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Incidence, Risk Factors and Treatment Outcomes of Glaucoma Post-Penetrating Keratoplasty: A 5-Year Lebanese Retrospective Descriptive Study

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General Overview

- **Corneal Blindness is the 5th Cause of Blindness Internationally:** 1.6M cases of Blindness Worldwide
- **Corneal transplant (Keratoplasty)** is the solution once the cornea has been destroyed.
- One of its types is **Penetrating Keratoplasty PKP**
- Like any procedure it has **many complications** one of them is **Post Penetrating keratoplasty Glaucoma (PKG).**

- Tan DT, Dart JK, Holland EJ, Kinoshita S. Corneal transplantation. The Lancet. 2012 May 5;379(9827):1749-61
- Wang H, Zhang Y, Li Z, Wang T, Liu P. Prevalence and causes of corneal blindness. Clinical &experimental ophthalmology. 2014 Apr;42(3):249-53

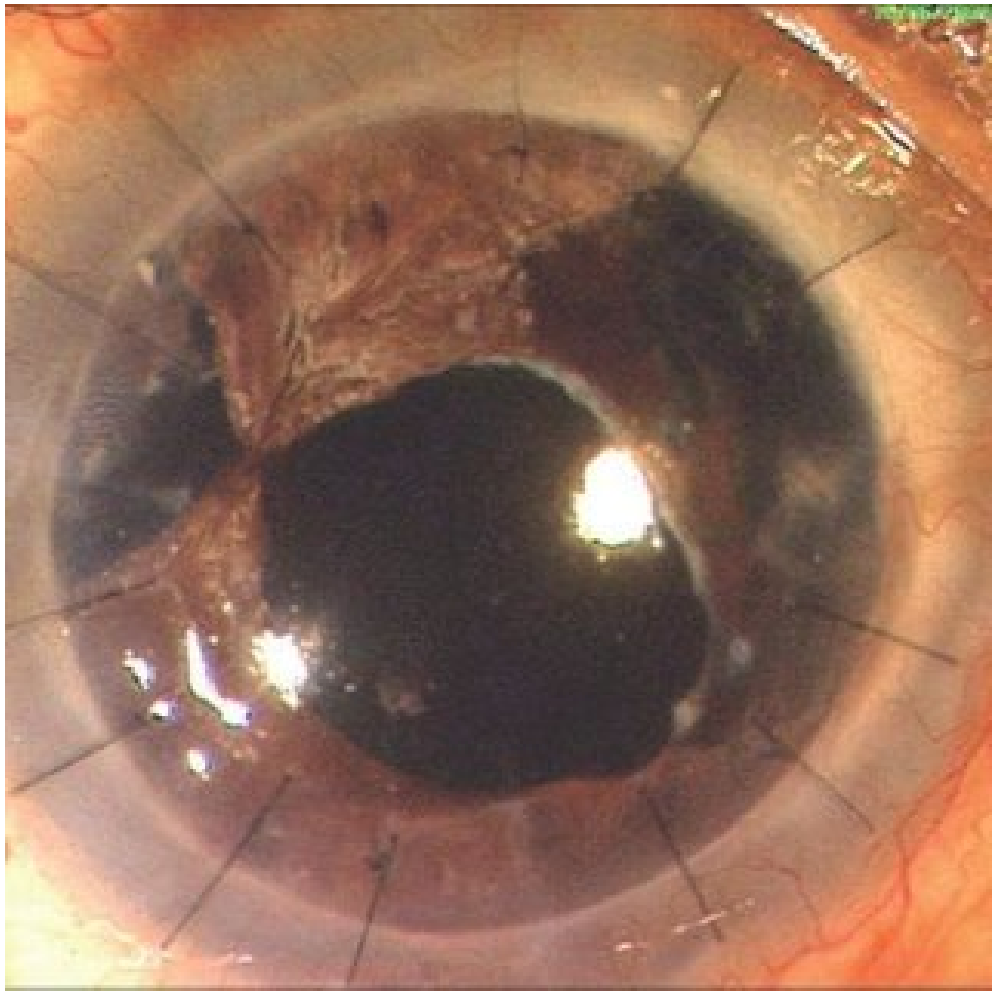
Purpose:

- Incidence, Risk Factors and Treatment Outcomes of Glaucoma Post-Penetrating Keratoplasty (PKG): A 5-Year Lebanese Retrospective Descriptive Study

PKG

Definition of PKG

- IOP > 21mmHG
- ± visual field changes
- ± optic nerve modifications
- Any elevated IOP that necessitate a treatment



Subjects and Methods

A total of 243 eyes of 205 patients who underwent PK in the Beirut Eye Specialist Hospital between 2012 and 2017 were reviewed and only 189 eyes of 159 patients were included.

A retrospective study including 189 single eyes of 159 patients that underwent PKP :

- **between January 2012 and November 2017**
- **at Beirut Eye & ENT Specialist hospital.**

Population

Inclusion Criteria

-Did PKP between 2012 and 2017 at the Beirut Eye Specialist Hospital.

