10,520	56 (44 – 65)	25%	4,110	59 (49 – 67)	30%
Illinois Eye Bank, Midwest Eye-Banks	2,081	54 (42 – 65)	23%	8,565	55 (44 – 64)	21%	4,176	58 (49 – 66)	26%
Minnesota Lions Eye Bank	1,448	57 (45 – 66)	27%	8,134	57 (45 – 67)	29%	2,666	57 (46 – 66)	25%
Texas (Lions Eye Bank of Texas at Baylor College of Medicine)	1,464	46 (27 – 58)	12%	8,622	50 (32 – 62)	17%	1,169	52 (34 – 63)	17%
Watson Gailey, Midwest Eye Banks	558	55 (43 – 65)	24%	2,768	56 (43 – 65)	22%	1,220	60 (49 – 67)	30%
West Virginia (Medical Eye Bank of Western Virginia – Vision Share)	628	52 (38 – 62)	15%	2,557	55 (44 – 63)	19%	608	54 (42 – 63)	18%
Total placed in US**	10,206	53 (39 – 63)	19%	43,456	54 (41 – 64)	21%	15,303	57 (46 – 66)	25%
Total placed internationally***	2,286	67 (58 – 72)	56%	11,976	63 (54 – 70)	42%	3,046	61 (53 – 68)	34%
Total	12,786	55 (42 – 66)	25%	55,440	56 (44 – 66)	25%	18,957	58 (47 – 66)	27%
<i>Eye Banks with Partial Data for Period 2000-2009</i>									
Sight Life									
Oregon (Lions Eye Banks of Oregon – Vision Share)				19,295	61 (51 – 69)	36%	7,102	62 (51 – 68)	36%
Georgia Eye Bank, Inc.				7,476	60 (50 – 67)	29%	3,000	61 (52 – 67)	33%
Utah Lions Eye Bank at the John A. Moran Eye Center – Vision Share				5,561	58 (46 – 66)	27%	2,852	57 (45 – 65)	24%
One Legacy				2,664	49 (30 – 60)	12%	1,428	52 (37 – 64)	21%
Cleveland Eye Bank – Vision Share				1,519	55 (43 – 64)	20%	2,516	56 (44 – 64)	19%
Eastern Virginia (Lions Medical Eye Bank & Research Center of Eastern Virginia, Inc. – Vision Share)				2,165	57 (48 – 65)	24%	1,457	56 (47 – 64)	20%
Rochester Eye & Human Parts Bank				1,605	57 (45 – 65)	22%	1,757	58 (45 – 67)	29%
				1,771	59 (49 – 67)	32%	561	59 (45 – 66)	26%

Eye Bank Name	Period Before CDS (1998-1999)		Period During CDS (2000-2007)		Period After CDS (2008-2009)	
	N	66 % Median (25 th -75 th percentile)	N	66 % Median (25 th -75 th percentile)	N	66 % Median (25 th -75 th percentile)
Total placed in US**			27,212	56 (44 – 65)	13,962	57 (45 – 65)
Total placed internationally***			14,509	64 (56 – 70)	6,562	63 (53 – 69)
Total			42,056	59 (48 – 67)	20,673	59 (48 – 67)

* Excludes corneas used in the CDS.

** Recipient location is unknown for 294 donors in period before CDS, 8 donors for period during CDS and 608 donors for period after CDS.

*** Recipient location is unknown for 335 donors for period during CDS and 149 donors for period after CDS.

Table 3
Distribution of Donor Age for CDS and Non-CDS Participating Eye Banks*

Participated in CDS**														Did Not Participate in CDS		
Year	Heartland	Illinois	Michigan	Minnesota	West Virginia	Texas	Watson Gailey									
Donor Age (Median, % 66)																
USA (n=68,965)																
Before CDS																
1998	55	19%	55	23%	52	20%	54	23%	51	16%	41	4%	52	20%		
1999	54	14%	53	21%	53	20%	57	26%	52	12%	49	18%	56	27%		
During CDS																
2000	55	21%	55	22%	51	19%	60	36%	50	12%	49	18%	55	20%		
2001	58	27%	54	22%	54	22%	58	30%	51	15%	49	14%	54	21%		
2002	58	25%	52	18%	53	18%	57	28%	55	15%	43	8%	55	23%		
2003	56	26%	54	19%	56	24%	55	24%	52	15%	42	11%	51	14%		
2004	54	20%	53	20%	55	23%	54	24%	54	21%	42	9%	55	19%		
2005	55	19%	54	18%	55	24%	55	23%	57	16%	44	11%	55	19%		
2006	57	22%	54	17%	57	24%	54	21%	54	18%	49	14%	57	20%		
2007	58	29%	56	23%	56	22%	55	23%	56	14%	55	20%	58	23%		
After CDS																
2008	59	27%	57	22%	57	26%	56	23%	52	17%	52	17%	60	30%		
2009	58	26%	59	27%	59	29%	56	22%	53	16%	52	16%	58	30%		
International (n=17,308)																
Before CDS																
1998	72	82%	65	47%	52	12%	NA	61	30%	–	–	–	NA			
1999	69	64%	61	35%	57	21%	61	41%	57	14%	58	28%	64	38%		
During CDS																
2000	70	66%	57	18%	59	29%	59	32%	58	23%	58	27%	60	20%		
2001	70	67%	58	24%	59	32%	59	31%	60	30%	61	30%	64	38%		
2002	68	59%	61	25%	57	29%	60	37%	60	29%	57	25%	58	26%		

Year	Participated in CDS**							Did Not Participate in CDS		
	Heartland	Illinois	Michigan	Minnesota	West Virginia	Texas	Watson Gailey			
	<i>Donor Age (Median, % 66)</i>									
2003	67	54%	61	36%	62	40%	61	24%	59	26%
2004	66	50%	61	31%	61	36%	62	38%	57	25%
2005	65	47%	59	25%	63	45%	62	40%	61	32%
2006	63	40%	62	34%	64	43%	63	40%	65	48%
2007	64	44%	65	42%	63	35%	62	43%	64	45%
After CDS										
2008	63	35%	61	35%	61	35%	62	41%	63	38%
2009	62	35%	58	24%	61	39%	60	33%	60	18%
									NA	
									NA	

* This table includes 7 eye banks with complete data for the period 1998 to 2009. Recipient location is unknown for 910 donors.

** Excludes corneas that were used in the CDS.

NA = results not presented for groups with n<20