Influencing Factors for Recurrence of Pterygium

Kosol Kampitak MD*,
Pawarit Wanichsetakul MD*, Wannisa Suphachearaphan MD*

** Department of Ophthalmology, Faculty of Medicine, Thammasat University, Rangsit Campus, Pathumthani, Thailand*

Background: *Recurrence of pterygium is a major common complication after surgical removal and there are many predisposing factors associated with the recurrence.*
Objective: *To evaluate the factors associated with recurrence of pterygium after excision.*
Material and Method: *A prospective study of 158 pterygium surgeries (158 patients) was performed. Age, gender, primary or secondary pterygium, size of pterygium, surgeon (staff or resident), and surgical technique, were analyzed by logistic regression analysis to find whether they had any influence of recurrence. The recurrence was defined as fibrovascular membrane extending onto the cornea.*
Results: *Eighty patients (50.6%) were women, and the mean age was 58.7±13.0 years. The mean horizontal size of pterygium was 3.3±1.3 mm. Forty-eight eyes (30.4%) had recurrence after excision. Only two factors were significantly found to be risk factors for pterygium recurrence. Secondary pterygium excision were found more recurrences than primary (odds ratio 8.4, 95% confidence interval 1.5 to 48.9). Pterygium excision surgery with bare sclera technique was associated with high rate of recurrence (odds ratio 37.9, 95% confidence interval 1.1 to 1,266.8).*
Conclusion: *Secondary pterygium and excision with bare sclera technique were the most important factors influencing pterygium recurrence after surgery.*

Keywords: *Pterygium, Surgery, Recurrence factors, Secondary pterygium, Bare sclera technique*

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Pterygium is an abnormal fibrovascular tissue extending onto the corneal surface and is a common disease found in the countries near the equator[1], including Thailand[2]. The possible reason may be ultraviolet radiation which induces cellular changes at the limbal area of cornea[1,3,4].

Many studies have shown the high prevalence of pterygium with increasing age[5-7]. Males were found to be more at risk for pterygium[5,7,8], and pterygium occurrence was also significantly associated with residing in rural regions[7,9] and having a low educational status[6,8]. Increasing age, male gender and living in rural regions usually has a correlation with outdoor work, which is associated with sunlight or ultraviolet exposure[7].

The treatment of pterygium generally starts with artificial tears to relieve irritation, but if the disease still progresses, surgical excision is the definite treatment. The challenging problem of pterygium surgery is postoperative recurrence which means failure of treatment. The previous report from Thammasat Hospital showed that the recurrence rate was as high as 24% after pterygium surgery[10]. The present study aimed to evaluate the factors associated with the recurrence of pterygium after excision. The knowledge of risk factors is important for ophthalmologists to improve their choices of surgical technique, postoperative care, and achieve the better surgical outcome.

Correspondence to:
Kampitak K, Department of Ophthalmology, Faculty of Medicine, Thammasat University, Rangsit Campus, Pathumthani 12120, Thailand.
Phone: +66-2-9269957, Fax: +66-2-9869212
E-mail: kosolkampitak@yahoo.com

Material and Method

An observational, prospective study was carried out from 2014 to 2015 at the Department of Ophthalmology, Thammasat University Hospital, Pathumthani, Thailand.

Inclusion criteria were patients older than 18 years old who had pterygium excision. Patients with intraoperative complications were excluded.

Pterygium excision was conducted by suitable methods depending on the surgeons' opinion. After operation, patients were observed for recurrence or other complications for at least six months. Recurrence was defined as fibrovascular tissue extending onto the corneal surface from limbal conjunctiva. The size of

pterygium was horizontally measured from limbus to the apex in millimeters, and was classified as small (<2.5 mm), medium (2.5 to 4.5 mm), and large (>4.5 mm).

Age and gender of patients, pterygium size, type of pterygium (primary or secondary), surgeon (resident or staff), methods of surgery (bare sclera technique, beta-radiation, mitomycin C, amniotic membrane transplantation, and conjunctival autograft) were recorded and evaluated to find whether they had any influence on recurrence.

Surgical procedures

Initial pterygium excision: the pterygium was excised after subconjunctival injection of 2% lidocaine hydrochloride. Residual pterygium on cornea was scraped and Tenon's capsule was extensively removed. Several techniques were:

1) Bare sclera technique: the sclera was not covered by any tissue after pterygium tissue removed.