-Males and females ranging in age **between 5 and 90 years old.**

Exclusion Criteria

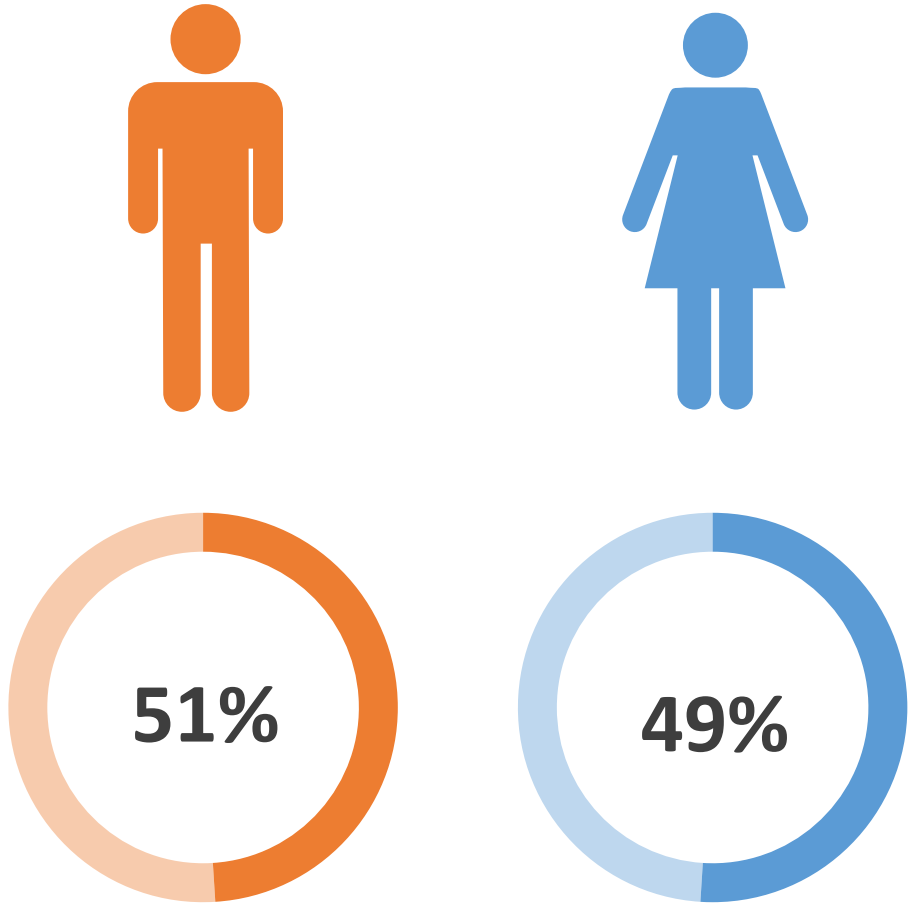
- Follow < 2 months or had incomplete records.

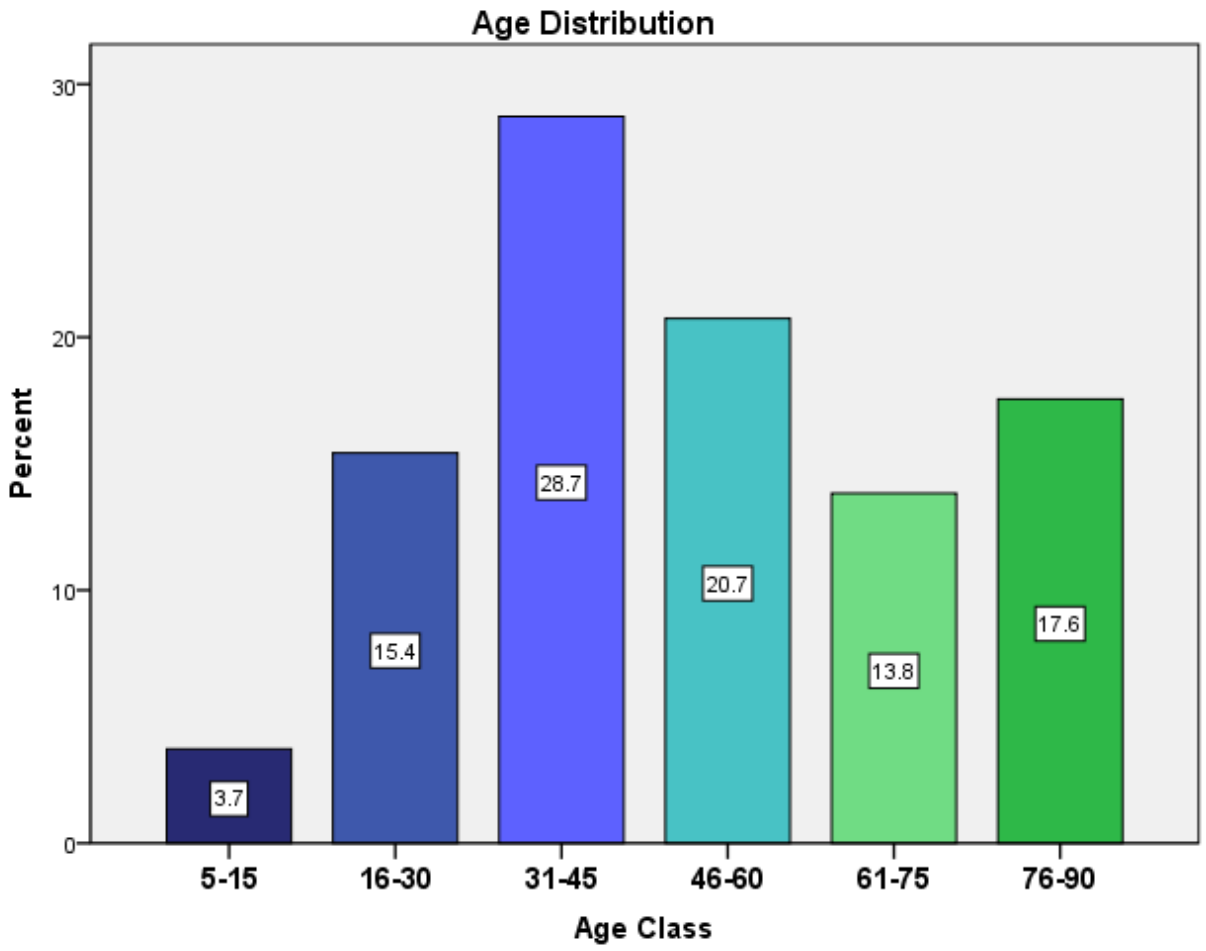
- **Pre-existing glaucoma.**

- History of treated glaucoma.

