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Ahmed Glaucoma Valve as a Risk Factor for Penetrating Keratoplasty Failure

Karwan Bakhtyar Mohammed* Kawa Khalil Ahmad**

Abstract

Background and objectives: Penetrating keratoplasty is a surgical procedure with a history spanning over a century. The objective is to identify the incidence and potential risk factor of graft failure after performing penetrating keratoplasty in eyes with Ahmed valve tube.

Methods: This retrospective study conducted on 24 patients whom penetrating keratoplasty and glaucoma shunt surgery have been performed for them from February 2017 to December 2022 at North eye center/ Erbil city. The follow up was obtained for determining the risk factors associated with keratoplasty failure.

Results: Half of the patients with glaucoma drainage devices have a successful penetrating keratoplasty surgery. Age was not a risk factor for penetrating keratoplasty failure, relative risk (RR)=0.85, CI=0.38-1.88, P=0.682). Also, the following factors were not a risk for keratoplasty failure; sex (RR=1,CI=0.45-2.23, P=1), sequence of surgery of Ahmed valve prior to penetrating keratoplasty (RR=0.57,CI=0.20-1.53, P=0.206), eye laterality (RR=1.23,95%CI=0.47-3.25, P=653), aphakia (RR=4.0,CI=0.12-136.95, P=0.215) and pseudophakia (RR=5.71,CI=0.52-62.66 P=0.154), history of vitreoretinal surgery is the risk factor for penetrating keratoplasty failure (RR=3.4,95%CI=1.63-7.10,P=0.002), chronic diseases (RR=0.79,95%CI=0.34-1.86,P=0.615) and intraocular pressure>21 mmHg (RR=1.214,95%CI=0.54-2.75,P=0.653) are also risk factors for decreasing success of penetrating keratoplasty.

Conclusion: In our study, Ahmed valve is a risk factor for failure of pentrating keratoplasty surgery which is 50%. Age, gender, Ahmed valve prior to penetrating keratoplasty, lens status and operated eye were not a risk factor in pentrating keratoplasty failure in those who underwent glaucoma drainage device. Whereas, vitreoretinal surgery, chronic diseases and intraocular pressure were observed as risk factors in penetrating keratoplasty failure.

Keywords: Ahmad valve, Penetrating keratoplasty, Risk factor

*MBChB, HDO, KHCMS, Department of Ophthalmology, Hawler Eye Teaching Hospital, Hawler Directorate of Health, Erbil, Iraq. Email: karwan.baxtiar@yahoo.com. Corresponding author
**MBChB, GBO, Consultant Ophthalmologist, Ministry of Health, Erbil, Iraq.Email: kawa.khoshnaw77@gmail.com

Introduction

Glaucoma, in itself, is recognized as a predisposing factor for the failure of corneal transplantation, and the existence of a glaucoma drainage device (GDD) is thought to exacerbate this susceptibility. Post-penetrating-keratoplasty glaucoma (PKPG) is a term used to describe an increased intraocular pressure (IOP) exceeding 21 mmHg following penetrating keratoplasty (PKP), with or without concurrent visual field impairment or alterations in the optic nerve head, conversely.[1] It is the predominant etiology of permanent visual impairment and ranks as the secondary most prevalent reason for transplant malfunction subsequent to rejection. This issue holds considerable clinical importance due to its high prevalence, diagnostic and surveillance challenges, as well as the intricacies involved in its treatment. Panda et al., have documented a post-keratoplasty glaucoma occurrence rate ranging from 9% to 31% during the initial phases following the surgical procedure.[2] Numerous individuals diagnosed with glaucoma are prone to the occurrence of corneal opacities, which may arise due to endothelial dysfunction post numerous intraocular procedures or due to the primary etiologies of glaucoma, including herpetic keratouveitis, trauma or congenital abnormalities.[3] The glaucoma linked to these conditions frequently proves resistant to conventional medical treatments, necessitating the insertion of a glaucoma drainage device (GDD) to manage intraocular pressure.[4] Therefore, penetrating keratoplasty is frequently carried out as a means of visual restoration on eyes that are either currently equipped with, or will eventually require, one or more glaucoma drainage devices (GDD) in place.[5] Alvarenga et al., were employing case-control methodology revealed a higher incidence of graft failure among individuals with a GDD compared to those whose IOP was managed through medical means.[6] That the investigation did not establish a causal relationship between GDD and graft failure, rather indicating that GDD may serve as proxies for a factor associated with more severe glaucoma. Nevertheless, existing research does suggest that the existence of a GDD can indeed result in the loss of endothelial cells.[7, 8] Several hypotheses have been proposed to explain the processes leading to endothelial cell injury and depletion, such as mechanical injury and immune-mediated damage resulting from changes in the immune microenvironment of the anterior eye segment. The failure of corneal transplantation in the context of a GDD is thought to involve multiple factors.[9] The enduring viability of corneal transplants in eyes with glaucoma drainage devices (GDD) is commonly perceived as low, with reported 1-year graft failure rates ranging widely from 8% to 51% in various studies, often involving diverse patient groups with different GDD types and timing of surgery.[3] Our study was conducted to quantify the success rate of PKP in patients with GDD and find the correlation between age and PKP failure. The evaluation of the impact of intraocular pressure (IOP) on the PKP final outcome would be also considered.

