Evaluation of the Efficacy of different pterygium surgeries in Polish Caucasian population. A retrospective case series.

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Abstract: The aim of our study was to compare the efficacy of the two most commonly used surgical methods for pterygium in the Polish population, conjunctival autograft versus amniotic membrane transplantation, and to evaluate the postoperative recurrence rate. We retrospectively analysed the medical records of 65 patients who underwent surgery for primary or recurrent pterygium at an ophthalmology clinic in Białystok, Poland between 2016 and 2020. Surgical success (no regrowth) occurred in almost half of the amniotic membrane patients (44%) and in most of the conjunctival autograft patients (79%); this was a significant relationship. The odds of successful surgery were 79% lower for subjects with amniotic membranes than for those with conjunctival autografts (OR with 95% CI = 0.21 (0.05; 0.94]; p = 0.045). Our study confirms that in Polish Caucasian population the success rate of the procedure using conjunctival autograft versus the use of amniotic membrane, is in favoured for the procedure with conjunctival graft.

Keywords: Pterygium, Pterygium surgery, Amniotic membrane, Conjunctival autograft, Polish Caucasian population

1. Introduction

Pterygium is a common disorder of the anterior eye surface. According to population studies, the prevalence of pterygium ranges from 1% to 30%.[1-3] It is a fibrovascular degenerative lesion of the ocular conjunctiva that presents clinically as triangular-shaped growth consisting of conjunctival epithelium and hypertrophied subconjunctival connective tissue with its apex facing the cornea. The most common location is the ocular conjunctiva, which is located in the projection of the palpebral fissure from the nasal side. As a result of changes in the local homeostasis of the ocular surface, major mechanisms of pterygium formation are triggered, including the formation of proliferative limbal stromal cell (LSC) clusters, epithelial metaplasia, formation of active fibrovascular tissue, inflammation, and disruption of
Bowman's layer along the infiltrating pterygium apex. In severe cases, pterygium can grow into the central part of the cornea, which can cause irregular corneal astigmatism, possibly resulting in decreased visual acuity, ranging from a significant decrease in visual acuity.

The most important risk factors for the development of pterygium and recurrences may include ethnicity, geographic latitude of residence and associated sun exposure, male sex, older age, smoking, rural origin, and darker skin complexion. Other factors include chronic irritation from dust and air pollutants, and anterior ocular surface surgery. Viral etiology, herpes simplex virus, human papilloma virus, cytomegalovirus, inflammation, and hereditary predispositions are also included among the risk factors for the development of pterygium. Although the pathogenesis of pterygium is not well understood, it is known to be related to ultraviolet (UV) radiation. By inducing reactive oxygen species, UVA causes indirect DNA damage and activates transcription factors that regulate the expression of many genes involved in extracellular matrix changes.

Pterygium can only be treated surgically. The main indications for surgical removal of a pterygium are deterioration of vision resulting from enlargement, increasing astigmatism, or recurrent inflammation. It is important to note that there is no "perfect" surgical method that guarantees no pterygium recurrence after removal. The most commonly used surgical techniques include conjunctival autografting, transposition of a pedicled conjunctival flap, and amniotic membrane transplantations. Adjuvant therapy in the form of antimetabolites, antiangiogenic agents, and radiation is used to reduce the risk of recurrence.

There are studies in the literature evaluating the effectiveness of conjunctival autograft versus amniotic membrane suturing that have been evaluated in Turkish, Chinese, Brazilian, or Indian populations, but there are no such reports relating to Caucasian populations to date. To date, there have been no such reports in relation to the Polish population. The aim of our study was to compare the efficacy of the two most commonly used surgical methods for pterygium in the Polish population, conjunctival autograft versus amniotic membrane suturing, and to evaluate the postoperative recurrence rate. To the best of our knowledge, this is the first study of its kind in Central and Eastern European populations.

