Post-Keratoplasty Glaucoma

Recognition, Prevention, Management

James D. Brandt, M.D.

Professor & Vice-Chair for
International Programs and New Technology
Director, Glaucoma Service
University of California, Davis

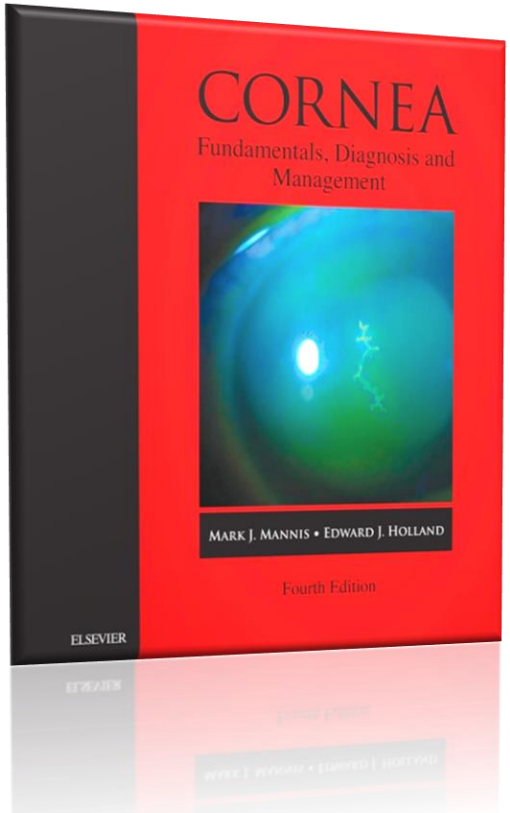
Sackler Faculty of Medicine
Tel Aviv University

The Institute for International Scientific Exchanges in Medical Sciences
Tel Aviv, Israel
14 February 2020

Financial Disclosures

None relevant to the topic of this talk

Cornea – Mannis & Krachmer, Eds.



Glaucoma after Corneal Transplantation

116

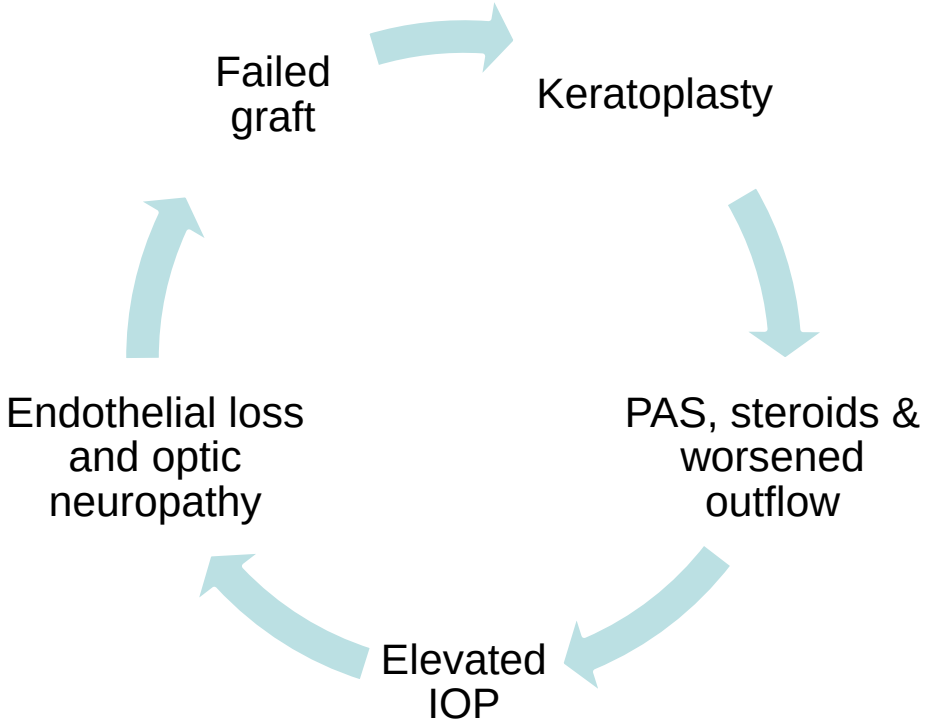
Michele C. Lim
James D. Brandt
Annie K. Baik

p. 1338

Chapter Outline

Fundamental Problem

- Performing keratoplasty in a patient with pre-existing glaucoma is guaranteed to make the glaucoma worse
- Uncontrolled glaucoma will reduce keratoplasty survival



Scope of the problem

- Elevated IOP after keratoplasty is common:
  - ≈ 25% both early & late
  - Pre-existing glaucoma is the primary risk factor, but there are others
- Identifying patients at risk and careful planning to maintain options to manage postoperative glaucoma is essential

Causes of elevated IOP

Early postop period

- Inflammation
- Retained viscoelastic
- Wound leak with angle closure
- Hyphema
- Operative technique
  - Tight suturing with long bites
  - Large recipient bed with same-size donor button
  - Increased peripheral corneal thickness
- Pupillary block
- Prior glaucoma
- Aphakia with mechanical angle collapse
- Combined ECCE

Late postop period

- PKP in aphakic eye
- Combined ECCE
- Chronic Angle Closure
- Pre-existing glaucoma
- Steroid-induced glaucoma
- Graft rejection with glaucoma
- Ghost cell glaucoma
- Aqueous misdirection

Kirkness CM & Ficker LA. (1992)
Risk factors for the development of postkeratoplasty glaucoma
Cornea 138:200-205

Preventing Problems and Managing Expectations

Pre-Op Evaluation of the Keratoplasty Patient

Pre-op Evaluation

- Optic Nerve Status
  - Afferent defect (rAPD)
  - Brightness sense
  - Flash VEP
- Gonioscopy
  - UBM if needed

Pre-op Evaluation

- Optic Nerve Status
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- Gonioscopy
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- IOP Target
- Preop IOP control
  - # of meds
  - Medication intolerances

Pre-op Evaluation

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- Gonioscopy
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- IOP Target
- Preop IOP control
  - # of meds
  - Medication intolerances

Question:

- IOP control is likely to worsen – what options will we have postop?