Results

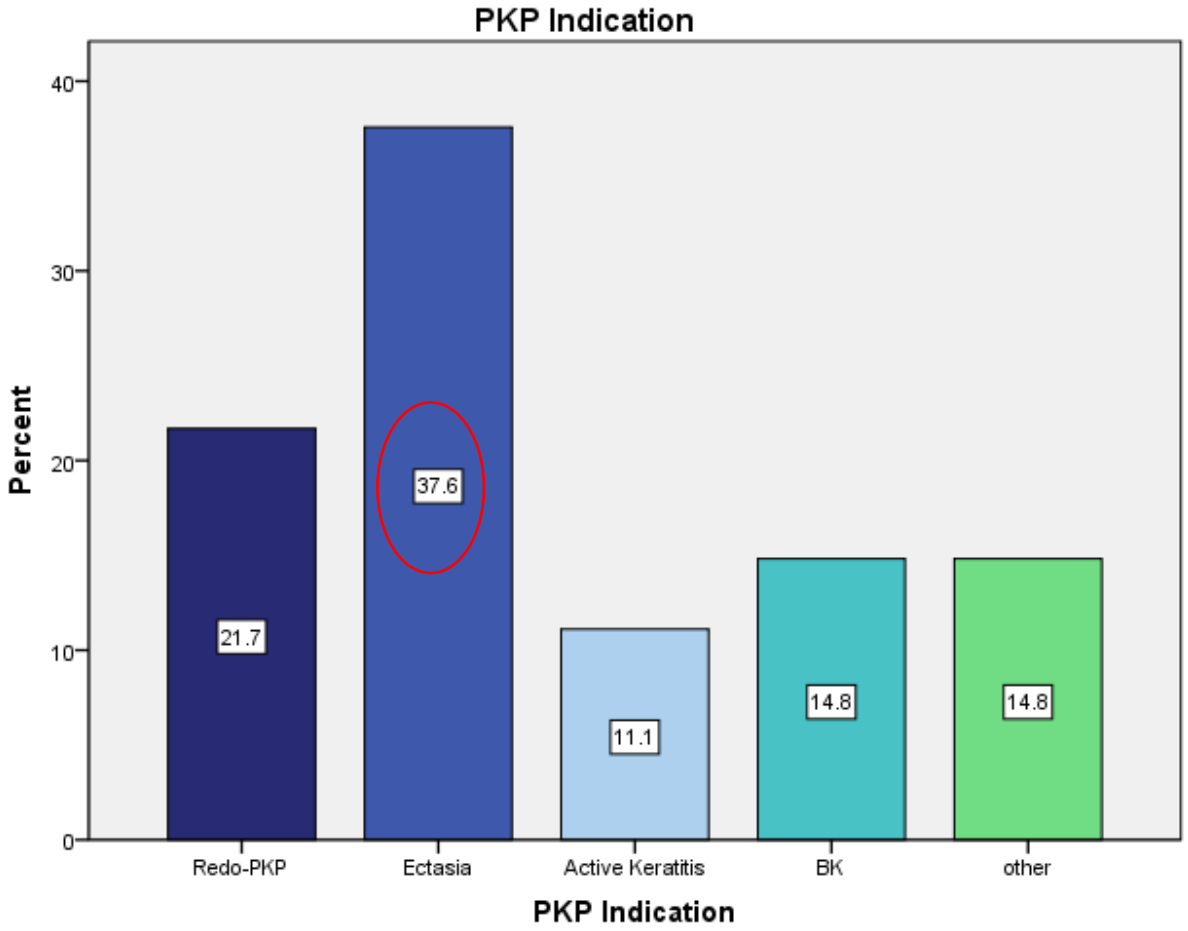
Population Distribution
Age and Gender





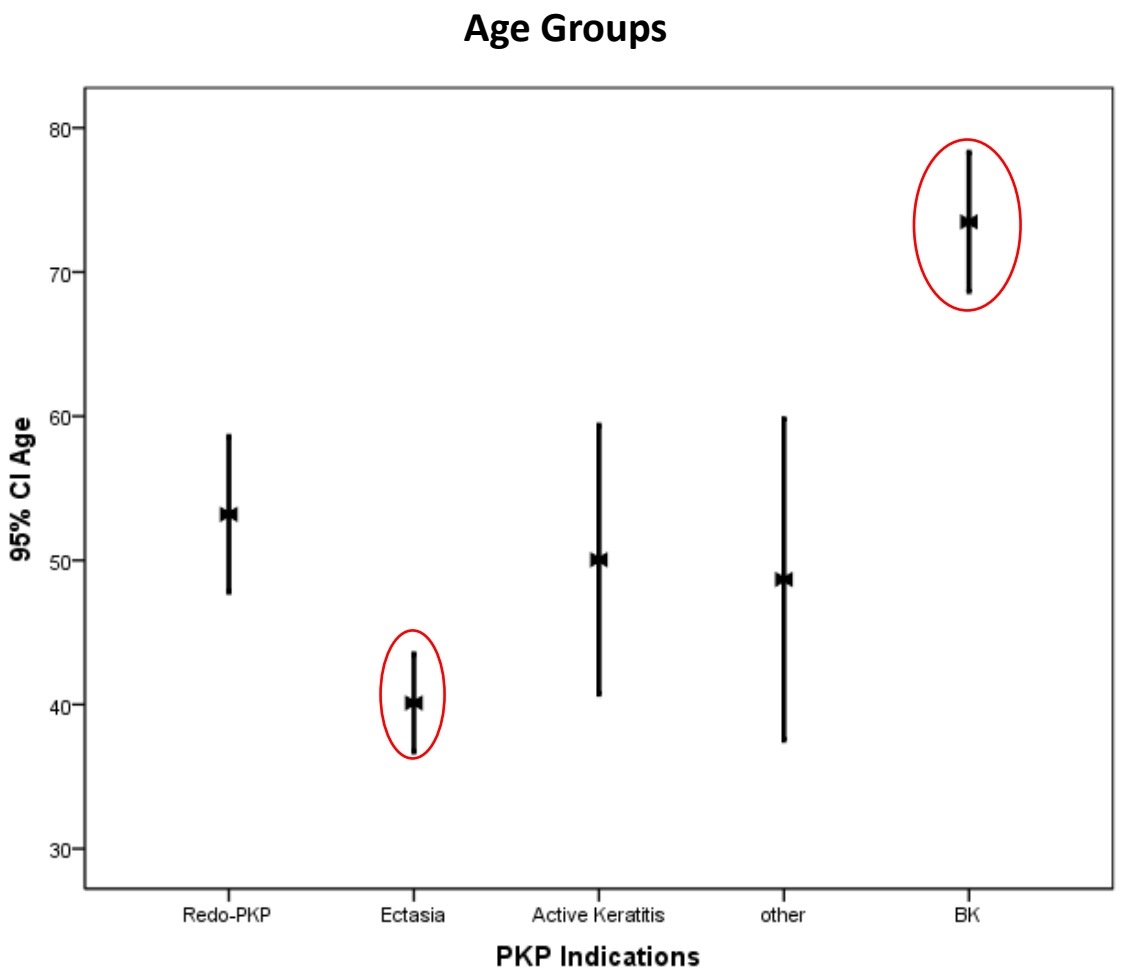
Population distribution

Based on indication for surgery

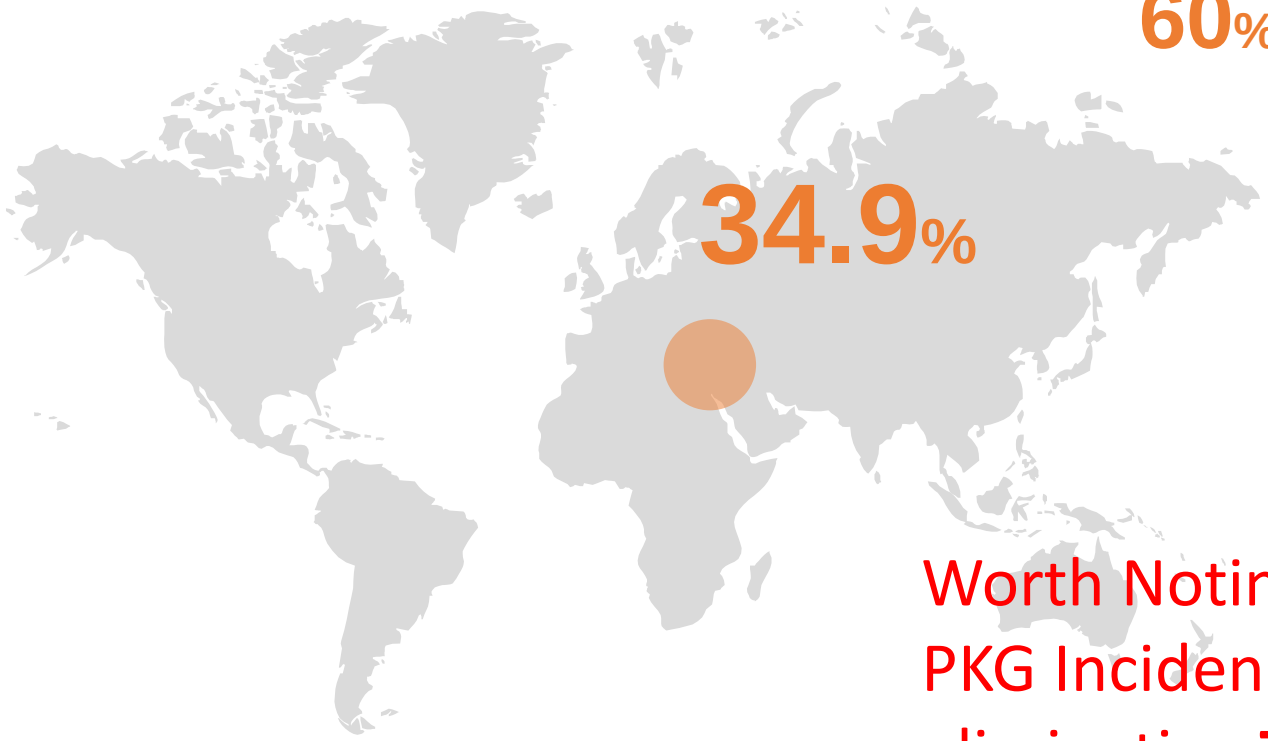


Population Distribution (Age)

Age Based on indication classification



Incidence of the PKG in Lebanon

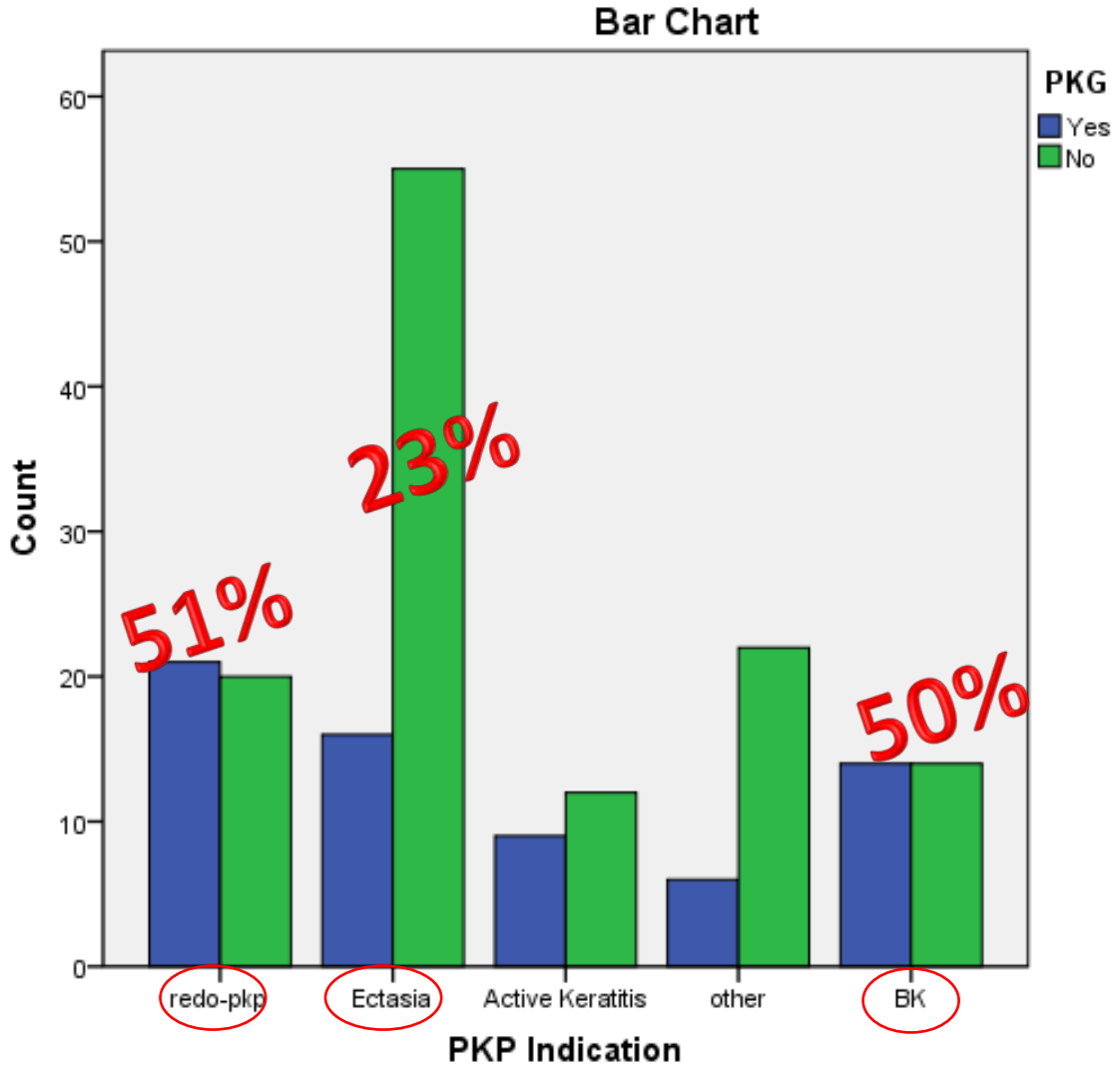


60% 40%

Worth Noting:
PKG Incidence decreases when eliminating **Transient high IOP pts**
34.9% → 28.5%

Population incidence and distribution

PKG in indication groups



The incidence of PKG varied according to the underlying indication for PKP and that different was **statically significant with P-Value <0.01**

Combined PROCEDURES

Additional procedures performed in combination with the keratoplasty in each of the groups.