2. Materials and Methods
We retrospectively analyzed the medical records of 65 patients who underwent surgery for primary or recurrent pterygium at an ophthalmology clinic in Bialystok, Poland between 2016 and 2020. The study was approved by the local bioethics committee of the Medical University of Bialystok and was conducted in accordance with the principles of the Declaration of Helsinki. The indication for the procedure was the presence of a nasally located pterygium of at least grade 1. [24]

Exclusion criteria included symblepharon, conjunctival scarring, and uncompensated glaucoma, which might require a filtering procedure in the future. Patients with a 6-month follow-up period were eligible for analysis. Prior to the procedure and at each follow-up visit after the procedure, each patient underwent a complete ophthalmological examination, including anterior segment photography of the eye in a lamp (Led Digital Vision HR, SL9900 ZOOM-D, C. S. O. Italy), and measurement of best-corrected visual acuity (BCVA) and intraocular pressure (IOP) using the Goldmann applanation tonometer (GAT; Haag-Streit, Bern, Switzerland). To ensure a similar quality in all photographs, the diffuse lamp light was set to a width of 2 mm, and the height was adjusted to the edges of the dilated pupil at a 45 ° angle to the lens surface at a magnification of 16 ×. The photograph is focused on the cornea. The degree of pterygium progression was assessed using a described previously (25).

Postoperative visits occurred 1 week, 2 weeks, 1 month, 3 months, 6 months, and 12 months after surgery. At the postoperative visits, corneal healing and the presence of possible recurrence were evaluated in addition to the tests mentioned earlier. Pterygium recurrence was defined as growth greater than 1 mm beyond the corneal limbus 6 months after surgery. Informed consent was obtained from all patients prior to the procedure. All procedures were performed by two experienced surgeons (A.B. and L.L.) under local anesthesia according to a previously described technique [12, 23]. In brief:

2.1 Excision with conjunctival autograft
After removal of the pterygoid head and body, the scleral bed at the site of the removed pterygoid was covered with a fragment of the patient’s conjunctiva taken from the superior temporal quadrant of the same or the other eye, with special care to avoid interrupting the conjunctiva in the middle. Each time a conjunctival graft was collected, Tenon’s tissue was carefully cleaned, as it is a source of fibroblast proliferation and a risk factor for pterygium regrowth. The graft was 1 mm larger on each side than on the dissected scleral bed. 8/0 absorbable sutures (Novosyn® 90/10; Braun) were used for conjunctival graft fixation.

2.2 Suturing the amniotic membrane
After removal of the head of the pterygium and cleaning of the sclera, a flap of amniotic membrane of size corresponding to the locus of the excised pterygoid increased by 1 mm was sutured onto the resulting bed. Amniotic membrane was laid down with its epithelial side facing up. A flap of the drained amniotic membrane was cut to fit the scleral pocket shape and size. Excess transplanted tissue was cut off with scissors and then fixed with absorbable sutures (Novosyn® 90/10, Braun). A dressing contact lens was applied to the cornea to improve graft adhesion and to reduce postoperative pain. All patients in both groups received moxifloxacin three times daily (Levomer, Adamed Pharma S.A) for the first week and dexamethasone three times daily (Dexafree, Baush, and Lomb) from the moment of corneal epithelialization at the site of the removed pterygium (on average 2 days after the surgery), with gradual tapering for 3 months after the surgery.

3. Statistical analysis
   The relationships between group and qualitative variables were analyzed using Fisher’s exact test. The number and percentage of observations and the odds ratio with a 95% confidence interval for the specific event occurrence were reported. The values of quantitative variables were compared between the groups using the Mann-Whitney U test. Differences between medians with 95% confidence intervals have also been reported. These calculations were performed using R statistical software version 4.1.2, with an assumed significance level of \( \alpha = 0.05 \).
   A post hoc analysis of the observed power was performed for the success of the operation, which was 0.54 for this study, with \( \alpha = 0.05 \). Post hoc analysis was performed using the G Power software, version 3.1.9.4.