2) Beta-radiation: beta-radiation was applied at 20 Gy after pterygium excision.

3) Mitomycin C: 0.02% mitomycin C was applied for 2 minutes intra-operation.

4) Amniotic membrane transplantation: Amniotic membrane from the Eye Bank of Thai Red Cross Society, Bangkok, Thailand, was sutured with 10-0 nylon to cover the bare sclera.

5) Conjunctival autograft: superior bulbar conjunctiva was removed from the same pterygium surgery eye and sutured with 10-0 nylon to cover the bare sclera.

Some operations were using the combination of two techniques.

Statistical analysis

Chi-squared test was used to analyze each influencing factor for recurrence or non-recurrence. Crude odds ratio of the influencing factors for recurrence was evaluated by univariate logistic regression. Only the factors that had *p*-value <0.1 from chi-squared test, and age and gender were analyzed again by multivariate logistic regression, Enter Method, to control confounding factors for adjusted odds ratio. The *p*-value <0.05 was determined as statistically significant.

Ethics

The study was approved by the Human Research Ethics Committee of Thammasat University, Thailand. The authors verified that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this study, adhering to the tenets of the Declaration of Helsinki. Before informed written consent was obtained, all of the participants had been told about the treatment process of pterygium, possible intraoperative and postoperative complications.

Results

A total of one-hundred and fifty eight participants (158 eyes) was included, 78 were males (49.4%) and 80 were females (50.6%). Mean age was 58.7±13.0 years old. Mean horizontal size of pterygium was 3.3±1.3 mm. There were 149 eyes (94.3%) with primary pterygium and 9 eyes (5.7%) with secondary pterygium.

Pterygium excision with amniotic membrane graft, the most common technique in this study, was performed in 87 eyes (55.1%). Other surgical techniques were pterygium excision with beta-radiation (36 eyes, 22.8%), with amniotic membrane graft transplantation plus mitomycin C adjunction (19 eyes, 12.0%), with conjunctival autograft transplantation alone (7 eyes, 4.4%), with conjunctival autograft transplantation and beta-radiation (6 eyes, 3.8%), and with bare sclera (3 eyes, 1.9%). The operations were performed by staff on 49 eyes (31.0%) and by residents on 109 eyes (69.0%).

Follow-up duration ranged from 6 to 11 months. The mean of follow-up duration was 6.8±1.2 months. The recurrence of pterygium was found in 48 eyes (30.4%), between 1 to 8 months postoperatively. The mean recurrence time was 4.4±1.7 months. Other complications included scleral thinning, symblepharon, and granulation tissue formation in 3 eyes (1.9%), 2 eyes (1.3%), and 1 eye (0.6%), respectively.

Type of pterygium was the only factor that had an influence on recurrence (crude odds ratio 5.1, 95% confidence interval 1.2 to 21.3, Table 2). The factors, including type of pterygium and method of surgery (*p*-value <0.1 from Chi-squared test, Table 1), and age and gender, were analyzed for adjusted odds ratio by using Enter Method of multivariate logistic regression. After controlling confounding factors, there were two factors which were significantly found to be influencing factors for pterygium recurrence. Recurrences were 8.4 times more in secondary than primary pterygium (95% confidence interval 1.5 to 48.9, Table 2). Pterygium surgery with bare sclera technique was associated with high recurrence 37.9 times (95% confidence interval 1.1 to 1,266.8, Table 2) when compared with conjunctival autograft plus beta-

Table 1. Number of recurrences according to influencing factors

Variable	Number of recurrence n (%)	*p*-value (pearson Chi-squared)
Age (years)		
≤40 (n = 17)	7 (41.2)	0.306
>40 (n = 141)	41 (29.1)	
Gender		
Male (n = 78)	20 (25.6)	0.201
Female (n = 80)	28 (35.0)	
Size (mm)		
<2.5 (n = 53)	17 (32.1)	0.795
2.5 to 4.5 (n = 85)	24 (28.2)	
>4.5 (n = 20)	7 (35.0)	
Type of pterygium		
Primary (n = 149)	42 (28.2)	0.015
Secondary (n = 9)	6 (66.7)	
Method of surgery		
Bare (n = 3)	2 (66.7)	0.029
Beta (n = 36)	4 (11.1)	
AMT (n = 87)	32 (36.8)	
AMT + MMC (n = 19)	8 (42.1)	
CAG (n = 7)	1 (14.3)	
CAG + Beta (n = 6)	1 (16.7)	
Surgeon		
Staff (n = 49)	14 (28.6)	0.740
Resident (n = 109)	34 (31.2)	

AMT = amniotic membrane transplantation; Bare = bare sclera technique; Beta = Beta-radiation; CAG = conjunctival autograft; MMC = application of intraoperative mitomycin C

radiation technique.