Post-Op Evaluation of the Keratoplasty Patient

Post-Keratoplasty Evaluation

- Re-evaluate glaucoma status as soon as possible
  - Tonometry is unreliable at best, especially early
    - Multiple techniques
    - Measure over graft and over host if possible
    - Pascal DCT *may* be the most accurate in post-PKP patients

Post-Keratoplasty Evaluation

- Document & Re-Stage optic nerve status
  - Re-document presence or absence of rAPD
  - Photos of optic nerve, comparison to prior photos when available
  - OCT utility variable depending on media

Treatment Options in the Keratoplasty Patient with Uncontrolled IOP

Treatment Options

- Trabeculectomy with MMC
- Goniosynechialysis
- Glaucoma Drainage Devices (GDDs)
  - Valved (e.g., Ahmed Glaucoma Valve)
  - Non-valved device (e.g., Baerveldt, Molteno)
    - Staged or single-stage implantation
- Cyclodestructive procedures (CPC, ECP)

Surgical Options: *Trabeculectomy*

- Trabeculectomy with MMC is a useful option for post-PKP glaucoma if:
  - Conjunctiva is not scarred
  - Patient is unlikely to be contact lens dependent
  - Patient unlikely to need further intraocular surgery
- Success rate for both IOP control and graft survival can be high in selected patients

Outcomes:
IOP Control vs. Graft Survival

TABLE 3

Review of Results and Complications After Mitomycin-C Trabeculectomy, Glaucoma Drainage Devices, and YAG Cyclophotocoagulation in Patients with Post-Keratopathy Glaucoma

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McDonnell[63] (Molteno single plate)	17	13	42	NA	71	29	41	NA	29
Beebe[10] (Molteno single- and double-plate 25 and ACTSEB 10)	35	24	34.5	14.7	86	51	34	5.5	6
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Levy[59] (YAG cyclophotocoagulation)	9	6	38	8.7	NA	NA	NA	33	33
Wheatcroft[110] (YAG cyclophotocoagulation)	13	19.8	37	15.2	69	38	NA	15	NA
Threkeld[102] (YAG cyclophotocoagulation)	39	27	31	17	77	44	NA	10	56
Ayyala[6] (YAG cyclophotocoagulation)	11	23	30	14.4	63	16.7	45.5	27	45

PKP = penetrating keratoplasty
ACTSEB = Anterior chamber tube shunt to encircling band

Trabeculectomy Tube Cyclophotocoagulation

Ayala RS (2000)
Penetrating Keratoplasty and Glaucoma
Survey of Ophthalmology 45:91-105

Surgical Options: Tubes

- GDDs offer an attractive option in eyes with complicated anterior segment issues, e.g.,
  - Scarred conjunctiva, distorted anterior segment
  - Need for simultaneous posterior segment surgery (PPV)
- Success rate for IOP control is high
- Success rate for graft survival is disappointing

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  - *Is it the tube or is it the kind of eyes that get tubes?*

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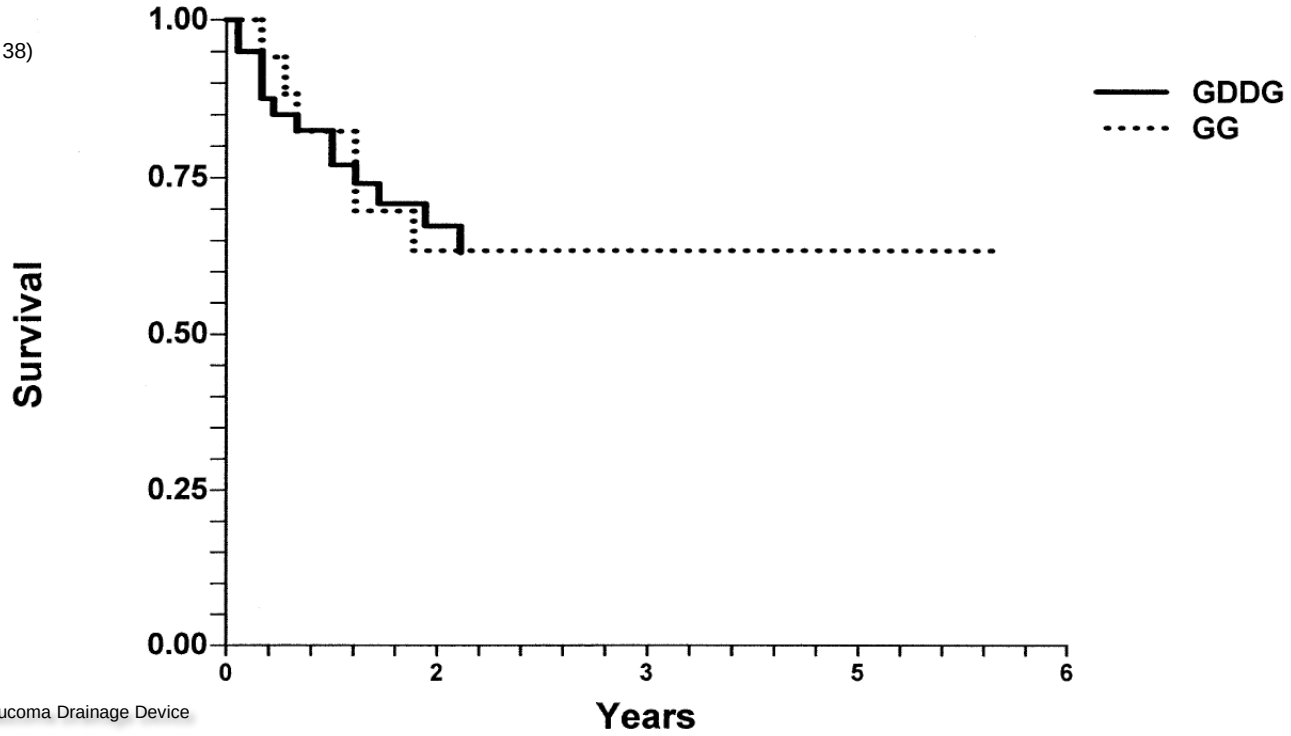
Tubes – IOP control

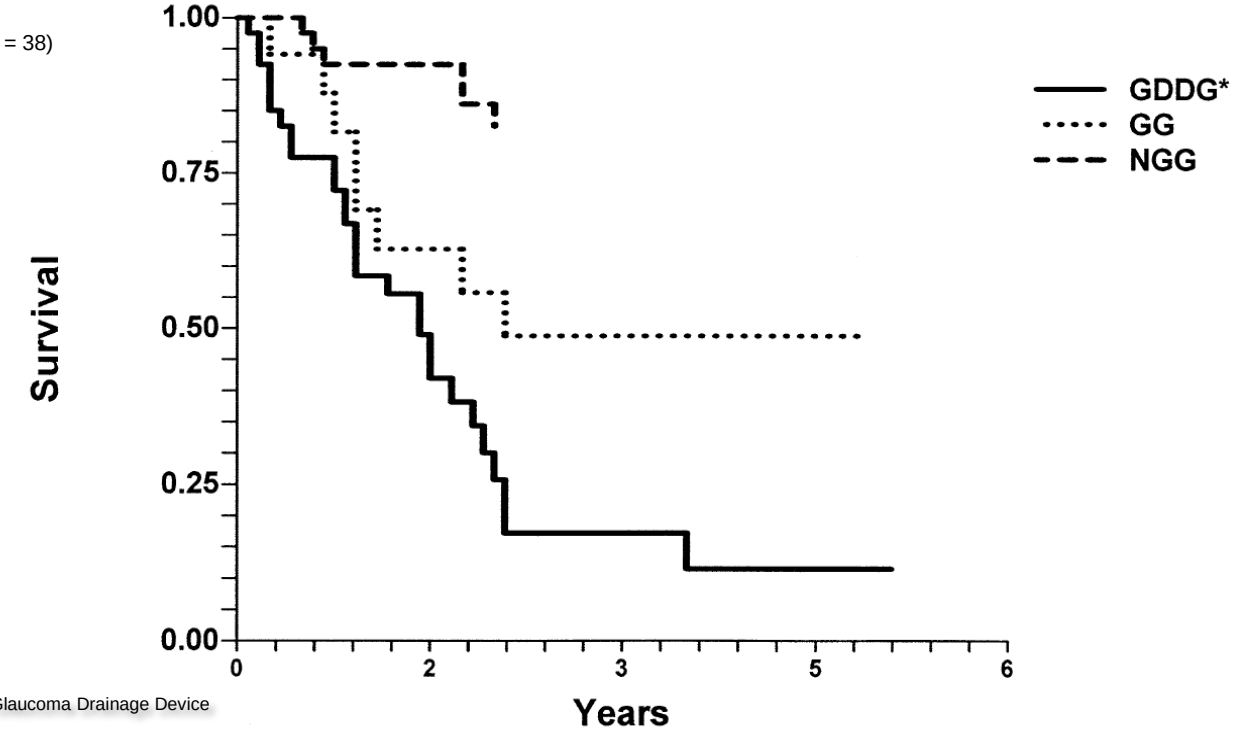
GDDG = Glaucoma Drainage Device Group (n = 38)
GG = Glaucoma Group (n = 17)