4. Results
   Table 1. Characteristics and comparison of groups (amniotic membrane vs. conjunctival autograft)

   | Variable                  | Amniotic membrane n = 9 | Conjunctival autograft | MD/OR 95% CI | p |
   |----------------------------|--------------------------|------------------------|--------------|---|
Women constituted a minority in both study groups (22% and 37%, respectively; p = 0.479). The respondents in the two groups did not differ significantly by age (p = 0.927) or follow-up time (p = 0.127). Pterygium in the right eye occurred in 22% of the subjects with amniotic membranes and in 33% of the subjects with conjunctival autografts (p = 0.707). The chance of primary pterygium occurrence was 90% lower in subjects with amniotic membrane than in those with conjunctival autograft (33% vs. 83%; OR with 95% CI = 0.10 (2.27; 53.27); p = 0.005), and the chance of recurrent pterygium was 11 times higher in subjects with amniotic membrane than in those with conjunctival autograft (67% vs. 15%; OR with 95% CI = 11.00 (2.27; 53.27); p = 0.003). Surgical success (no regrowth) occurred in almost half of the amniotic membrane patients (44%) and in most of the conjunctival autograft patients (79%); this was a significant relationship. The odds of successful surgery were 79% lower for subjects with amniotic membranes than for those with conjunctival autografts (OR with 95% CI = 0.21 (0.05; 0.94); p = 0.045) (Table 1).

There were no differences in the number of pterygium progression grades between the two groups. Grade 1/Grade 2/Grade 3 (p>0.05)

5. Discussion

In the literature, the incidence of pterygium varies considerably among countries. [26] The prevalence can reach 22% in these equatorial areas and less than 2% at latitudes above 40° (0.9% in the German population) [7]. It is important to note that there is no "gold standard" in pterygium surgery. Postoperative recurrence is a significant problem in ophthalmic practice. In our study, we presented the effectiveness of pterygium treatment using two
surgical methods: conjunctival autograft versus amniotic membrane suturing in the Polish population. Our results corroborate those of other studies, in which greater efficacy in preventing pterygium recurrence was observed with conjunctival autografts. [22] In our study, the recurrence rate for both surgical methods (21.2% and 55.6% for autograft and amniotic membrane suturing, respectively) was higher than that reported by other authors, which may be due to the lack of adjuvant use.

Removal of the pterygoid with conjunctival autograft involves covering the sclera in the area of the removed pterygoid with a fragment of the patient’s conjunctiva, taken from another quadrant of the same or the other eye. This procedure is technically longer and more difficult than the simple excision method; however, it is also associated with a much lower postoperative recurrence rate. When harvesting a conjunctival graft, it is important to thoroughly remove Tenon’s tissue, as it is a source of fibroblast proliferation and a risk factor for pterygium regrowth. Reported rates of pterygium recurrence after conjunctival autografting range from 1% to approximately 40% (19). For primary pterygium, many studies have reported recurrence rates of less than 15%, whereas for recurrent pterygium, recurrence rates range from 30-33 to%. [14] Absorbable sutures, tissue adhesives, and autologous patient blood can be used for conjunctival graft fixations. In the first case, the transplanted conjunctival flap is fixated with absorbable sutures, usually 8/0 vicryl, which is associated with postoperative discomfort and irritation of the eyeball, while the most common complications of using tissue adhesive or autologous blood include graft dislocation. Recurrence rates may also vary depending on the fixation method used; however, there are conflicting reports in this regard. In a study by Sati et al. [12] there was no significant difference in pterygium recurrence among the three forms of conjunctival graft fixation. The study by Hall et al.[13], comparing the method using sutures with the method using tissue adhesive, showed a slightly higher recurrence rate when sutures were used (8.7% versus 0%, respectively). When comparing the tissue adhesive method with the method involving autologous blood [27] in a prospective randomized study, Nadarajah et al. obtained a slightly lower rate of pterygium recurrence, at 3.4% in the 12-month follow-up for the tissue adhesive surgery group and 10.6% for the autologous blood group. In our study, the autograft was fixed using absorbable sutures in all cases.

