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Donor Cornea Tissue in Cases of Drowning or Water Submersion: Eye Banks Practice Patterns and Tissue Outcomes

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Abstract

Surgical use of donor corneal tissue from victims of water submersion (drowning or submersion secondary to death) remains controversial due to limited evidence about the quality of these tissues. To assess the safety of donor corneal tissue from victims of water submersion, an investigation of eye banks' practice patterns and tissue outcomes was conducted. All 79 Eye Bank Association of America accredited eye banks were contacted for a phone interview of practices regarding tissue from victims of water submersion. A retrospective review of corneal tissues from 2014–2016 from a large eye bank network was performed to identify all donors submerged in water. Corneal epithelial integrity, endothelial cell density (ECD), rim cultures, and adverse events were analyzed for associations with water submersion characteristics. 49 eye banks (62% response) participated in the survey. 55% of these eye banks had specific, written protocol for tissue eligibility from donors submerged in water. With or without specific protocol, eye banks reported considering water type (84%) and length of time submerged (92%) to determine eligibility. 22% of eye banks reported medical director involvement when eligibility determination was unclear. 79 tissues from 40 donors who were submerged were identified in 2014–2016 eye bank data. No donor tissues had pre-processing corneal infiltrates, positive rim cultures, or adverse events post-keratoplasty. Corneal epithelial integrity and ECD were not associated with water type or length of time submerged. In conclusion, data from a large eye bank network showed no adverse events or outcomes, indicating these tissues may be safe.

Keywords

cornea; eye bank; transplantation; drowning

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Conflicts of Interest

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Introduction

A unified policy or medical standard for donated corneal tissue from victims of drowning for corneal transplantation has not been established by the governing body, the Eye Bank Association of America (EBAA), or by corneal surgeons and eye bank specialists. Policy and protocols have not been established due to limited evidence on the safety or risks associated with using tissue for corneal transplantation from donors who drowned. Some surgeons worry that submersion in water adversely affects tissue quality and carries an additional risk of infection, impacting safety for transplant recipients. Eversight, a large eye bank serving Connecticut, Illinois, Michigan, New Jersey, and Ohio, addresses instances of drowning in its policy by stating that all tissues must meet EBAA Medical Standards, and additionally, “death by drowning does not, of itself, rule out donation for potential surgical use. Consult a Medical Director on a case by case basis” (Eversight 2016).

Currently, the decision to procure and offer tissue from victims of drowning rests on the judgment of eye bank technicians and, in some cases, with input from the eye bank medical director. Once procured, tissue is evaluated by technicians to ensure its safety and quality for transplantation. All potential donor tissue is treated with antimicrobials to prevent possible infection in recipients, but if infiltrates are visible on inspection, they are presumed to be infections and are cause for exclusion (Eversight 2015).

To evaluate infection risk to recipients, in 1995 Lindquist et. al. examined the ocular surface flora of tissues from drowning victims. The research team found a higher incidence of streptococcus and gram-negative bacteria in these tissues. Researchers highlighted this finding because streptococcus is one of the most common causes of infection after corneal transplant (Eye Bank Association of America 2016). However, the Lindquist group found no adverse events in the 11 recipients of tissue from donors who drowned (Lindquist 1995). One hypothesis is that since corneal infiltrates are so rare, on average 5.5 infections (endophthalmitis or infectious keratitis) per 10,000 grafts performed each year for tissue examined from 2001–2015 (Eye Bank Association of America 2016), the antibiotic storage solution minimizes corneal infections effectively even in tissues of drowning victims. As documented in the EBAA Medical Standards, “bacteriologic contamination of donor eyes does not necessarily lead to infection”, and rim cultures may not correlate with postoperative infections, should they occur (Eye Bank Association of America 2015). The limited information we have presents a murky picture on the risk of adverse events to recipients of tissue from donors who were submerged in water.

We performed a survey of eye banks’ policies and considerations for tissue procurement, and pursued a retrospective investigation from a large, multi-state eye bank of tissues from victims of drowning or water submersion secondary to death in order to clarify safety and guide eye-bank policy regarding these tissues.

Materials and Methods

Survey of EBAA-accredited eye banks

All 79 EBAA accredited eye banks were contacted by telephone in an attempt to survey their policies and processes for making donation eligibility decisions from victims of drowning or water submersion. If the eye bank agreed to participate, a corneal fellow (PP) conducted a semi-structured interview with the director of procurement or lab manager (if a director was unavailable). Four main questions were investigated: (1) Is there a written protocol with clear parameters for tissue from victims of drowning or water submersion?; (2) Does the type of water determine whether donor tissue is eligible?; (3) Does the amount of time submerged determine whether donor tissue is eligible?; and (4) In cases where the eligibility protocol is absent or subject to interpretation, is the case referred to the eye bank medical director?