Additional surgeries	Group 1 Ectasia	Group 2 Redo-PKP	Group 3 Bullous Keratopathy	Group 4 Active Keratitis	Group 5 Other	Total
Pupilloplasty	-	1	4	-	2	7
Anterior vitrectomy	-	1	4	2	3	10
Cataract surgery	5	4	-	3	6	18
IOL manipulation*	1	2	5	1	2	11
Limbal cell transplant	-	3	-	-	2	5
Total with additional surgery	6	11	8	6	15	46(24%)
Total without additional surgery	65	30	20	15	13	143(75.6%)

*IOL manipulation includes: fixation, exchange, and removal.

- No significant difference was found in IOP following PKP between patients who underwent a combined procedure and those who did not **(Chi X^2 P=0.491>0.05; odds ratio: 1.2)**

Combined PROCEDURES (sub-Groups)

The incidence of PKG between the groups divided by surgical indication that underwent additional surgeries or not.

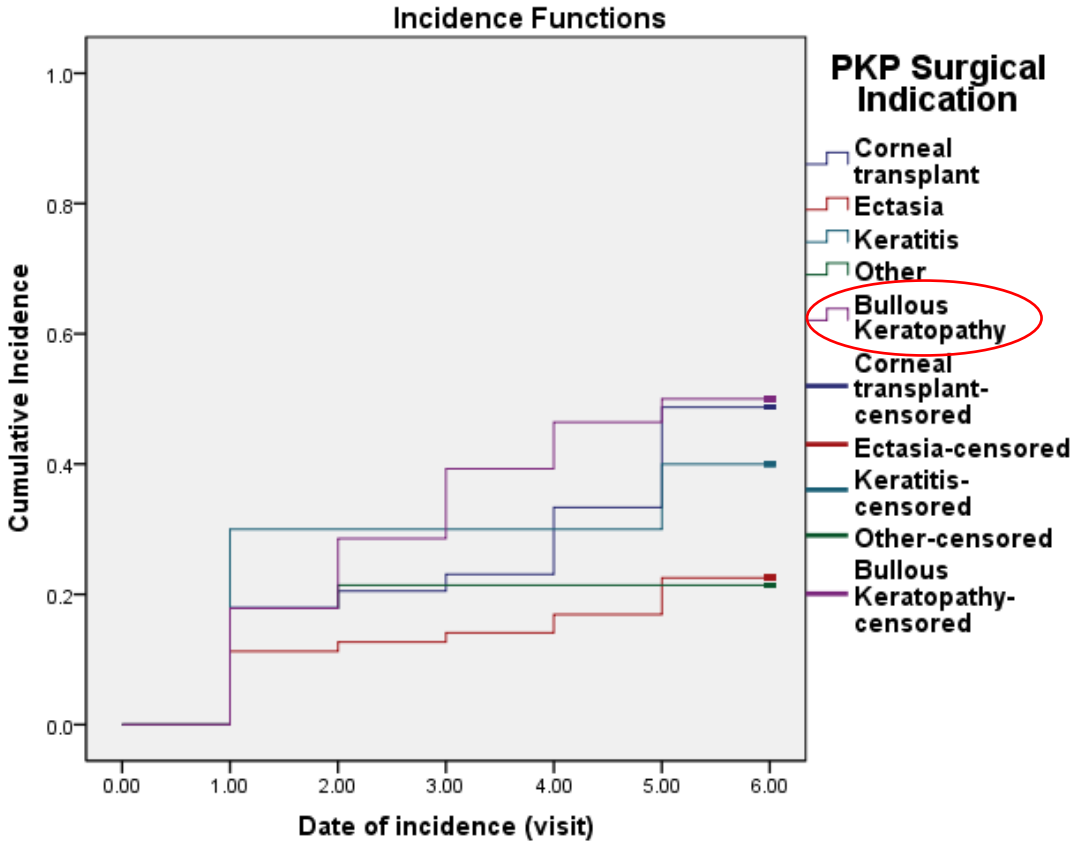
			High IOP Incidence				
Group	Ophthalmic History	Additional surgery	Yes	No	Total	P-value	Odds Ratio
1	Ectasia	Yes	0(0%)	6(100%)	6	0.2*	1.3
		No	16(25%)	49(75%)	65		
2	Redo- PKP	Yes	9(81%)	2(18%)	11	**0.018***	6.8
		No	12(40%)	18(60%)	30		
3	Bullous keratopathy	Yes	6(75%)	2(25%)	8	0.1*	4.5
		No	8(40%)	12(60%)	20		
4	Keratitis	Yes	1(17%)	5(83%)	6	0.18*	0.18
		No	8(53%)	7(47%)	15		
5	Other	Yes	2(13%)	13(87%)	15	0.25*	0.35
		No	4(31%)	9(69%)	13		

PKP: Penetrating Keratoplasty; IOP: Intraocular pressure; *P-value for Chi X^2 test

- In the sub-group Analysis, **Redo-PKP** was the only one to show a **significant increase** in the risk of developing PKG when combined with other surgery (odds ratio: 6.8)

Incidence of Glaucoma post-PKP

Comparing mean times to developing PKG for the PKP indication, the presenting diagnosis (indication), and previous risk factors (HTN, DM)



Kaplan–Meier survival study

Significant relation

Indication of PKP and developing PKG

study1 (LogRank: P=0.011 < 0.01)