As the innermost layer of the placenta, the amniotic membrane is used for the treatment of pterygium owing to its unique structure. It consists of a single epithelial layer, together with a basal membrane and a stromal layer of extracellular matrix (ECM), consisting of a compact cell-free layer and a loose layer of fibroblasts. [28] Owing to its biological properties, the amniotic membrane can be used as a graft with anti-inflammatory and anti-fibrotic
properties, capable of delivering numerous growth factors and promoting epithelial cell proliferation and differentiation without the risk of immune reactions. [29] The use of amniotic membrane appears to be safe and effective and is associated with lower recurrence rates compared with the simple excision technique. [30] Reported recurrence rates with amniotic membrane transplantation range from 3.8% to 40.9%. In a prospective study, Prabhasawat et al. reported a recurrence rate of 10.9% after amniotic membrane transplantation. [31] Studies comparing the use of autograft with amniotic membrane transplantation (AMT) after pterygium excision have shown that AMT is associated with a higher risk of recurrence 6 months after surgery, compared with conjunctival autograft, and the inferiority of AMT occurs in both primary and recurrent pterygium. [32-38] According to the authors, pterygium recurrence at 3 and 6 months after the surgery with AMT ranges from 4.76% to 26.9%, and from 2.6% to 42.3%, respectively. Amano et al. demonstrated a recurrence rate of 8.7% when mitomycin C was used intraoperatively (0.04 %). [39] Conjunctival autograft may be a source of conjunctival epithelium, while the amniotic membrane appears to play a role in inhibiting the progenitor cells involved in pterygium recurrence. [40] During the procedure, the amniotic membrane may be fixed with absorbable sutures or a tissue adhesive. This is the method of choice in cases of large pterygoids, patients with post-inflammatory conjunctival lesions, or in patients who may require future anti-glaucoma surgery.

When comparing the success rate of the procedure using conjunctival autograft versus the use of amniotic membrane, the data favored the procedure with conjunctival graft at 7.4% versus 19.2%. [41] Similar to that in our study (21.2% vs. 55.6%)

Our study has some limitations. First, it was a retrospective study, which has lower evidence power at its design stage. Second, the groups were not very large, and adjuvant treatment was not used. We also have no information on the timing of exposure to factors that may promote pterygium recurrence in patients after surgery. However, it was conducted on a homogeneous group of patients and is the first study of subject in an Eastern European population.

Conclusion: Our study confirms that in Polish Caucasian population the success rate of the procedure using conjunctival autograft versus the use of amniotic membrane, is in favoured for the procedure with conjunctival graft. Further studies are needed to investigate the newer surgical techniques. Newer surgical techniques, the efficacy and long-term effects of which should be investigated (there are currently no reliable results), including limbal-conjunctival autografting and the combination of the limbal autografting method with simultaneous covering of the defect after excision of the pterygoid with amniotic membrane.
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References:

1. Cajuc-com-Uy H, Tong L, Wong TY, Tay WT, Saw SM. The prevalence of and risk factors for pterygium in an urban Malay population: the Singapore Malay Eye Study (SiMES). Br J Ophthalmol. 2010;94(8):977-81.
2. West S, Muñoz B. Prevalence of pterygium in Latinos: Proyecto VER. Br J Ophthalmol. 2009;93(10):1287-90.
3. Bachelor MA, Bowden GT. UVA-mediated activation of signaling pathways involved in skin tumor promotion and progression. Semin Cancer Biol. 2004;14(2):131-8.
4. Shahraki T, Arabi A, Feizi S. Pterygium: an update on pathophysiology, clinical features, and management. Ther Adv Ophthalmol. 2021;13:25158414211020152.
5. Sekundo W, Droutsas K, Cursiefen C. [Operative techniques for surgical treatment of primary and recurrent pterygia]. Ophthalmologe. 2010;107(6):525-8.
6. Shusko A, Schechter BA, Hovanesian JA. Pterygium Surgery Utilizing Limbal Conjunctival Autograft and Subconjunctival Amniotic Membrane Graft in High-Risk Populations. Clin Ophthalmol. 2020;14:2087-90.
7. Hampel U, Wasielica-Poslednik J, Ries L, Faysal R, Schulz A, Nickels S, et al. Prevalence of pterygium and identification of associated factors in a German population - results from the Gutenberg Health Study. Acta Ophthalmol. 2021;99(1):e130-e1.
8. Di Girolamo N, Chui J, Coroneo MT, Wakefield D. Pathogenesis of pterygia: role of cytokines, growth factors, and matrix metalloproteinases. Prog Retin Eye Res. 2004;23(2):195-228.
9. Islam SI, Wagoner MD. Pterygium in young members of one family. Cornea. 2001;20(7):708-10.
10. Hilgers JH. Pterygium: its incidence, heredity and etiology. Am J Ophthalmol. 1960;50:635-44.
11. Chao SC, Hu DN, Yang PY, Lin CY, Nien CW, Yang SF, et al. Ultraviolet-A irradiation upregulated urokinase-type plasminogen activator in pterygium fibroblasts through ERK and JNK pathways. Invest Ophthalmol Vis Sci. 2013;54(2):999-1007.
12. Sati A, Shankar S, Jha A, Kalra D, Mishra S, Gurunad VS. Comparison of efficacy of three surgical methods of conjunctival autograft fixation in the treatment of pterygium. Int Ophthalmol. 2014;34(6):1233-9.
13. Hall RC, Logan AJ, Wells AP. Comparison of fibrin glue with sutures for pterygium excision surgery with conjunctival autografts. Clin Exp Ophthalmol. 2009;37(6):584-9.
14. Koranyi G, Seregard S, Kopp ED. The cut-and-paste method for primary pterygium surgery: long-term follow-up. Acta Ophthalmol Scand. 2005;83(3):298-301.
15. Fernandes M, Sangwan VS, Bansal AK, Gangopadhyay N, Sridhar MS, Garg P, et al. Outcome of pterygium surgery: analysis over 14 years. Eye (Lond). 2005;19(11):1182-90.
16. Ma DH, See LC, Liau SB, Tsai RJ. Amniotic membrane graft for primary pterygium: comparison with conjunctival autograft and topical mitomycin C treatment. Br J Ophthalmol. 2000;84(9):973-8.
17. Al Fayed MF. Limbal versus conjunctival autograft transplantation for advanced and recurrent pterygium. Ophthalmology. 2002;109(9):1752-5.
18. Bilge AD. Comparison of conjunctival autograft and conjunctival transposition flap techniques in primary pterygium surgery. Saudi J Ophthalmol. 2018;32(2):110-3.
19. Kaufman SC, Jacobs DS, Lee WB, Deng SX, Rosenblatt MI, Shtein RM. Options and adjuvants in surgery for pterygium: a report by the American Academy of Ophthalmology. Ophthalmology. 2013;120(1):201-8.
20. Nganga Ngabou CGF, Makita C, Ndalla SS, Nkokolo F, Messe Ambia Koulimaya R, Diatewa B. [Pterygium surgery by conjunctiva autograft with autologous blood fixation]. J Fr Ophtalmol. 2018;41(5):425-32.
21. Yu J, Feng J, Jin T, Tian L, Zhu L, Cao K, et al. The Effect of a Novel Strategy in Treating Primary Pterygium: A Prospective Randomized Clinical Study. Am J Ophthalmol. 2021;225:108-16.
22. Liang W, Li R, Deng X. Comparison of the efficacy of pterygium resection combined with conjunctival autograft versus pterygium resection combined with amniotic membrane transplantation. Eye Sci. 2012;27(2):102-5.