Chart Review

Eversight is a large, multi-state eye bank serving Connecticut, Illinois, Michigan, New Jersey, and Ohio. Eversight has no specific policy on tissue from donors who drowned or were submerged in water at death, other than consulting the medical director on a case by case basis. Eversight records of all procured tissue from donors who drowned or were submerged in water secondary to death between January 1, 2014 and December 31, 2016 were obtained from an in-house database (Midwire) for retrospective analysis. More detailed information was collected from the medical chart documentation, when available. Information collected regarding the circumstances surrounding drowning included: whether the victim had primary drowning or secondary drowning (water submersion after death), the time spent submerged, and type of water in which the submersion occurred. The types of water were categorized as freshwater, saltwater, and decontaminated water (such as tap water, swimming pool water, hot tub water, etc.). All corneas are stored at 5 degrees Celcius in monitored refrigerators. Data collected on tissue after procurement included the presence of corneal infiltrates, epithelial defects, epithelial surface irregularities on eye bank slit-lamp bio-microscopy evaluation, and ECD) by specular microscopy. All ECD values were recorded at initial tissue processing, not at the time of tissue release. Post-transplant adverse events and results of rim cultures, when available, were also collected.

Statistical Methods

For the phone survey to EBAA accredited eye banks, results were summarized as frequency and percent of participating eye banks that reported specific policy regarding tissue from donors of drowning or water submersion. For the Eversight retrospective chart review, characteristics of the identified sample, including donor demographics, circumstances surrounding the drowning or water submersion, and clinical measures of the tissue were summarized with descriptive statistics (means and standard deviations, SD, for continuous measures; frequencies and percentages for categorical measures). Characteristics of the drowning or water submersion were assessed for associations with tissue quality and transplant outcomes. Linear mixed regression, repeated measures logistic regression, and repeated measure ordinal logistic regression were used to test for associations of water submersion characteristics with the outcomes of ECD, epithelial defect, and severity of

epithelial irregularity, respectively. These models all accounted for the correlation between tissues of the same donor. Simple descriptive statistics were reported for any tissue or transplant outcomes with small sample sizes which would prohibit a more sophisticated analysis. SAS version 9.4 statistical software (SAS Institute, Cary, NC) was used for all analysis.

Results

Survey of Practice Patterns

All 79 EBAA accredited eye banks were contacted, and 49 (62%) agreed to participate in the survey. Table 1 summarizes responses to the survey questions regarding policy for tissues from victims of drowning or water submersion. Of the surveyed eye banks, 55% (n=27) have a written protocol describing inclusion and exclusion factors for tissue eligibility specific for victims of drowning. The majority of eye banks assessed characteristics of the water submersion, including 84% (n=41) that take into account the type of water and 92% (n=45) that consider the length of time the donor was submerged in water. In cases where protocol is absent or open to interpretation, 22% (n=11) of eye banks involve the eye bank medical director. Although most eye banks reported that they considered type of water and length of time the donor was submerged when making decisions about tissue procurement, the way they used this information varied. Some only accepted tissue from donors drowned in particular types of water, or submerged for less than a certain cut-off time, but most eye banks used the characteristics surrounding the drowning in culmination with other EBAA criteria to form a subjective decision on tissue procurement.

Chart Review

From January 1, 2014 to December 31, 2016, a total of 79 tissues were procured from 40 donors who drowned or were submerged in water secondary to death in the Eversight network of eye banks. Donors were on average 43.3 years old at the time of death (range=7–80 years) and 68% male (Table 2). Of the 79 procured tissues, 63 (80%) met EBAA and Eversight eligibility criteria for surgical use, as described in their policy. Fourteen of the sixteen ineligible tissues were reviewed by a medical director who made the decision to not proceed with surgical use with no specific indication, beyond drowning or submersion, as a listed cause of surgical intent denial. The remaining two tissues were deemed ineligible for donation by the processing technician due to an “epithelial foreign body,” although no epithelial defect or infiltrate was noted.

The type of submersion was noted as primary drowning for 31 donors (77.5%) and submersion secondary to death for 9 donors (22.5%). Time submerged was available for 25 donors (mean=38 minutes, range=1–120, median=15), which included both primary drowning and submersion secondary to death. Type of water in which drowning occurred was available for 38 donors (15 of these occurred in decontaminated water, 21 occurred in freshwater, and 2 occurred in saltwater).