Patients and methods

In the current study; we retrospectively reviewed the records of all patients who underwent PKP from February 2017 to December 2022 in North eye center in Erbil/ Iraq. All of the patients were studied who underwent PKP and Ahmed valve (AV) implantation surgery for controlling glaucoma and the interval between both surgeries was 2 months to 30 months, the data and questioner were obtained including age, gender, chronic disease, PKP, interval between AV surgery and PKP, vitreoretinal (VR) surgery, and pre and post operative IOP. To evaluate the failure and success rate of PKP, also, to find the correlation between

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age and PKP failure, as well as the impact of IOP on the PKP final outcome. We included all cases with penetrating keratoplasty (PKP) surgery whom they have glaucoma shunt tube in a preoperative and postoperative data. Exclusion Criteria involved any PKP out of North eye center as well as any follow up lower than nine months were excluded in this study. The Statistical Package for the Social Sciences (SPSS, IBM, Chicago, USA, version 27) was used. The data were expressed as numbers (%) for categorical data and mean (St. deviation) for numerical data. Chi-square test was used for categorical variables; paired t test was used for determine the difference in numerical variables. Relative risk (RR) and 95% Confidence Interval (CI) was used to determine the relationship of the risk factors to the PKP failure. P- value ≤ 0.05 was considered statistically significant. The ethical study protocol was approved by the Kurdistan Higher Council for Medical Specialists (KHCMS).

Results

In the current study a total of 24 patients were studied, with an average age 42.67 ± 22.43 year (7 to 81), the majority (*n*=13, 54.2%) was ≤ 40 years, while 11 (45.8%) were older than 40 years. The males and females were equally distributed in our study. The predominant operated eye was right (*n*=17, 70.8%) rather than left (*n*=7, 29.2%). As shown in Table (1).

Table (1): Demographic characteristics of the patients.

Demographic characteristics	Frequency *n* (%)
Age (year)	
Mean ± SD	42.67 ± 22.43
≤ 40 years	13 (54.2%)
> 40 years	11 (45.8%)
Gender	
Female	12 (50.0%)
Male	12 (50.0%)
Operated eye	
Right	17 (70.8 %)
Left	7 (29.2 %)

n= number; %= percentage; SD= standard deviation.

As listed in Table (2), two (8.3%) patients were hypertensive, only 1 (4.2%) was diabetic and 2 (8.3%) were both diabetic and hypertensive. Two-third of the patients (*n*=16, 66.7%) were penetrating keratoplasty surgery (PKP) done prior and the other (*n*=8, 33.3%) were Ahmed valve tube (glaucoma tube) surgery done prior. The interval from index AV to index PK was 8.27 ± 8.04 months. The dominant of the lens status was pseudo phakic (*n*=17, 70.8%) followed by phakic (*n*=5, 20.8%) then aphakic (*n*=2, 8.3%). 17 (70.8%) were underwent vitreoretinal surgery and the other were not. The successful rate of PKP surgery in those patients with AV tube was (*n*=12, 50.0%).

Table (2): Clinical and ophthalmologic characteristics of the patients.