Alvarenga LS, Mannis MJ, Brandt JD *et al.* (2004)
The Long-term Results of Keratoplasty in Eyes With a Glaucoma Drainage Device
American Journal of Ophthalmology 138:200-205

Tubes – Graft Survival

GDDG = Glaucoma Drainage Device Group (n = 38)
GG = Glaucoma Group (n = 17)
NGG = Non-glaucoma Group (n = 48)



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Why do grafts fail with tubes?

- Direct mechanical damage to endothelium
  - Long tube tip can touch graft
  - Tube entry site through host cornea may continuously destroy endothelium
- ? Immune mechanisms
  - Two-way communication of aqueous with subconjunctival space
  - Ahmed valve does ***not*** prevent retrograde flow

A/C versus Pars plana

Study	GDD Tube Location	IOP control (%)	Graft Survival (%)
Sidoti *et al.* (2001)	Pars plana	85	64
Kwon *et al.* (2001)	Anterior Chamber	89	≈ 82
Arroyave *et al.* (2001)	Anterior Chamber	89	48
	Pars Plana	100	83

Table adapted from:
Lee RK & Fantes F (2003)
Surgical management of patients with combined glaucoma and corneal transplant surgery
Current Opinion in Ophthalmology 14:95-99

GDDs – Technical challenges

- Conjunctival scarring
  - Buttonholes
  - Wound breakdown in setting of limbal stem cell deficiency (aniridia, chemical burn)
- Positioning and length of the tube
  - Difficult to gauge at time of PKP

Staged Approach

- Original description of Molteno Implant was as a ‘staged’ device
- GDD plate placed externally, tube tucked out of the way
- Capsule allowed to form over plate to provide resistance to aqueous outflow once device connected to intraocular space

Staged Approach

- Used in eyes identified prior to PKP to be at high risk of postoperative glaucoma
  - Trauma, chemical burns
  - Anterior segment dysgenesis (e.g., Peters anomaly, aniridia, sclerocornea)
- Used in eyes with media opacity too severe to assess anterior segment structures

Staged Approach

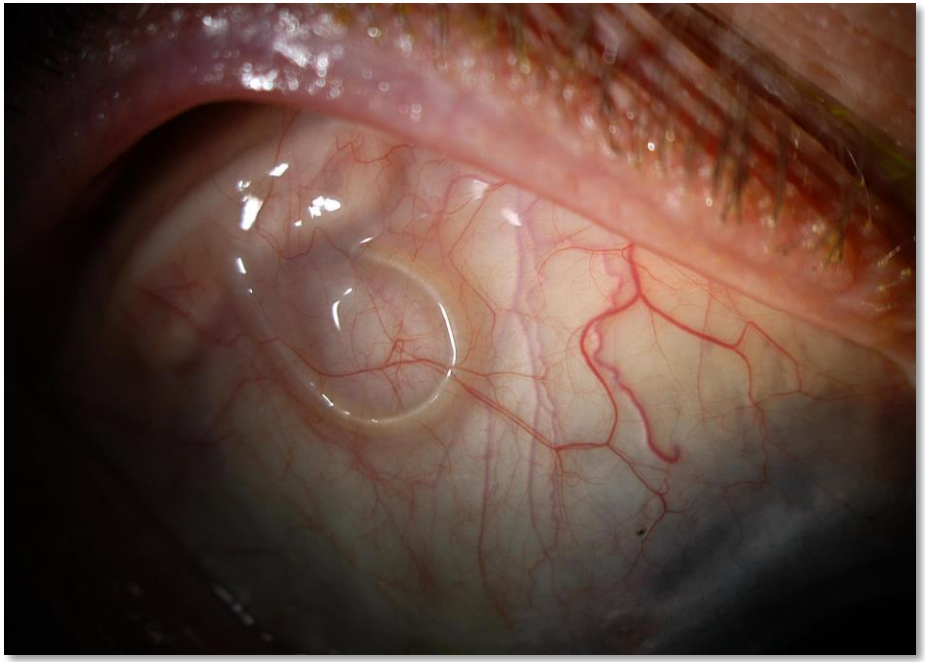
Advantages

- Avoids risk of early hypotony or hypertensive phase
- Allows placing of tube under better visualization
  - Avoids placing tube too close to graft (or in pars plana)
- IOP control after Stage II is very consistent, hypertensive phase rare

Disadvantages

- Prolongs initial surgery
  - Stage I placement can be done before or after graft
- Hardware placed which may never be needed
- Requires 2nd trip to OR if Stage II needed
  - But quick (< 30 min)