Discussion

The recurrence of pterygium after excision is a challenging problem since it means not only new occurrence of the previous disease but also worse complications in some cases, such as a bigger or more inflamed pterygium. There are many factors associated with the recurrence of pterygium, and age is an important one. Younger people tend to have a higher recurrence of pterygium[11-13]. Fernandes et al found more recurrence of pterygium in patients under 40 years of age compared with those over 40 years (25.2% vs. 14.8%, $p = 0.003$)[11]. Mahar and Manzar also reported that a younger group of patients (<50 years) was significantly correlated with the recurrence of pterygium ($p = 0.04$)[12]. In contrast, our study did not show a significant difference in recurrence rates between young (≤40 years) and old patients (>40 years) with pterygium.

The present study found that gender was not a significant risk factor for the recurrence of pterygium, However, there are some studies that show a higher recurrence among men[11,14]. Femandes et al reported men were more susceptible than women to a recurrence of pterygium, in both primary (23.3% vs. 10.7%, $p<0.0001$) and secondary (26.7% vs. 0%, $p = 0.034$) pterygium groups[11]. In addition, Torres-Gimeno et al stated that males had 72 times more recurrence of pterygium than females (62% vs. 0%, odds ratio 72.6, 95% confidence interval 3.6 to 1,458.2, $p<0.001$)[14].

Our study did not detect the correlation between size of pterygium and recurrence rate. However, compared to previous reports, Marhar and Manzar found that higher level of corneal involvement by pterygium significantly correlated with the recurrence ($p = 0.01$)[15]. Moreover, Yamada et al's study also showed that pterygium involving pupillary area had higher rate of recurrence[16].

Our study found that pterygium tended to recur again in patients who had secondary pterygium, which had 8.4 times more recurrence than those with primary pterygium (95% confidence interval 1.5 to 48.9, Table 2). This result corresponds with Mahar and Manzar's study, which showed that secondary pterygium significantly correlated with the recurrence ($p = 0.05$)[12].

Surgical experience is another important factor to be considered for recurrence of pterygium. Our study did not show a difference in recurrence of pterygium when excision was performed by staff or residents. However, previous studies reported surgical experience was associated with the recurrence of pterygium. Ti et al found that rates of recurrence varied widely (5% to 82%) and were inversely related to surgical experience[17]. In addition, Masuda et al also found significant correlation between the skill of surgeons and the recurrence of pterygium ($p = 0.022$)[13].

Choices of surgical techniques clearly affect the recurrence of pterygium. The present study confirms that pterygium excision with bare scleral technique had a recurrence rate as high as 66.7% and had a risk of recurrence 37.9 times more than conjunctival autograft plus beta-radiation technique (95% confidence interval 1.1 to 1,266.8, Table 2). In accordance with previous studies, Kareem et al found that pterygium excision with bare scleral technique had a high recurrence rate as 32% to 34%[18], same as other

Table 2. Risk analysis for influencing factors of pterygium recurrence

Variable	Crude odds ratio	95% confidence interval		*p*-value	Adjusted odds ratio	95% confidence interval		*p*-value
		Lower	Upper			Lower	Upper	
Age (years)								
≤40	1.7	0.6	4.8	0.310	2.7	0.7	9.9	0.138
>40	1.0							
Gender								
Male	0.6	0.3	1.3	0.202	0.5	0.2	1.1	0.105
Female	1.0							
Size (mm)								
<2.5	1.0							
2.5 to 4.5	0.8	0.4	1.8	0.631				
>4.5	1.1	0.4	3.4	0.813				
Type of pterygium								
Primary	1.0							
Secondary	5.1	1.2	21.3	0.026	8.4	1.5	48.9	0.018
Method of Surgery								
Bare	10.0	0.4	250.4	0.161	37.9	1.1	1,266.8	0.042
Beta	0.6	0.1	6.8	0.699	1.6	0.1	24.2	0.729
AMT	2.9	0.3	26.0	0.339	6.6	0.5	79.9	0.139
AMT + MMC	3.6	0.4	37.5	0.278	5.6	0.4	78.7	0.204
CAG	0.8	0.0	17.0	0.906	0.9	0.0	30.9	0.945
CAG + beta	1.0							
Surgeon								
Staff	1.0							
Resident	1.1	0.5	2.377	0.740				

AMT = amniotic membrane transplantation; Bare = bare sclera technique; Beta = beta-radiation; CAG = conjunctival autograft; MMC = application of intraoperative mitomycin C

studies that reported high recurrence rate of pterygium in bare scleral technique[11,19].