Clinical and ophthalmologic characteristics	Frequency *n* (%)
Chronic disease	
No	19 (79.2%)
DM	1 (4.2%)
HTN	2 (8.3%)
DM with HTN	2 (8.3%)
PKS status	
PKP prior	16 (66.7%)
Ahmed valve tube prior	8 (33.3%)
Interval from index AV to index PKP (month)	
Mean ± SD	8.27 ± 8.04
Lens status	
Aphakic	2 (8.3%)
Phakic	5 (20.8%)
Pseudo phakic	17 (70.8%)
VR	
No	17 (70.8%)
Yes	7 (29.2%)
Outcome	
Succes	12 (50.0%)
Fail	12 (50.0%)

n= number; %= percentage; SD= standard deviation; DM= Diabetes mellitus; HTN= Hypertension; PKP= penetrating keratoplasty; VR= Vitreoretinal surgery.

Table (3) and Figure (1) show the pre and postoperative intraocular pressure (IOP) measurements. IOP was significantly higher

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in preoperative (27.1 ± 8.7 mm Hg) than the post operative IOP (19.1 ± 8.3 mm Hg), p value= 0.001. In respect of the IOP of the preoperative, the majority (*n*=15, 62.5%) were >21 mm Hg and 9 (37.5 %) were ≤ 21 mm Hg, on the other hand, the majority of the IOP of the postoperative patients 17 (70.8%) was ≤ 21 mm Hg and only 7 (29.2%) were >21 mm Hg.

Table (3): Comparison of pre and postoperative IOP.

IOP mm Hg	Preoperative	Postoperative	p value
Mean ± SD	27.1 ± 8.7	19.1 ± 8.3	0.001 *
≤ 21 mm Hg	9 (37.5%)	17 (70.8%)	
>21 mm Hg	15 (62.5%)	7 (29.2%)	

n= number; %= percentage; SD= standard deviation; mm Hg= millimeter mercury; IOP= intraocular pressure; *= significant difference.

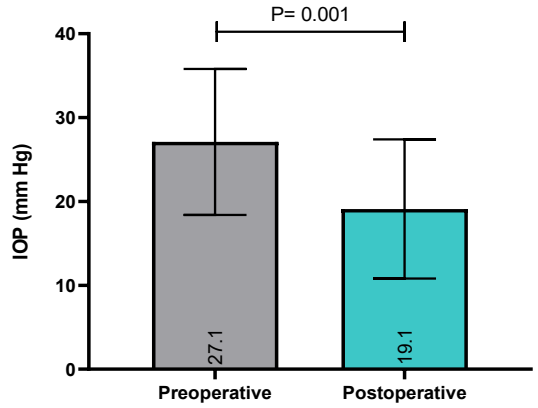

Figure (1): Comparison of preoperative and postoperative IOP.

Table (4) displays the potential risk factors of PKP failure, The mean age of the PKP failure patients was slightly higher (43.8 ± 24.4 years) than success (41.58 ± 21.2 years), 54.5% (n=6) of the > 40 years patients was associated with PKP failure, on the other hand, 45.5% (n=5) of the > 40 years patients was success PKP. Despite that, increasing age was no a potential significant risk factor for PKP failure statistically, relative risk (RR)= 0.85, 95% CI= 0.38- 1.88, P= 0.682). Also, the following factors were not estimated as a risk factor for PKP failure; gender (RR= 1, 95% CI= 0.45- 2.23, P=1), surgery of Ahmed tube prior to PKP (RR= 0.57, 95% CI= 0.20 - 1.53, P= 0.206), operation of right eye (RR= 1.23, 95% CI= 0.47- 3.25, P= 653) and aphakic lens status (RR= 4, 95% CI= 0.12- 136.95, P= 0.215) as well as pseudo phakic lens (RR= 5.71, 95% CI= 0.52- 62.66, P= 0.154). Notably, history of vitreoretinal surgery is the potential risk factor for PKP failure (RR=3.4,95%CI=1.63-7.10, P=0.002), also presence of diabetes mellitus and hypertension (RR= 0.79, 95% CI= 0.34- 1.86, P=0.615) have effect on the failure of PKP. The mean of post operative IOP of the PKP failure patients was somewhat higher (19.79 ± 10.33 years) than PKP success patients (18.38 ± 5.90 years), 33.3% (n=4) of the PKP failure had IOP of greater than 21 mm Hg, conversely 25.0% (n=3) of the success PKP had IOP of > 21 mm Hg, the relative risk (RR) relying on > 21 mm Hg= 1.214, 95% CI= 0.54- 2.75, P= 0.653).