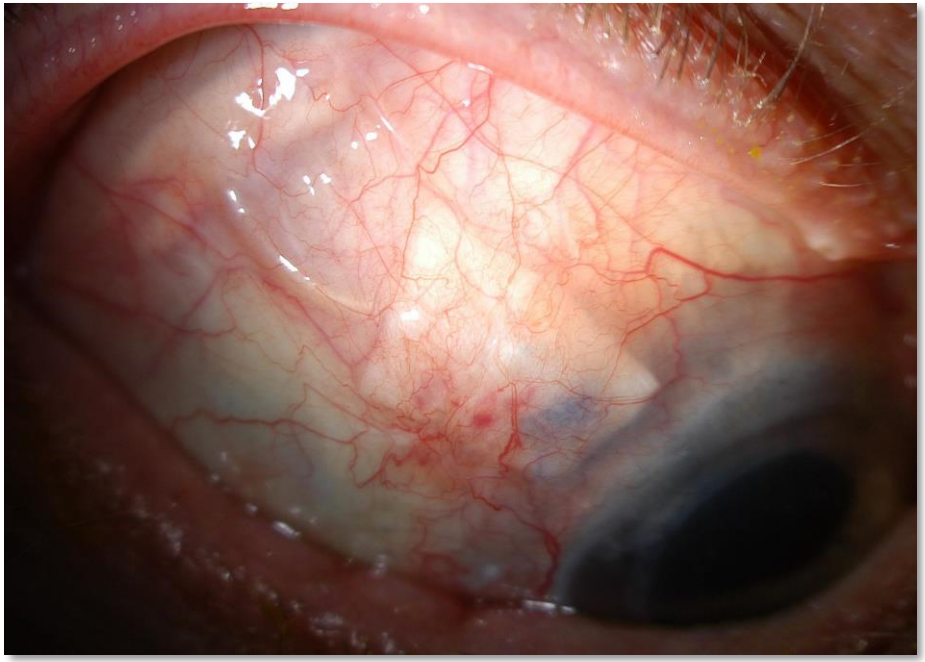
Stage I Baerveldt Implant



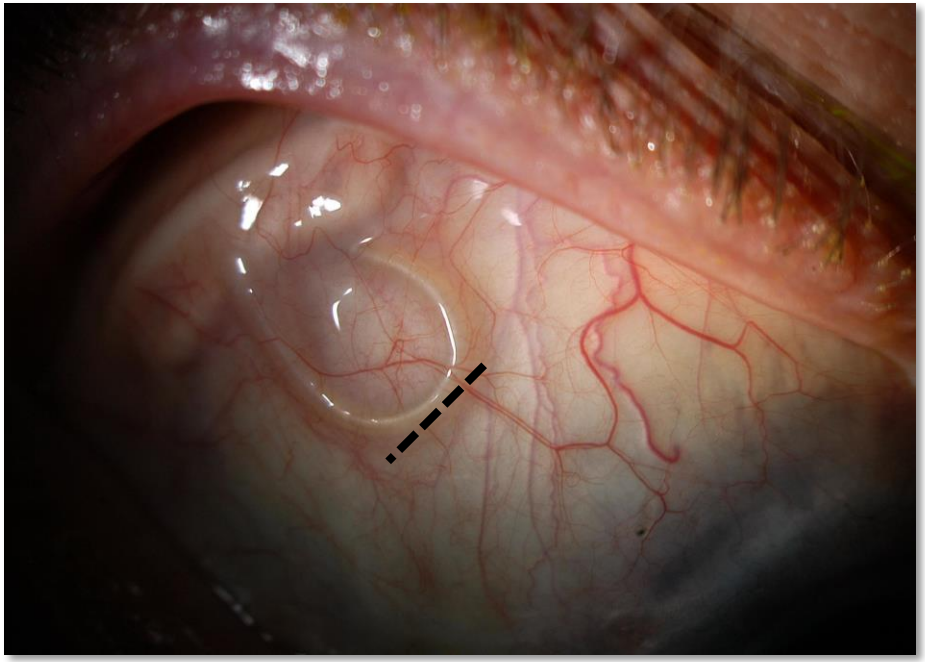
- 40 year old male with corneo-scleral laceration, lens injury
- One year after primary repair, underwent Stage I Baerveldt Implant, PKP, vitrectomy, sewn-in PCIOL
- Good vision, IOP controlled medically for 5 years

Stage II Baerveldt Implant

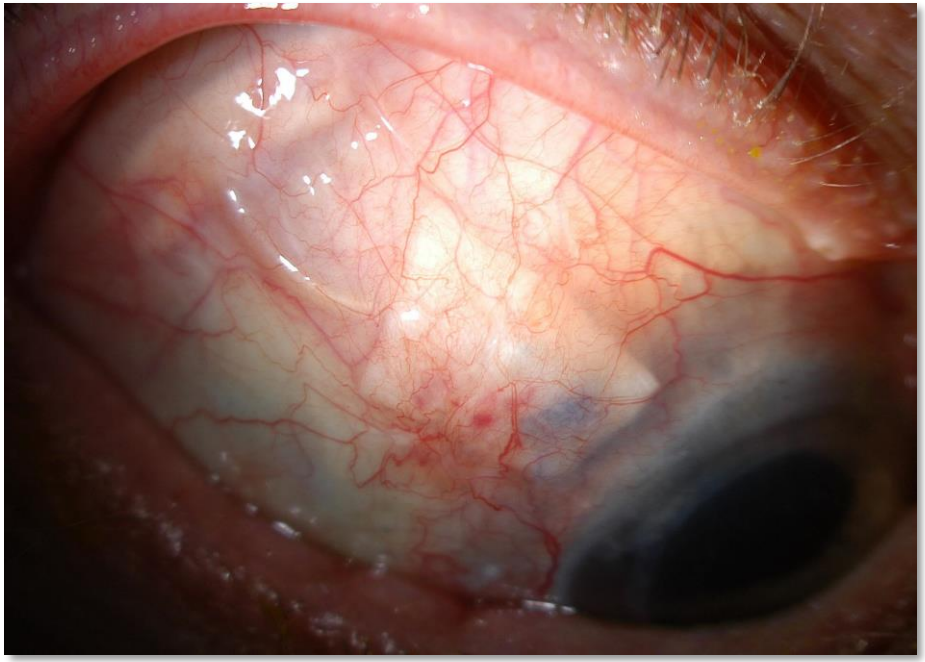
- Patient returns ~5 years later with IOPs in the 40s despite MTMT
- Stage II implant performed
- Tube inserted behind Iris, in front of PCIOL
- IOP in low teens on no meds ~3 years later
- Graft remains clear



Stage I & II Baerveldt Implant



Small (< 1 cm) conjunctival incision needed to retrieve tube from Stage I implant



4 months postop, tube is nicely covered by pericardial patch graft (Tutoplast™)

Surgical Options: CPC

- Trans-scleral cyclophotocoagulation (tsCPC) a useful adjunct to medications
  - IOP success ≈ 2/3
  - graft failure ≈ 40%
  - Hypotony 20% - 30%
- tsCPC generally reserved for poor-prognosis eyes
  - Causes moderate inflammation, increased steroid coverage mandatory to preserve graft
- Outcomes with Micro-Pulse CPC not yet reported