Conclusion

Pterygium excision with bare sclera technique and secondary pterygium condition significantly appeared to be influencing factors for recurrence after surgery.

What is already known on this topic?

Influencing factors for recurrence of pterygium may be young age, male gender, large size of pterygium, secondary pterygium, method of surgery, and experience of surgeon.

What this study adds?

This study confirms that secondary pterygium and surgery with bare sclera technique are influencing factors for pterygium recurrence after surgery.

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Potential conflicts of interest

None.

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ปัจจัยที่มีอิทธิพลต่อการกลับเป็นใหม่ของต้อเนื้อ

โกศล คำพิทักษ์, ปวริศร์ วาณิชยเศรษฐกุล, วรรณิศา ศุภเจียรพันธ์

ภูมิหลัง: *การกลับเป็นใหม่ของต้อเนื้อเป็นภาวะแทรกซ้อนที่พบได้บ่อยภายหลังลอก มีปัจจัยหลายชนิดที่มีผลต่อการกลับเป็นใหม่*

วัตถุประสงค์: *เพื่อหาปัจจัยที่เกี่ยวข้องกับการกลับเป็นใหม่ของต้อเนื้อภายหลังผ่าตัด*

วัสดุและวิธีการ: *เป็นการศึกษาไปข้างหน้าเฝ้าดูข้อมูลใน 158 ตา (ผู้ป่วย 158 ราย) ที่ได้รับการผ่าตัดลอกต้อเนื้อ ตัวแปรด้านอายุ เพศ ต้อเนื้อที่เป็นครั้งแรกหรือต้อเนื้อที่เคยได้รับการผ่าตัดมาแล้วและกลับเป็นใหม่ ขนาดต้อเนื้อ แพทย์ผู้ผ่าตัด (อาจารย์แพทย์หรือแพทย์ประจำบ้าน) และวิธีการผ่าตัด ถูกนำมาวิเคราะห์ด้วยวิธีการถดถอยโลจิสติก เพื่อหาว่ามีอิทธิพลต่อการกลับเป็นใหม่ของต้อเนื้อภายหลังผ่าตัดหรือไม่ การกลับเป็นใหม่ของต้อเนื้อหมายถึงการที่มีเนื้อเยื่อพังผืดงอกเข้าไปบนกระจกตา*

ผลการศึกษา: *ผู้ป่วย 80 ราย (ร้อยละ 50.6) เป็นหญิงอายุเฉลี่ยเท่ากับ 58.7±13.0 ปี ขนาดเฉลี่ยของต้อเนื้อในแนวนอนเท่ากับ 3.3±1.3 มิลลิเมตร ภายหลังผ่าตัด เกิดการกลับเป็นใหม่ของต้อเนื้อ 48 ตา (ร้อยละ 30.4) มีเพียงสองปัจจัยเท่านั้นที่พบว่ามีความเสี่ยงอย่างมีนัยสำคัญต่อการกลับเป็นใหม่ของต้อเนื้อ ต้อเนื้อที่เคยลอกมาแล้วและกลับเป็นใหม่มีโอกาสกลับเป็นใหม่อีกครั้ง ภายหลังลอกมากกว่าต้อเนื้อที่เป็นครั้งแรก (odds ratio 8.4, 95% confidence interval 1.5 ถึง 48.9) การผ่าตัดด้วยวิธี bare sclera มีความเสี่ยงที่จะกลับเป็นใหม่สูง (odds ratio 37.9, 95% confidence interval 1.1 ถึง 1,266.8)*

สรุป: *ต้อเนื้อที่เคยลอกมาแล้วและกลับเป็นใหม่และการผ่าตัดด้วยวิธี bare sclera เป็นปัจจัยสำคัญที่มีอิทธิพลต่อการกลับเป็นใหม่ของต้อเนื้อภายหลังผ่าตัด*