23. Khan FA, Niazi SPK. Effect of Pterygium Morphology on Recurrence with Preoperative Subconjunctival Injection of Mitomycin-C in Primary Pterygium Surgery. J Coll Physicians Surg Pak. 2019;29(7):639-43.
24. Sodhi PK, Verma L, Ratan SK. The treatment of pterygium. Surv Ophthalmol. 2004;49(5):541-2; author reply 2-3.
25. Tan DT, Chee SP, Dear KB, Lim AS. Effect of pterygium morphology on pterygium recurrence in a controlled trial comparing conjunctival autografting with bare sclera excision. Arch Ophthalmol. 1997;115(10):1235-40.
26. Rezvan F, Khabazkhoob M, Hooshmand E, Yekta A, Saatchi M, Hashemi H. Prevalence and risk factors of pterygium: a systematic review and meta-analysis. Surv Ophthalmol. 2018;63(5):719-35.
27. Nadarajah G, Ratnalingam VH, Mohd Isa H. Autologous Blood Versus Fibrin Glue in Pterygium Excision With Conjunctival Autograft Surgery. Cornea. 2017;36(4):452-6.
28. McLaren J, Malak TM, Bell SC. Structural characteristics of term human fetal membranes prior to labour: identification of an area of altered morphology overlying the cervix. Hum Reprod. 1999;14(1):237-41.
29. Nuzzi R, Tridico F. How to minimize pterygium recurrence rates: clinical perspectives. Clin Ophthalmol. 2018;12:2347-62.
30. Arain MA, Yaqub MA, Ameen SS, Iqbal Z, Naqvi AH, Niazi MK. Amniotic membrane transplantation in primary pterygium compared with bare sclera technique. J Coll Physicians Surg Pak. 2012;22(7):440-3.
31. Elwan SA. Comparison between sutureless and glue free versus sutured limbal conjunctival autograft in primary pterygium surgery. Saudi J Ophthalmol. 2014;28(4):292-8.
32. Besharati MR, Miratashi SAM, Ahmadi AB. Pterygium surgery: amniotic membrane or conjunctival autograft transplantation. International Journal of Ophthalmology. 2008;1(4):362-6.
33. Keklikci U, Celik Y, Cakmak SS, Unlu MK, Bilek B. Conjunctival–Limbal Autograft, Amniotic Membrane Transplantation, and Intraoperative Mitomycin C for Primary Pterygium. Annals of Ophthalmology. 2007;39(4):296-301.
34. Kheirkhah A, Nazari R, Nikdel M, Ghassemi H, Hashemi H, Behrouz MJ. Postoperative conjunctival inflammation after pterygium surgery with amniotic membrane transplantation versus conjunctival autograft. American Journal of Ophthalmology. 2011;152(5):733-8.
35. Fernandes L, Paes J, de Morais B, da Costa C, de Oliveira E, Felix F, et al. Surgical Treatment of Primary Pterygium: Comparison Between Techniques of Autologous Conjunctival Transplant and Transplantation of Amniotic Membrane. Investigative Ophthalmology & Visual Science. 2007;48(13):5296-.
36. Parra ZP, Pérez AC, Leyva EE, Hernández SL, Villalón SM. Conjunctival autograft versus amniotic membrane graft in primary pterygium surgery [Autoinjerto conjuntival versus injerto de membrana amniótica en la cirugía del pterigión primario]. Revista Cubana de Oftalmología. 2008;21(1):0.
37. Katırcıoğlu YA, Altparmak UE, Duman S. Comparison of three methods for the treatment of pterygium: amniotic membrane graft, conjunctival autograft and conjunctival autograft plus mitomycin C. Orbit. 2007;26(1):5-13.
38. Kim H-J, Lee S-Y. The comparative study of clinical results in surgically treated pterygium patients with amniotic membrane transplantation versus limbal autograft. Investigative Ophthalmology & Visual Science. 2008;49(13):6031-.
39. Amano S, Motoyama Y, Oshika T, Eguchi S, Eguchi K. Comparative study of intraoperative mitomycin C and beta irradiation in pterygium surgery. Br J Ophthalmol. 2000;84(6):618-21.
40. Ye J, Kook KH, Yao K. Temporary amniotic membrane patch for the treatment of primary pterygium: mechanisms of reducing the recurrence rate. Graefes Arch Clin Exp Ophthalmol. 2006;244(5):583-8.
41. Schreiber SL, Crabtree GR. The mechanism of action of cyclosporin A and FK506. Immunol Today. 1992;13(4):136-42.
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