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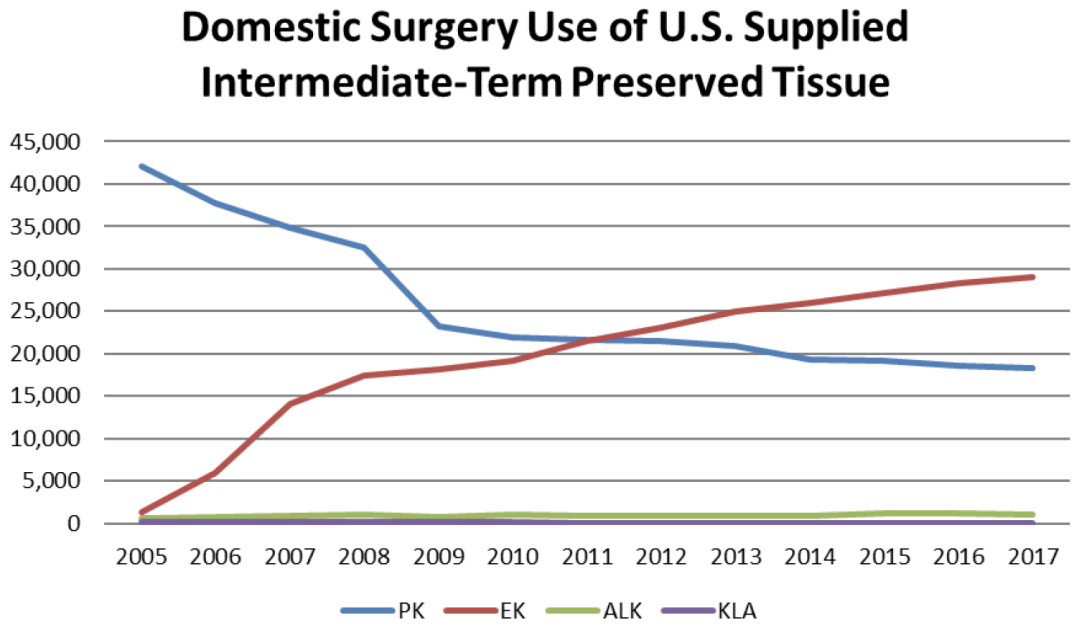
What about DSAEK?

DSAEK

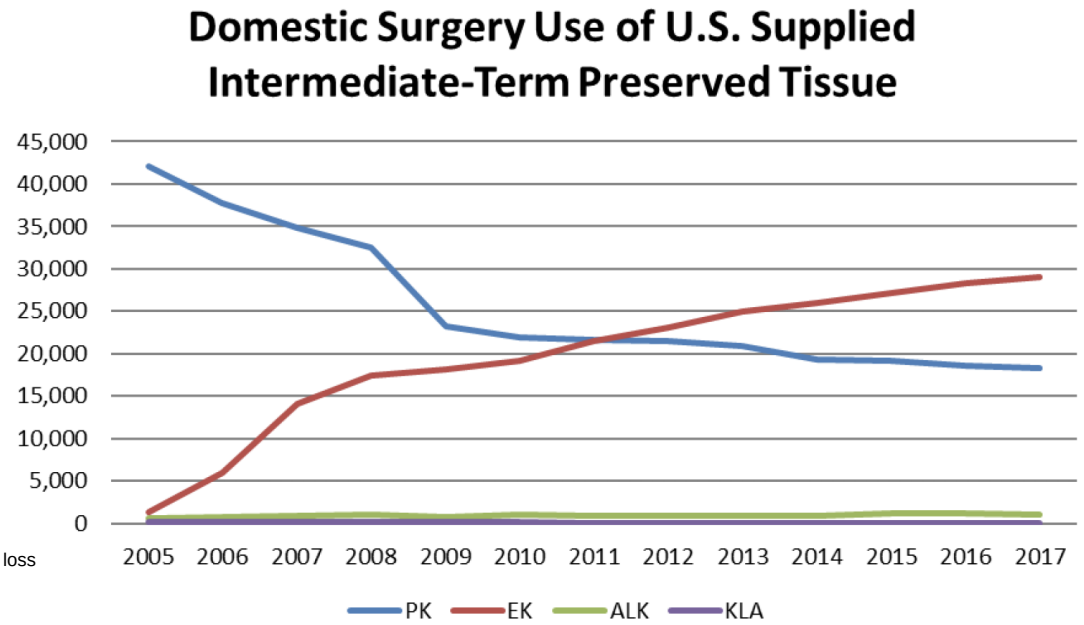
- Descemet stripping automated endothelial keratoplasty (DSAEK): most common form of corneal transplantation in US*



* Eye Bank Association of America (EBAA) 2016 Eye Banking Statistical Reports

Introduction

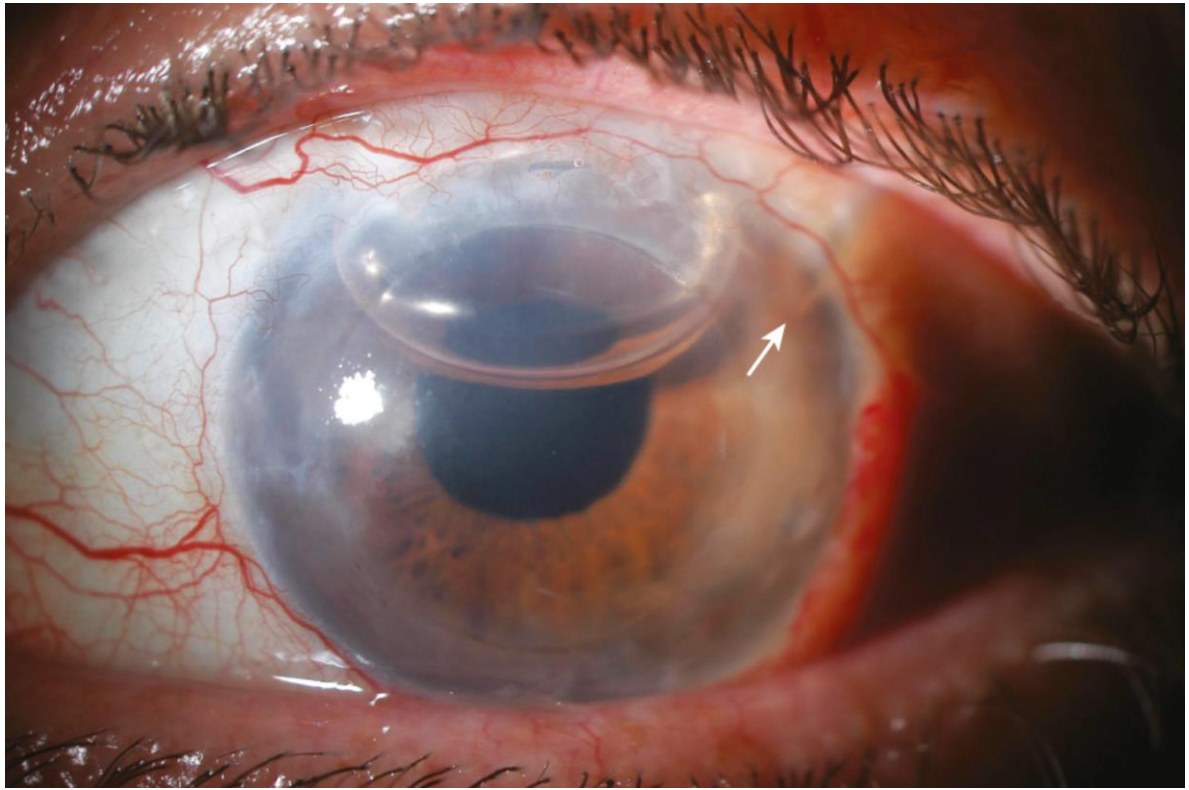
- DSAEK failure: 4-9% of eyes up to 5 years after surgery*†