Table (4): Risk factors associated with penetrating keratoplasty failure.

Variables	Fail (*n*=12)	Success (*n*=12)	RR	95 % CI	p value
Age					
Mean ± SD	43.8 ± 24.4	41.58 ± 21.2	0.85	0.38 – 1.88	0.682 ns
≤ 40 years	6 (46.2%)	7 (53.8%)			
> 40 years	6 (54.5%)	5 (45.5%)			
Gender					
Male	6 (50.0%)	6 (50.0%)	1	0.45 - 2.23	1.0
Female	6 (50.0%)	6 (50.0%)			
Chronic disease					
No	3 (60.0%)	2 (40.0%)	0.79	0.34 - 1.86	0.615 ns
Yes	9 (47.4%)	10 (52.6%)			
PKS status					
PKP prior	9 (60.0%)	6 (40.0%)	0.57	0.20 –	0.206 ns

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Tube prior	3 (33.3%)	6 (66.7%)		1.53	
Operated eye					
Right	9 (52.9%)	8 (47.1%)	1.23	0.47 – 3.25	0.653 ns
Left	3 (42.9%)	4 (57.1%)			
Lens status					
Phakic	1 (20.0%)	4 (80.0%)	4.00 5.71	0.12 – 136.95 0.52 – 62.66	0.215 ns 0.154 ns
Aphakic	1 (50.0%)	1 (50.0%)			
Pseudo phakic	10 (58.8%)	7 (41.2%)			
VR surgery					
No	5 (29.4%)	12 (70.6%)	3.4	1.63 - 7.10	0.002 *
Yes	7 (100.0)	0 (0.0%)			
IOP					
Mean ± SD	19.79 ± 10.33	18.38 ± 5.90			
≤ 21 mm Hg	8 (47.1%)	9 (52.9%)	1.214	0.54 – 2.75	0.653 ns
>21 mm Hg	4 (57.1%)	3 (42.9%)			

n= number; %= percentage; SD= standard deviation; RR= Relative Risk for PKP failure; CI= Confidence of interval; PKP=penetrating keratoplasty; VR= Vitreoretinal surgery; ns= No significant difference; *= Significant difference.

Discussion

In previous times, a unified agreement was lacking regarding the optimal timing for performing penetrating keratoplasty (PK) and glaucoma drainage device (GDD) placement in individuals necessitating both interventions. Numerous investigations have indicated that initiating GDD placement before PK could potentially result in enhanced longevity of the graft.[3] This sequence offers enhanced IOP management during PK, reduces the risk of corneal graft trauma associated with GDD placement. Coleman et al., revealed detailed outcome for 31 eyes that received Ahmed Valve implants either sequentially or concurrently with PKP.[10] This study revealed that the preoperative IOP measurements was significantly higher (27.1 ± 8.7 mm Hg) than to post operative IOP (19.1 ± 8.3 mm Hg), p value= 0.001. In their prospective clinical study, Panda et al., reported that the mean preoperative IOP was 42.95 ± 10.24 mmHg, and 13.04 ± 4.42 mmHg at the end of the first week. A gradual rise in IOP was noted at 1 month (16.94 ± 3 mmHg).[2] A retrospective observational cohort study conducted by Hollander et al., showed that the mean of preoperative IOP of 77 patients with Ahmed valve who underwent PK was 29.6 ±10.8 mmHg and reduced to16.5 ± 8.7 mmHg.[3] The aim of our study is to quantify the success rate of PKP in patients with GDDs and find the impact of IOP on the PKP final outcome. Evaluating the age factor on the final results and correlation between the sequence of both surgeries and PKP failure would be also considered. Indeed, among 24 PKP patients, 50.0% (n=12) were success, unfortunately, the others were failed. The failure rate was much higher than the rate of Tai et al., who recorded that the PKP failure rate after 1 month of PKP surgery was 28.0%.[11] Whereas, our result was near to the result conducted by Hollander et al., who observed the probability of a graft failure at 1, 2, and 3 years to be 42.4% (95% confidence interval (CI): 32.0% - 54.6%), 57.1% (95% CI: 45.6%-69.1%), and 59.1% (95% CI: 47.5%-71.2%), respectively.[3] The findings of this study have demonstrated that the age older than 40 years old was not risk for PKP failure in patients with GDDs; (Relative risk (RR)= 0.85, 95% CI= 0.38- 1.88, P= 0.682), in agreement of our result was a study conducted by Hollander et al, recorded a weak association between decreased risk of graft failure and older age at baseline (RR 0.91, 95% CI 0.81-1.02, P = 0.095, per 10 years).[3] Furthermore, Williams et al., on Australian Corneal Graft found no notable correlation between the age and graft