The 79 procured tissues were evaluated for corneal infiltrates, epithelial irregularities, epithelial defects, and ECD (Table 2). No corneal infiltrates were present on eye bank

technician slit lamp examination. Epithelial irregularities were noted in 77 tissues (97%), including 35 tissues (44.3%) with mild irregularities, 34 (43.0%) with moderate irregularities, and 8 (10.1%) with severe irregularities. In evaluating epithelial defects, 48 (60.8%) had no defects, and 31 (39.2%) had a defect. The average ECD was 2687 cells/mm² (range=1550–3876).

Table 3 displays associations between characteristics of the drowning (water type, submersion type, time submerged) and tissue outcomes (epithelial defect, severity of epithelial irregularity, and ECD). All data is displayed at the tissue-level. Type of water ($p=0.4$), type of submersion ($p=1.0$), and time submerged ($p=0.07$) were not significantly associated with the probability of an epithelial defect. Similarly, water type ($p=0.5$), submersion type ($p=0.8$), and time submerged ($p=0.3$) were not significantly associated with the probabilities of less severe epithelial irregularity. Although tissue from donors who drowned or were submerged in decontaminated water had lower ECD (mean cell count $\pm$ SD = 2527 ± 381 cells/mm²) than those who drowned or were submerged in fresh water (2804 ± 409 cells/mm²) or salt water (3342 ± 275 cells/mm²), tissue from those donors was also significantly older (50.5 ± 14.7 years, 38.9 ± 20.3 years, vs. 20.0 ± 2.3 years, respectively). After adjusting for age, water type was not significantly associated with ECD ($p=0.2$). In addition, no significant associations for submersion type ($p=0.6$) or time submerged ($p=1.0$) with ECD were noted.

Of the 63 transplanted tissues, rim culture results were available for 20 tissues, and post-operative outcomes forms were returned for 28 tissues. None of the surgeons of these transplanted tissues reported positive rim cultures or adverse events related to tissue characteristics (Table 2).

Discussion

Our study addresses the knowledge gap around the procurement and integrity of corneal tissue from drowned or submerged donors. Nationally, there is no formal protocol on tissue procurement from victims of drowning or water submersion. Of the surveyed EBAA accredited eye banks in the United States, more than half (55%) have written protocols in place about tissue eligibility from drowned or submerged donors. With or without formal protocol in place, the majority of these eye banks consider the type of water (84%) and length of time submerged (92%) to determine tissue eligibility for procurement. Additionally, only 22% of eye banks involve the medical director in cases of ambiguity around tissue procurement.

Our results suggest that drowning or submersion in water was not associated with corneal contamination or altered integrity. We did not compare characteristics of eligible to ineligible tissues because a large pool of ineligible tissue were never processed at the eye bank. Based on retrospective evidence from a large, multi-state eye bank, the majority of procured tissue (79.7%) from victims of drowning or water submersion was eligible for surgical use. There were no noted post-transplant adverse effects or positive rim cultures. However, surgeons only took rim cultures and reported results back to the eye bank in 32% of the tissues (20 of 63 tissues). Fundamentally, this limits our ability to conclude that these

tissue are, indeed, safe. In addition, no procured tissues had corneal infiltrates upon slit lamp evaluation at the eye bank. In some cases, there were abnormal epithelial findings by slit lamp examination, but these were not associated with the length of time submerged in water or the type of water where submersion occurred.

Most eye banks consider the length of time submerged for victims of drowning. For all tissues, eye banks evaluate the death-to-procurement time in eligibility decisions. This practice has been debated because controversial evidence surrounding the risks to the transplant recipient. A study by Linke et al. (2013), of the Hamburg eye bank, suggests that longer death-to-procurement times are associated with greater corneal contamination, possibly due to transfer of flora from skin and environment. However, a study by Khouani et al. (2014) found no association between these factors. These differences are possibly due to variation in mean time before tissue collection. The study by Linke et al. (2013) had a mean time to collection of 40 hours and found an association with contamination, while the Khouani et al. (2014) had a much shorter mean time to collection (9.7 hours) and found no association with contamination. Instances of drowning may lead to longer time before tissue collection than hospital deaths, but the approximate added mean time of submersion (prior to the victim being pronounced deceased) for our sample was 38 min, and thereby likely minimal enough to not affect corneal contamination.