* Price MO, Fairchild KM, Price DA, *et al.*
Descemet's stripping endothelial keratoplasty five-year graft survival and endothelial cell loss
Ophthalmology 2011;118:725–729

† Rosenwasser GO, Szczotka-Flynn LB, Ayala AR, *et al.*
Effect of Cornea Preservation Time on Success of Descemet Stripping Automated Endothelial Keratoplasty: A Randomized Clinical Trial
JAMA Ophthalmol. 2017;135(12):1401–1409

DSAEK, Bubbles & Tubes



From: Lim MC, Brandt JD & Baik AK
Glaucoma after Corneal Transplantation, Chapter 116 in
"Cornea, 4th Edition", Mannis MJ & Holland EJ, Eds., Elsevier 2017

Background

- Glaucoma seems linked to DSAEK failure:
  - Aqueous shunts and trabeculectomies
  - Glaucoma drainage devices and trabeculectomies
  - Glaucoma drainage devices, NOT topical meds
  - Elevated IOP

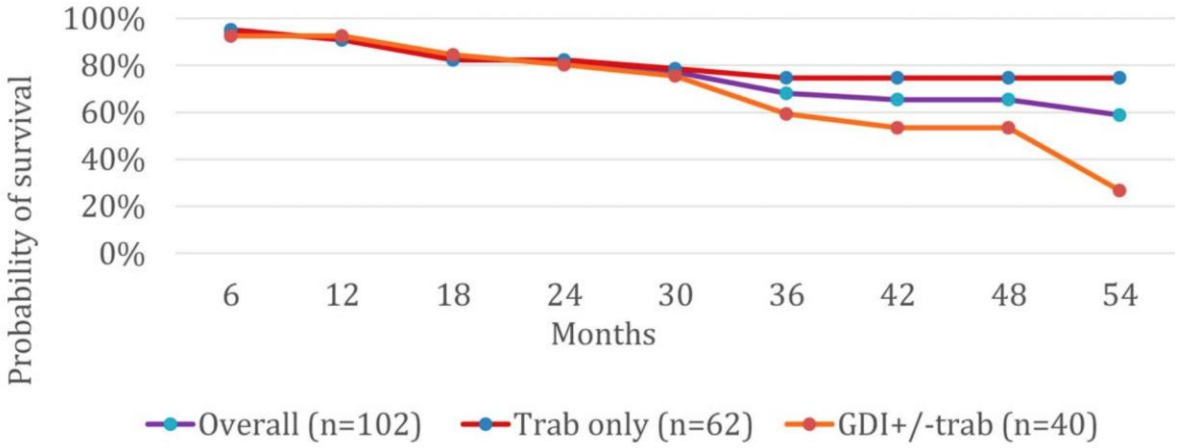
Nahum Y *et al.*
Risk Factors Predicting the Need for Graft Exchange after DSAEK
Cornea 2015;34(8):876-879

Anshu A, Price MO, Price FW
Descemet's stripping endothelial keratoplasty: long-term graft survival and risk factors for failure in eyes with preexisting glaucoma
Ophthalmology 2012;119(10):1982–1987

Kang JJ *et al.*
DSAEK in eyes with previous glaucoma surgery
Cornea 2016;35(12):1520-1525

Nguyen P, Khashabi S, Chopra V, et al.
DSAEK: A comparative study of outcome in patients with preexisting glaucoma
Saudi J Ophthalmol 2013;27(2):73–78

Glaucoma Surgery & DSAEK



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Cornea 2016;35(12):1520-1525

DSAEK Failure in eyes with Pre-existing Glaucoma

The UC Davis Experience

Jennifer Y. Li, M.D.
Jefferson D. Berryman, M.D.

Purpose

- To identify risk factors for DSAEK failure unique to glaucomatous eyes
- Secondary analysis:
  - Re-bubbling rates

Methods

- Retrospective chart review of all DSAEK cases by single surgeon (JYL) 2012-2018
  - Exclusion: Follow-up <6 months
  - Primary endpoint – graft failure
  - Secondary endpoint – re-bubbling

Results

282 eyes underwent DSAEK

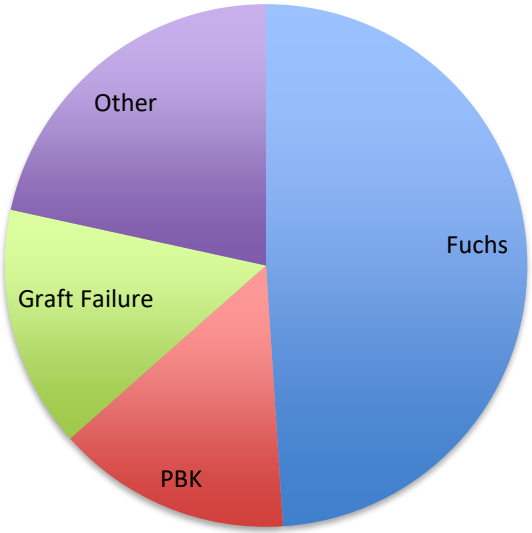
41 eyes excluded for follow-up <6 months

241 cases included (176 patients, 223 eyes)

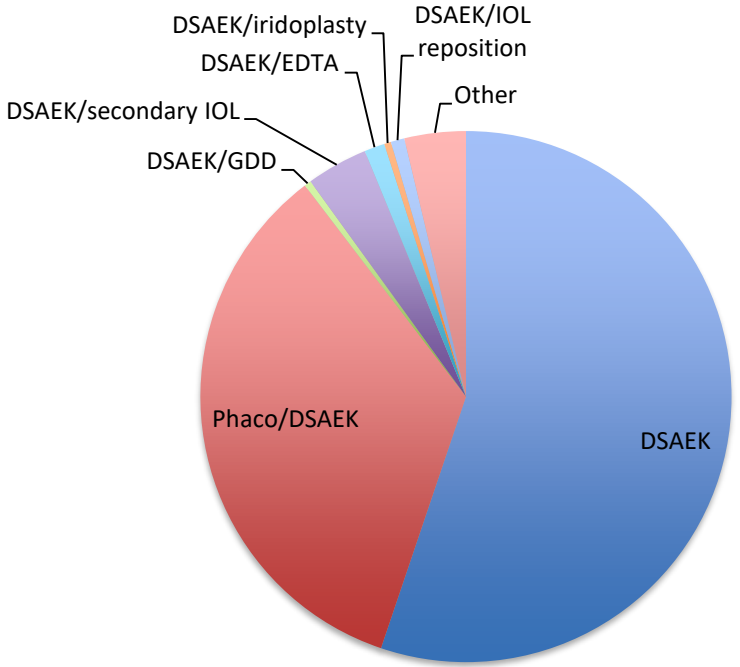
116 with glaucoma

125 no glaucoma

Indications & Procedures



Indication for DSAEK



Procedures performed

Results – Overall failure rates

	Total number (n)	Failures	Early failures (<3 months)	Failure rate
All eyes (total grafts)	223 (241)	31 (41)	4 (4)	13.9% (17.0%)
No history of glaucoma	124 (125)	3 (3)	0 (0)	2.4% (2.4%)
History of glaucoma	99 (116)	28 (38)	4 (4)	28.2% (32.8%)