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failure.[12] The current study revealed that the gender is not defined as a risk factor for PKP failure (RR for male= 1, 95% CI= 0.45- 2.23, P=1). This result is in line with other study like, Barraque et al., Previous research conducted by the authors did not yield any statistically significant findings in relation to donor gender, as indicated by both univariate and multivariate analyses.[13] On the other hand, certain research indicates that male grafts may experience alloimmune responses in female recipients due to the expression of Y gene antigens exclusively in males and not in females.[14] Among the five our patients who associated with chronic disease like Diabetes mellitus (DM) and hypertension (HT), 3 (60.0%) was PKP failure and the other 2 (40.0%) was success for PKP (RR= 79, 95% CI= 0.34- 1.86, P=0.615), The presence of chronic diseases may potentially increase the risk of penetrating keratoplasty (PKP) graft failure. A study conducted by Vieira-Potter., reported that, in diabetic patients, the success rate of corneal transplantation is comparatively reduced in contrast to other conditions like keratoconus. A primary contributing factor to this disparity lies in the fact that individuals with diabetes tend to experience a delayed wound healing mechanism, leading to a faster failure of grafts. Furthermore, diabetic patients exhibit a heightened susceptibility to corneal infections, such as fungal keratitis, which can further exacerbate the rejection of grafts.[15, 16] Notably, surgery of Ahmed tube prior to PKP is not a potential risk factor for PKP failure (RR= 0.57, 95% CI= 0.20 - 1.53, P= 0.206). Numerous studies have examined how the sequence of PK and GDD affects graft survival. Rapuano et al., observed evidence suggesting a trend towards reduced graft survival when a GDD was implanted following a PK procedure.[17] Nevertheless, Coleman et al., Discovered that outcomes were similar whether an Ahmed Glucoma Valve (AGV) was implanted simultaneously with or after a PK.[10] Kwon et al., Reported that eyes with a GDD implanted before PK have a higher risk of graft failure.[18] In this study, there is evidence that operated eye (right or left) is not a risk factor (RR= 1.23, 95% CI= 0.47- 3.25, P= 653) also aphakia (RR= 4, 95% CI= 0.12- 136.95, P= 0.215) as well as pseudophakia (RR= 5.71, 95% CI= 0.52- 62.66, P= 0.154). A study carried out by Fasolo et al. found that the hazard ratio (HR) with a 95% confidence interval (CI) for pseudophakic individuals was 1.99 (1.61–2.46), P<0.001, while for aphakic individuals, it was 7.97 (2.85–8.64), P<0.001.[19] Also, post operative IOP greater than 21 mm Hg was a relative risk factor for PKP failure based on our data (RR= 0.824, 95% CI= 0.36- 1.86, P= 0.653). This result is in agreement with the study conducted by Hollander et al., they hypothesized that reduced minimum IOP (HR 0.92, 95% CI 0.86-0.98, P < 0.01, per mm Hg) was identified as a factor linked to a notably lower risk of graft failure.[3] Despite this, they mentioned that studying IOP as a risk factor for graft failure was challenging due to variations in measurements over time, differences in follow-up procedures.[3]

Interestingly, the current study out of the 24 patients, 7 was underwent VR surgery, all of them was failed to PKP failure, indicating that the history of vitreoretinal surgery is a risk factor for PKP failure (RR= 3.4, 95% CI= 1.63- 7.10, P= 0.002).

Conclusions

In conclusion of our study in which all 24 cases underwent both penetrating keratoplasty (PKP) and Ahmed valve (AV) surgery, AV tube was found to be a risk factor for failure of PKP surgery. Age, gender, Ahmed valve surgery prior to PKP surgery, operated eye, as well as lens status were not a significant risk factor in PKP failure. On the other hand, IOP, chronic disease and vitreoretinal surgery were observed as a risk factor in the failure of PKP surgery.

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However, in the future further studies with larger sample size is recommended.

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Conflict of interest
The authors declare no conflict of interest.

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