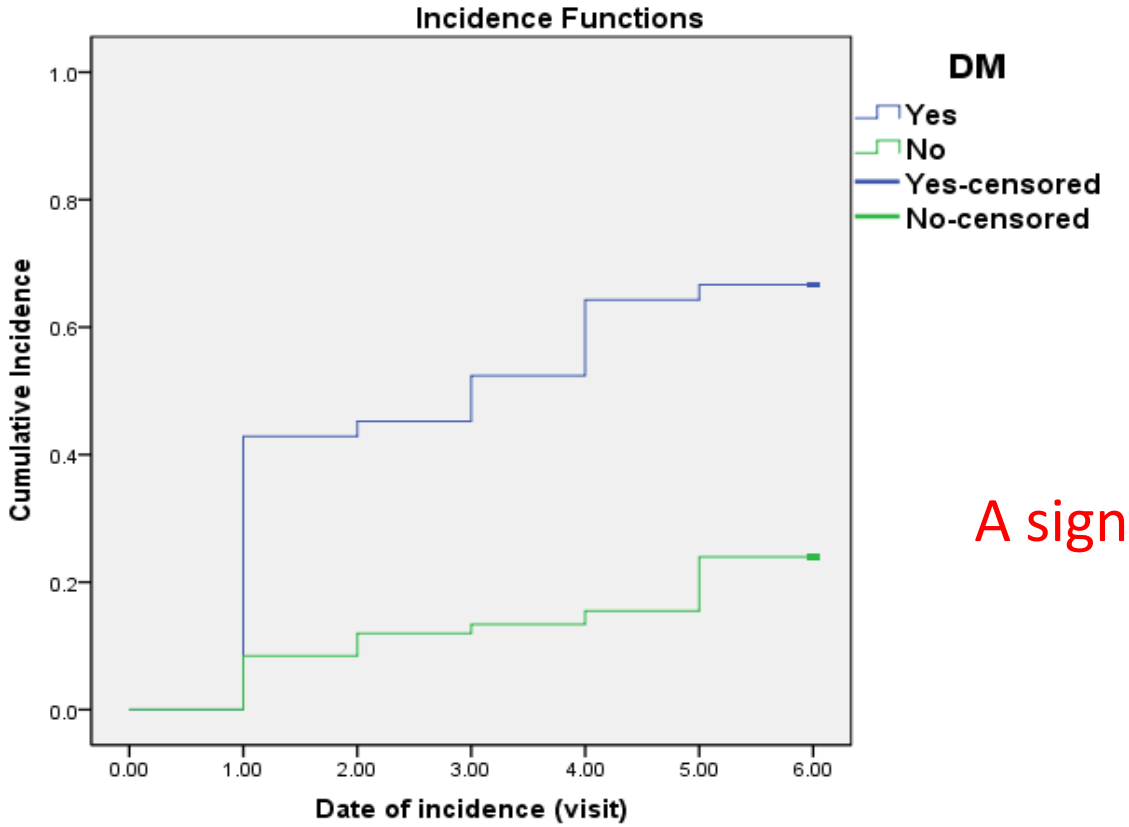
Early incidence

Bullous keratopathy (BK) (3.7 months)

Later indidence

Ectasia (6.7 months).

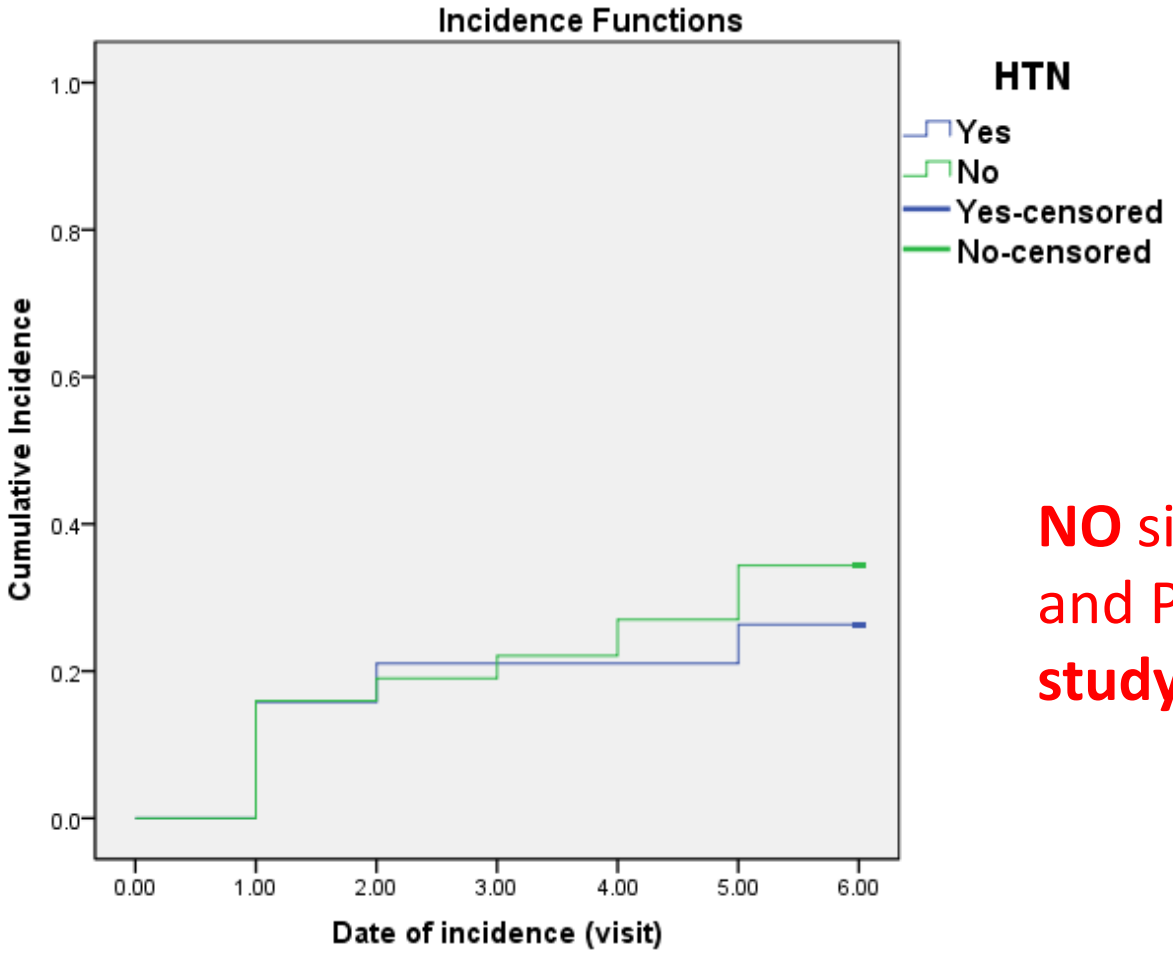
Relation between DM and PKG



Of the total population, 22% of patients were Diabetics: 67.4% developed PKG

A significant relation was found between DM and PKG

Relation between HTN and PKG



NO significant relation was found between HTN and PKG (5/19)

study 3 (LogRank: P=0.5 < 0.05)

Visual acuity

Comparing mean visual acuity between pre and 25.3 ± 15 months post operatively, in patients with and without glaucoma.