Failure Rate by Glaucoma subtype

	Failures	Failure rate	Hazard ratio [95% CI]	p value
All glaucoma	**38/116**	**32.8%**	**12.65 [4.33 – 43.02]**	**<0.0001**
POAG	**14/36**	**38.8%**	**2.95 [1.73 – 5.07]**	**0.0001**
CACG/Narrow angles	**11/22**	**50.0%**	**3.65 [2.14 – 6.23]**	**<0.0001**
Uveitic	3/8	36.5%	2.30 [0.90 – 5.89]	0.0828
Steroid	1/5	20.0%	1.180 [0.20 – 6.97]	0.855
Pigmentary	1/2	50.0%	2.99 [0.73 – 12.29]	0.129
PXF	1/8	12.5%	0.73 [0.11 – 4.65]	0.738
JOAG/congenital	**4/7**	**57.1%**	**3.61 [1.78 – 7.32]**	**0.0004**
Ocular hypertension	1/11	11.1%	0.64 [0.17 – 2.42]	0.506
Aniridia	1/1	100%	6.00 [4.52 – 7.96]	<0.0001
ICE	1/2	50.0%	2.99 [0.73 – 12.29]	0.1294
Other	1/11	9.0%	0.52 [0.08 – 3.46]	0.5011

95% CI = 95% confidence interval

POAG = primary open angle glaucoma
CACG = chronic angle closure glaucoma
PXF = pseudoexfoliative
JOAG = juvenile open angle glaucoma
ICE = iridocorneal endothelial syndrome

Failure rate by prior glaucoma surgery

	Failures	Failure rate	Hazard ratio [95% CI]	p value
No prior surgery	15/181	8.3%	1.0	n/a
***Any* glaucoma surgery**	**26/60**	**43.3%**	**5.23 [2.96 – 9.20]**	**<0.0001**
Baerveldt GDD	16/28	57.1%	4.87 [2.99 – 7.93]	<0.0001
Ahmed GDD	5/11	45.5%	2.90 [1.42 – 5.93]	0.0034
***Any* GDD**	**23/44**	**52.3%**	**4.84 [2.89 – 8.10]**	**<0.0001**
Trabeculectomy	**11/24**	**45.8%**	**3.32 [1.92 – 5.73]**	**<0.0001**
CPC	**10/21**	**47.6%**	**3.38 [1.94 – 5.89]**	**<0.0001**
ECP	**8/11**	**72.7%**	**5.07 [3.14 – 8.91]**	**<0.0001**
Canaloplasty	0/1	0.0%	N/A	N/A

95% CI = 95% confidence interval

GDD = Glaucoma Drainage Device
CPC = trans-scleral cyclophotocoagulation
ECP = endoscopic cyclophotocoagulation

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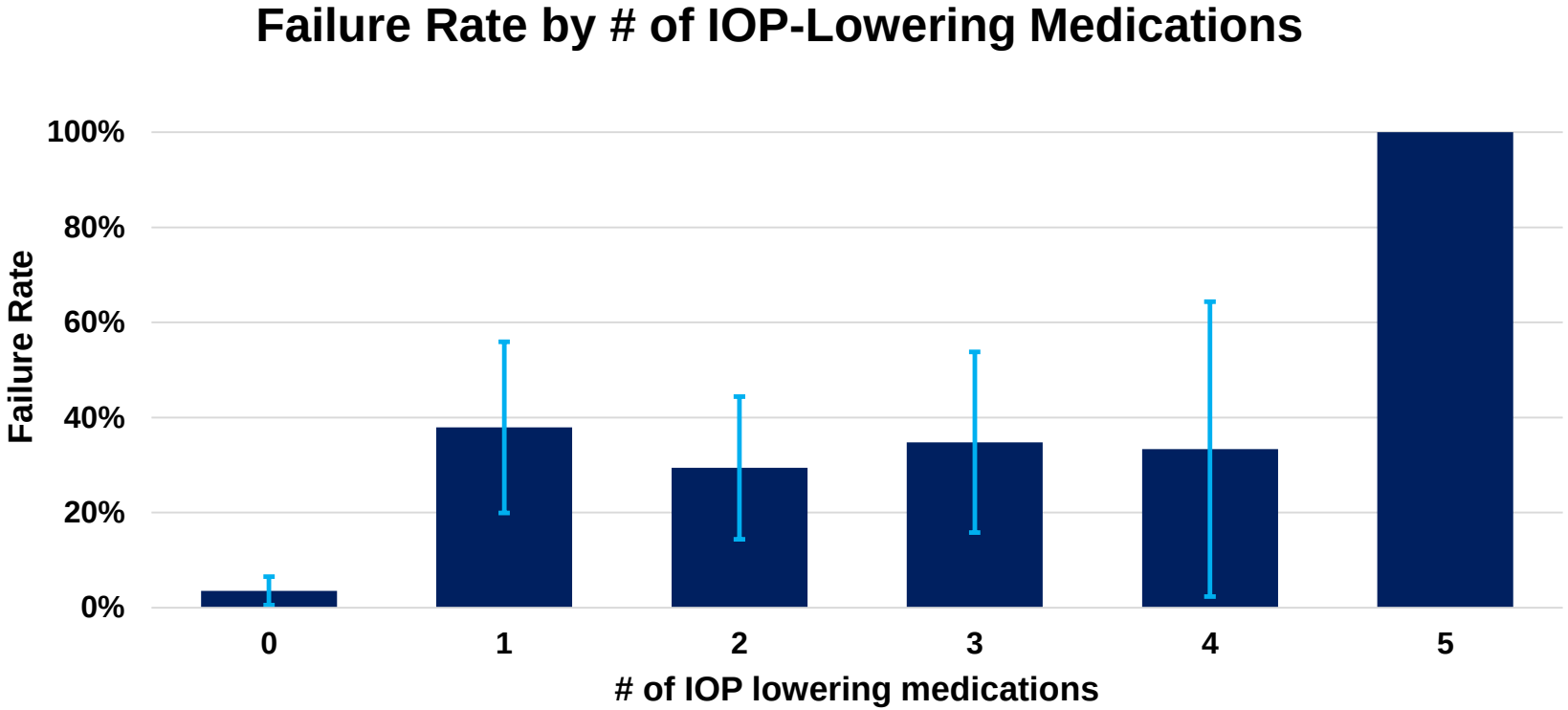
Canaloplasty	0/1	0.0%	N/A	N/A
≥2 above surgeries	**16/31**	**51.6%**	**4.34 [2.63 – 7.17]**	**<0.0001**

95% CI = 95% confidence interval

GDD = Glaucoma Drainage Device
CPC = trans-scleral cyclophotocoagulation
ECP = endoscopic cyclophotocoagulation