Our results are also consistent with evidence from the broader transplantation literature for organs from victims of drowning. Most evidence is from the lung transplantation literature – a particularly vulnerable organ for microbial contamination due to their high vascularity and aspiration-hazard in cases of drowning or water submersion. In lungs, donor asphyxiation or drowning was not associated with poor long-term survival or incidence of rejection in transplant recipients (Whitson et al. 2014), despite the presence of pathogens isolated in the lung or bloodstream that correspond to the those found at the site of submersion (Bonatti et al. 2012). Focusing on microbial contamination, infected and uninfected lung tissue had no outcome differences, so long as any potential infection was treated with appropriate antibiotics (Bonatti et al. 2012). Gram-negative *Aeromonas* spp. is the bacteria most commonly found in lung transplantation donor victims of saltwater and freshwater drowning or submersion, and is highly susceptible to antibiotics (Bonatti et al. 2012; Hoetzenecker et al. 2010). Case studies have illustrated instances of recipient infection after transplant from a drowned donor; however, in both cases the infection was identified and was successfully managed (Hoetzenecker et al. 2010; Kim et al. 2015). Prophylactic treatment of corneal tissue with antimicrobials and screening for tissue integrity, which is currently standard protocol for tissues from all donors, likely minimizes risk adequately.

This study is limited by its retrospective nature. Our sample is susceptible to selection bias because only donor tissue approved by the eye bank technician or medical director was procured and thus included in this study. The tissues that were not procured or rejected before processing by the manager or medical director may have been lower quality or had higher infection rates. Further, there was not information on the water type and length of time submerged in all charts, limiting our power to detect significant associations with tissue quality. We also could not control slit lamp examination assessment of the tissue, such as the technician's subjective determination of extent of epithelial irregularity. Also, without a

control group we cannot assess any differences in tissue outcomes or risk to recipients from donors who were submerged in water prior to death versus those who were not. However, there were no adverse events after transplantation, so missing donor data and lack of a control group would likely not affect our results.

Overall, our results indicate that characteristics surrounding drowning and post-death submersion in water were not associated with tissue quality or transplant outcomes in a sample of donor transplant tissues. Almost 4,000 individuals die from primary drowning each year in the United States, with more subject to secondary drowning (Xu 2014). Many potential donor tissues are not procured because of concerns for possible recipient harm, so we do not know the risks these tissues would infer. This study indicates that current practices, from a single, large, multi-state eye bank appear to be safe and a more inclusive eye bank policy for procurement may be appropriate with proper medical director oversight. As a result of this work, the new policy at Eversight eye bank is to procure all tissues from donors who drowned or were submerged in water that also meet existing EBAA quality and safety standards and review all cases with the medical director prior to tissue release for surgical use. This early data warrants a larger prospective study to evaluate tissue quality and safety in a broader range of corneal tissues, including tracking rim culture results and post-operative adverse effects.

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Table 1

Survey Results from EBAA accredited Eye Banks in the United States (N=49)

Question	Yes
Is there a written protocol with clear parameters for tissue from victims of drowning or water submersion?	27/49 (55%)
Does the type of water determine whether donor tissue is eligible?	41/49 (84%)
Does the amount of time submerged determine whether donor tissue is eligible?	45/49 (92%)
In cases where the eligibility protocol is absent or subject to interpretation, is the case referred to the eye bank medical director?	11/49 (22%)

Descriptive statistics of the donor sample and of quality and outcome measures of tissues – 79 tissues of 40 donors