	N	t	Mean logMAR preoperative	Mean logMAR postoperative	▲Mean (logMAR)	P-value
Without PKG	65	4.4	**1.37± 0.85**	**0.84± 0.96**	0.53±0.98	**0.000***
With PKG	35	1.2	**1.30±0.83**	**1.02±0.94**	0.34±1.23	0.20*
Total	100	4.07	1.34± 0.84	.90± 0.95	0.47±1.07	**0.000***
P-value					0.43**	

*P-values of Paired samples T-test to compare IOP,

LogMAR	Visual acuity
0.70	20/100
1.00	20/200
1.30	20/400 CF6m
1.4	CF5m

- Improvement in visual acuity

- Patients without PKG → very high significance

t(65)= 4.4, p=0.00<0.01

- Patients with PKG → the clinical improvement was statistically non-significant

t(35)= 1.2, p= 0.2>0.05

- But comparing Means differences (pre-op vs post-op)

-> showed no statistical difference between the improvement of both groups

t (100)= 0.792, p=0.43>0.05

Corneal size

Comparing mean donor's corneal size between patients developing PKG or not.

		N	t	mean donor's corneal size (mm)	P-value
PKG	Yes	67	1.5	8.04±0.66	0.136*
	No	122		7.89±0.51	
	Total	189		7.94±0.57	

PKG: Post-Keratoplasty Glaucoma.*P-value of independent t-test

No significance was found relating to corneal size to PKG.

t(189)= 1.5, p=0.136>0.05

The distribution of eyes according to suture number and PKG development

	Sutures			Total	P-value
	combined	16	More than 16		
With PKG	4(20%)	55(35.9%)	7(85%)	66	**0.003***
Without PKG	16(80%)	98(64.1%)	1(15%)	115	
Total	20(100%)	153(100%)	8(100%)	181	

PKP: Penetrating Keratoplasty; IOP: Intraocular pressure;* P-value for Chi X^2 test

- Having more than 16 sutures was highly associated with PKG
- Less sutures combined with running showed lesser incidence of PKG (Relations were very significant P=0.003)
- On average sutures were removed after **12.5±9.3** in patients.
  - IOP was measured before and after suture removal in 15 patients
  - A **drop** of IOP was detected in most of these patients (**5** ±7.5 mmHg)
  - **Suggesting a role of suturing and suture removal in controlling and/or measuring postoperative IOP.**

PKP Complication

The Incidence of other post-keratoplasty complications in patients with and without PKG.

Post-PKP complications	With PKG	Without PKG	Both groups	P-value
Graft rejection	**5 (7.6%)**	**2 (1.6%)**	7 (3.7%)	
Graft failure	2 (3%)	6 (4.9%)	8 (4.2%)	
Infections	3 (4.5%)	4 (3.3%)	7 (3.7%)	0.014***
Epithelial defects*	**9 (13.6%)**	**5 (4.1%)**	14 (7.4%)	
Others**	5 (7.6%)	4 (3.3%)	9 (4.7%)	
Total	24/66 (36.4%)	21/123(17%)	45/189 (23.8%)	0.003***

PKP: Penetrating Keratoplasty; IOP: Intraocular pressure;
*Epithelial defects include: pterygium, opacification, hyperopia, scaring, and ulcers;
** Others include: retinal detachment, leakage, choroidal detachment, allergic reactions
*** P-value for Chi X^2 test

- PKG patients developed more complications
- Corneal epithelial defect and Graft rejections

Treatment options

Treatment of post keratoplasty glaucoma in each of the analyzed groups according to ophthalmological history.

Mode of postoperative treatment	G 1 Ectasia	G 2 Redo- PKP	G 3 Bullous Keratopathy	G 4 Keratitis	G 5 Other	Total	P-value
Spontaneous resolution	3	5	2	1	1	12	
Continued medical treatment	12	13	8	6	3	42	0.81**
Surgically treated Trabeculectomy	1	3	4	2	2	12	
Total	16	21	14	9	6	66	

PKP: Penetrating Keratoplasty; * P-value for Chi X^2 test;

- Treatment with anti-glaucoma eye drops proved effectiveness in controlling IOP in the majority of our patients:
  - spontaneous resolution (12/66: 18%)
  - Continued (42/66: 63.6%)
  - Surgical intervention (Trabeculectomy) (12/66: 18%)

- No significance was found relating the PKP indication to post-operative effective type of treatment **(Chi X^2, Exact test: P=0.81> 0.05)**

Discussion

- We excluded patients with previous glaucoma history so to consider other risk factors independently.
- Regarding the incidence of PKP, our results were within the upper limit with an incidence of 34.9%:
  - When eliminating cases of transient Hight IOP incidence dropped by 6% (28.5%)
  - Higher rates of Redo-PKP surgeries (tertiary referral center) as an indication (21.7%) of our population predisposing by itself to having higher risk of PKG.
- Patients in our population with **Bullous keratopathy and previous graft rejection** were shown to be at high risk for PKG (50% and 51.2%) compared to the reported data by Nilgun Yildirim et al (43% and 45%)
- The lowest incidence of PKG was in the patients presenting with Ectasia (Keratoconus, Keratoglubous…) as revealed in our results (22.5%) and that is similar to what was previously reported (20%) by Haddin RI et al.

- Haddadin RI, Chodosh J. Corneal transplantation and glaucoma. In Seminars in ophthalmology 2014 Sep 1 (Vol. 29, No. 5-6, pp. 380-396). Taylor & Francis
- Yildirim N, Gursoy H, Sahin A, Ozer A, Colak E. Glaucoma after penetrating keratoplasty: incidence, risk factors, and management. Journal of ophthalmology. 2011 Nov 30;2011.