Failure & Glaucoma Medications



Failure rate by IOP-lowering medication

Univariate Model	Failures (%)	Hazard ratio [95% CI]	p value
Topical beta blocker	30/68 (44.1%)	6.94 [3.69-13.05]	<0.0001
Topical CAI	16/40 (40.0%)	3.22 [1.90 – 5.45]	<0.0001
PGA	11/47 (23.4%)	1.51 [0.82 – 2.79]	0.1852
Topical alpha-2 agonist	22/50 (44%)	4.42 [2.61 – 7.51]	<0.0001
Oral CAI	8/16 (50%)	3.41 [1.20 – 6.11]	<0.0001
Topical pilocarpine	0/1 (0%)	N/A	N/A

95% CI = 95% confidence interval
CAI = carbonic anhydrase inhibitor
PGA = prostaglandin analogue

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95% CI = 95% confidence interval
CAI = carbonic anhydrase inhibitor
PGA = prostaglandin analogue

Failure rate by IOP-lowering medication

Multivariate Model	Hazard ratio [95% CI]	p value
Topical beta blocker	3.18 [1.22 – 8.31]	0.019
Topical CAI	0.71 [0.32 – 1.56]	0.394
Topical alpha-2 agonist	1.48 [0.54 – 4.07]	0.452
Oral CAI	1.54 [0.64 – 3.70]	0.335
Surgery	2.86 [1.20 – 6.84]	0.018

95% CI = 95% confidence interval
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Failure rate by IOP-lowering medication

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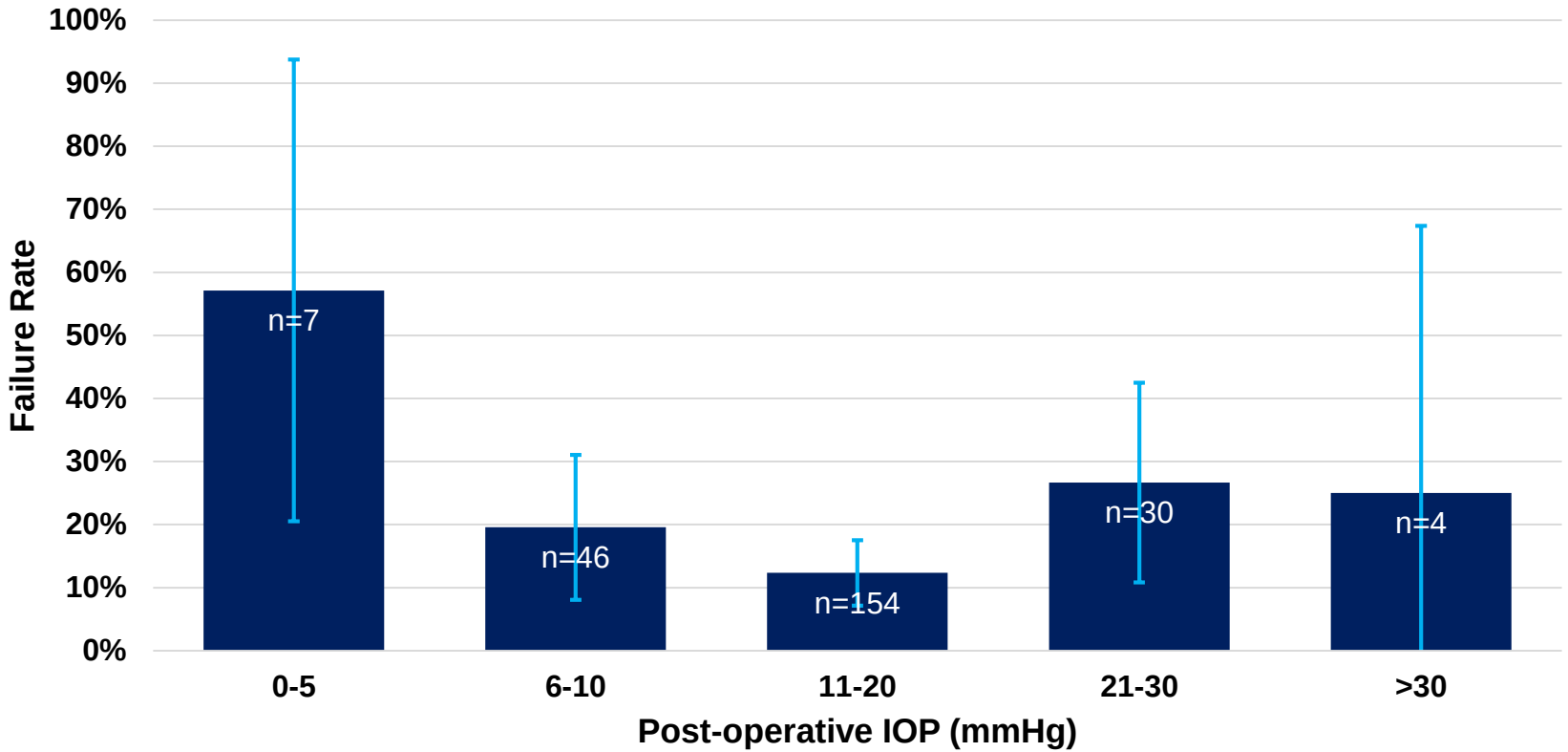
95% CI = 95% confidence interval
CAI = carbonic anhydrase inhibitor

Failure rate by Post-op IOP



Rebubbling rates by risk factor

	Rebubbling (%)	Hazard ratio [95% CI]	p value
All patients	12/241 (4.9%)	1.0	
Hypotony (IOP<5)	2/7 (28.6%)	6.69 [1.79 – 15.0]	0.0048
Elevated IOP (IOP >20)	1/34 (2.9%)	0.55 [0.07 – 4.15]	0.565
Glaucoma	6/116 (5.2%)	1.08 [0.36 – 3.25]	0.8944
GDD	2/43 (4.6%)	0.92 [0.21 – 4.05]	0.9132
Trabeculectomy	1/24 (4.2%)	0.82 [0.11 – 6.09]	0.8479
Any IOP medication	6/142 (4.2%)	0.70 [0.23 – 2.10]	0.5212

95% CI = 95% confidence interval
IOP = Intraocular pressure
GDD = Glaucoma Drainage Device

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95% CI = 95% confidence interval
IOP = Intraocular pressure
GDD = Glaucoma Drainage Device

Conclusions

PKP & Glaucoma

- Identifying eyes at risk of post-PKP glaucoma *prior to surgery* is crucial, and allows:
  - Planning for various options (e.g. Trabeculectomy after PKP if needed, Stage I tube, ECP before PKP, etc.)
  - Better informed consent and discussion of realistic prognosis for visual outcomes

PKP & Glaucoma

- We have a broad choice of surgical techniques for treating post-PKP glaucoma
- *All* are associated with reduced graft survival

DSAEK & Glaucoma

- Just as with PKP, identifying glaucoma *prior to surgery* is crucial for planning & prognosis
- Glaucoma significantly increases the risk of DSAEK failure
- GDDs significantly increase failure risk
- Beta blockers, use of multiple meds, and hypotony may lead to poorer outcomes

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