Table 2

Continuous Measures	Total Sample (79 Tissues of 40 Donors)				Eligible for Donation (63 Tissues of 32 Donors)				Not Eligible for Donation (16 Tissues of 8 Donors)			
	n	Mean (SD)	Min, Max	Median	n	Mean (SD)	Min, Max	Median	n	Mean (SD)	Min, Max	Median
Age at Death (years)	40	43.3 (19.6)	7, 80	46	32	41.3 (19.3)	7, 80	44	8	51.4 (20.0)	23, 75	54
Time Submerged (mins)	25	38.3 (42.8)	1, 120	15	19	43.1 (46.8)	1, 120	20	6	23.2 (23.7)	2, 60	13.5
Endothelial Cell Density	79	2687 (462)	1550, 3876	2667	63	2764 (429)	1946, 3876	2681	16	2386 (477)	1550, 3030	2381
Categorical Measures												
		Frequency (percent total)				Frequency (percent eligible)				Frequency (percent not eligible)		
Gender		(n=40 donors)				(n=32 donors)				(n=8 donors)		
Male		27 (67.5)				19 (59.4)				8 (100.0)		
Female		13 (32.5)				13 (40.6)				0 (0.0)		
Type of Submersion		(n=40 donors)				(n=32 donors)				(n= donors)		
Primary Drowning		31 (77.5)				24 (75.0)				7 (87.5)		
Submersion After Death		9 (22.5)				8 (25.0)				1 (12.5)		
Water Type		(n=38 donors)				(n=31 donors)				(n=7 donors)		
Decontaminated		15 (39.5)				12 (38.7)				3 (42.9)		
Freshwater		21 (55.3)				17 (54.8)				4 (57.1)		
Saltwater		2 (5.3)				2 (6.5)				0 (0.0)		
Corneal Infiltrate		(n=79 tissues)				(n=63 tissues)				(n=16 tissues)		
Absent		79 (100.0)				63 (100.0)				16 (100.0)		
Epithelium Irregularity		(n=79 tissues)				(n=63 tissues)				(n=16 tissues)		
None		2 (2.5)				2 (3.2)				0 (0.0)		
Mild		35 (44.3)				31 (49.2)				4 (25.0)		
Moderate		34 (43.0)				24 (38.1)				10 (62.5)		
Severe		8 (10.1)				6 (9.5)				2 (12.5)		
Epithelial Defect		(n=79 tissues)				(n=63 tissues)				(n=16 tissues)		
Absent		48 (60.8)				38 (60.3)				10 (62.5)		
Present		31 (39.2)				25 (39.7)				6 (37.5)		
Positive Rim Culture		(n=20 tissues)				(n=20 tissues)						
Absent		20 (100.0)				20 (100.0)				N/A		

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Continuous Measures	Total Sample (79 Tissues of 40 Donors)			Eligible for Donation (63 Tissues of 32 Donors)			Not Eligible for Donation (16 Tissues of 8 Donors)		
	n	Mean (SD)	Min, Max	n	Mean (SD)	Min, Max	n	Mean (SD)	Min, Max
Adverse Event			(n=28 tissues)			(n=28 tissues)			
Absent		28 (100.0)			28 (100.0)				N/A

SD, Standard Deviation; Min, Minimum; Max, Maximum; Mins, Minutes; N/A, Not Applicable

Table 3

Descriptive statistic and tests of association between characteristics of the drowning (water type, submersion type, time submerged) and tissue outcomes (epithelial defect, severity of epithelial irregularity, and endothelial cell count)

Variable	Epithelial Defect			Severity of Epithelial Irregularity			Endothelial Cell Density	
	No	Yes	χ^2	None	Mild	Moderate	Severe	χ^2
Water Type								
	freq (row %)	freq (row %)		freq (row %)	freq (row %)	freq (row %)	freq (row %)	mean (SD)
Decontaminated	20 (66.7)	10 (33.3)		0 (0.0)	17 (56.7)	10 (33.3)	3 (10.0)	2527 (381)
Fresh	23 (56.1)	18 (43.9)	0.4	2 (4.9)	14 (34.2)	20 (48.8)	5 (12.2)	2804 (409)
Salt	1 (25.0)	3 (75.0)		0 (0.0)	2 (50.0)	2 (50.0)	0 (0.0)	3342 (275)
Submersion Type								
	freq (row %)	freq (row %)		freq (row %)	freq (row %)	freq (row %)	freq (row %)	mean (SD)
Primary Drowning	37 (60.7)	24 (39.3)	1.0	2 (3.3)	26 (42.6)	27 (44.3)	6 (9.8)	2707 (464)
Submersion after Death	11 (61.1)	7 (38.9)		0 (0.0)	9 (50.0)	7 (38.9)	2 (11.1)	2620 (462)
Time Submerged (min)								
	mean (SD)	mean (SD)		mean (SD)	mean (SD)	mean (SD)	mean (SD)	slope* (SE)
	47.2 (47.8)	23.5 (24.9)	0.07	–	46.0 (43.5)	38.8 (45.5)	15.3 (14.9)	–0.11 (2.17)
								1.0

^aP-value testing the effect of “Variable” in a repeated measures logistic regression modeling the probability of an epithelial defect

^bP-value testing the effect of “Variable” in a repeated measures ordinal logistic regression modeling the probabilities of less severe epithelial irregularity, models exclude the “none” category due to small sample size

^cP-value testing the effect of “Variable” in a linear mixed regression modeling endothelial cell count. P-value for the model testing the effect of water type is adjusted for age.

* slope estimate is for cells/mm² for every 1 minute increase in time submerged

freq, frequency; SD, standard deviation; min, minute; SE, standard error