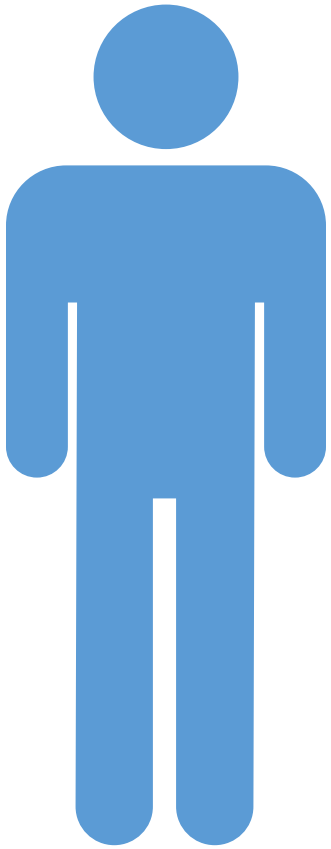
Discussion

- Except for the re-do PKP, no significant difference was found in IOP following PKP alone and PKP with combined procedure; which was supported by the publication of Ramjat et al and Yildirim et al.
- The average period between surgery and the first documented IOP elevation was 5±6 months similar to what was found by Ammar et al
- Re-assess after suture removal
- The use of topical medications to control IOP is the main treatment of PKG, which was also documented by Kardage et al.

- Haddadin RI, Chodosh J. Corneal transplantation and glaucoma. In Seminars in ophthalmology 2014 Sep 1 (Vol. 29, No. 5-6, pp. 380-396). Taylor & Francis
- Karadag O, Kugu S, Erdogan G, Kandemir B, Ozdil SE, Dogan OK. Incidence of and risk factors for increased intraocular pressure after penetrating keratoplasty. Cornea. 2010 Mar 1;29(3):278-82
- Ramjat Sihota et al, Post-penetrating management and keratoplasty glaucoma: Risk factors, visual outcome, Australian and New Zealand Journal of Ophthalmology (1998) 26, 305-309
- Yildirim N, Gursoy H, Sahin A, Ozer A, Colak E. Glaucoma after penetrating keratoplasty: incidence, risk factors, and management. Journal of ophthalmology. 2011 Nov 30;2011

Conclusions

Incidence and Risk Factors For PKG + Management and complications



PKG Incidence

One over three patients **1/3**

Pre-Op Risk Factors

DM Type II , BK, Redo-PKP

NOT in Ectasia

Intra-Op Risk Factors

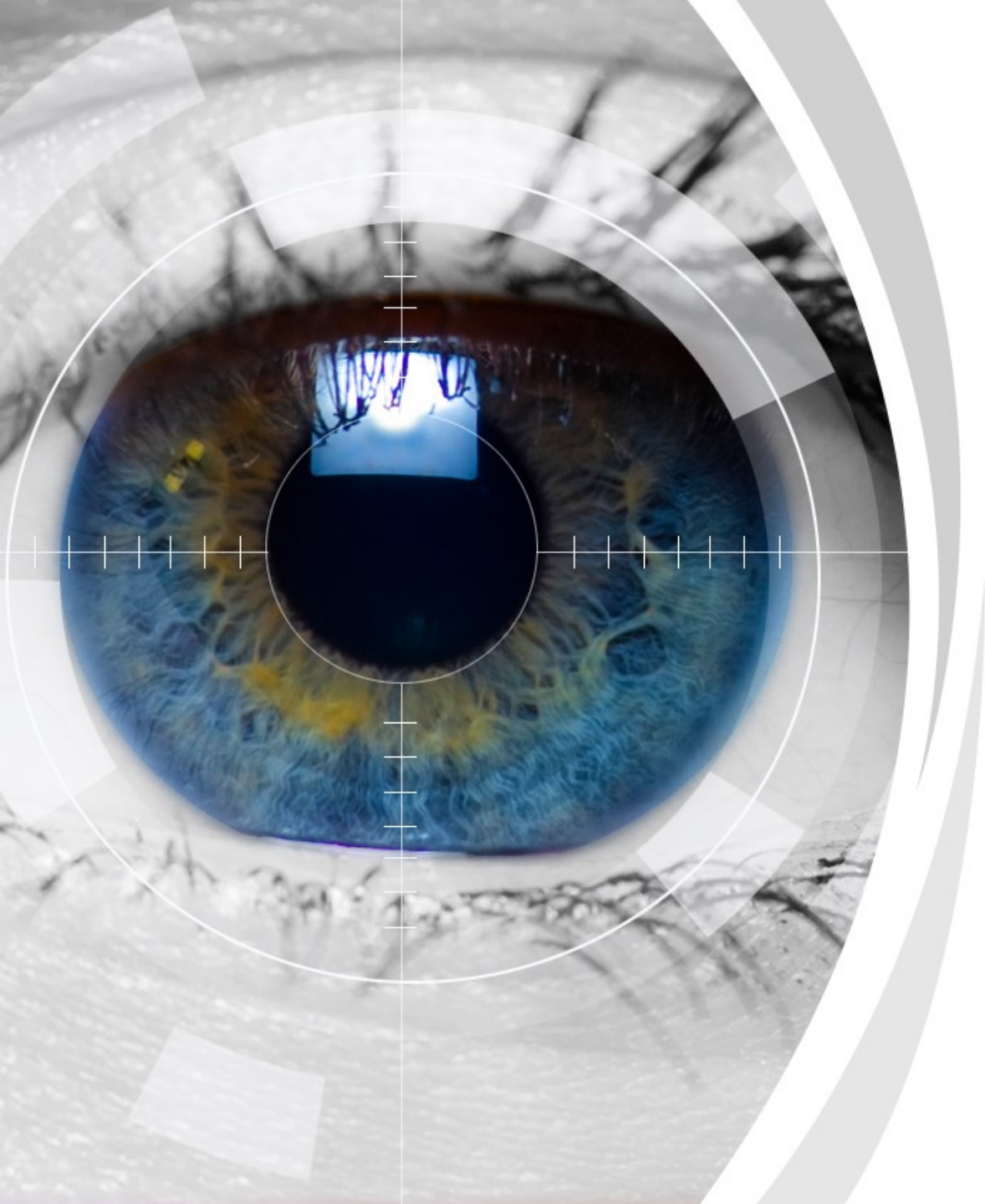
Combining PKP with other surgeries in Redo-PKP

Having higher number of sutures

Post-Op Factors

Medical and surgical treatment were equally effective regardless of PKP indication

Corneal epithelial defect and graft rejection were directly related to PKG



Thank you