LITERATURE REVIEW

SCLERAL WOUND HEALING IN PARS PLANA VITRECTOMY : A NARRATIVE REVIEW

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ABSTRACT

Background: *Scleral wound healing involves cell death, migration, proliferation, differentiation, and ECM remodeling. Damaged connective tissue and blood arteries produce extravasation of blood cells, platelets, and plasma proteins when incisions are made in the conjunctiva and sclera (e.g. fibronectin, fibrinogen and plasminogen).*

Aims: *This literature review aims to elaborate scleral wounds constructions in general, wound healing process, and closure of the scleral wound after pars plana vitrectomy.*

Methods: *This literature review conducted 35 research publications from 2013-2022 who cited from some reputable sources using "wound healing", "scleral", "sutureless", and "vitrectomy" as keywords.*

Results: *The self-healing process that takes place after scleral wounds are closed. On the second day, fibrous tissue grows to fill in the wound gap, marking the beginning of the wound healing process. On the third day, the connective tissue was then expanded to span the entire thickness of the wound. On day five, the connective tissue begins to thicken and begins to align with the lamellae of the normal connective tissue that is around it. This process continues until day seven. On the seventh day, it looked that the wound had healed and normal tissue creation had taken place.*

Conclusion: *Transconjunctival sutureless vitrectomy accelerated scleral wound healing. Small trocars and Zorro incisions speed scleral healing. Otherwise, silicone oil didn't affect scleral wound healing.*

Keyword: *pars plana vitrectomy; sclerotomy; wound healing.*

INTRODUCTION

The sclera is an avascular structure that covers about 90% of the outer part of the eye.[1] The sclera is the outermost layer of the wall and occupies five-sixths of the eyeball. The anterior part is seen under the conjunctiva as the white part of the eye, but on closer examination can be seen the blood vessels that supply the episclera, especially in the area of the anterior segment of the eyeball between the conjunctiva and the sclera. The function of the sclera is to give shape to the eyeball and is a strong supporting tissue.[2,3,4]

Vitrectomy methods and techniques are always developing towards smaller surgical instruments, leading to better function and less trauma to the eye. Pars plana vitrectomy (PPV) was first introduced in 1971 by Machemer et al. using a 17G trocar through a 2.3 mm-wide scleral incision and considered as the best option for self-sealing incisions in vitreoretinal surgery.[5] As the technique develops, the transconjunctival sutureless vitrectomy (TSV) offers stabilization of intraocular pressure during sealed-system surgical procedure and reduction of the surgical time required to perform suturing.[6] TSV was introduced in 2020, using a micro cannula, trocar, and 25G or 23G instrument.[7] The use of the smaller instruments minimizes vitreoretinal invasiveness compared to conventional pars plana vitrectomy (PPV), reducing eye trauma and postoperative inflammation, and speeds up patient recovery.[8] Sutureless pars plana sclerotomy enables stabilization of intraocular pressure (IOP) during surgery with a completely sealed system and reduction of surgical time, thereby eliminating the need for sutured wound closure. Wound and suture-related complications such as leakage, irritation, and scleral pigment changes could also be avoided. However, wound complications in sutureless procedures still raise some concerns. Therefore, several modifications have been developed, such as changing the conventional incision direction.[9] This literature review aims to elaborate scleral wounds constructions in general, wound healing process, and closure of the scleral wound after pars plana vitrectomy.

METHODS

This narrative review of scleral tissue alterations following pars plana vitrectomy was prepared via the process of literature review by compiling a variety of credible sources. The keywords "wound healing", "scleral", "sutureless", and "vitrectomy" were used to get 35 research papers that served as standards for the compilation of this literature review. The journals cited in this literature review originate from reliable scientific sources as following scientific sources Pubmed, Medline, Crossref and Google Scholar. The citations were published between 2013 and 2022. The acquired information was examined utilizing a critical approach to case-related issues.

RESULTS

Scleral Wound Healing on Sclerotomy: General Mechanism

The activation of the innate immune system initiates wound healing, a complex and dynamic series of related events. The coagulative and inflammatory phases of the healing process, followed by the proliferative phase, and finally, the remodelling phase of the wounded tissue, can be separated into several phases.[10,11]

Damaged connective tissue and blood arteries produce extravasation of blood cells, platelets, and plasma proteins when incisions are made in the conjunctiva and sclera (e.g. fibronectin, fibrinogen and plasminogen). Platelet aggregation occurs when a blood artery ruptures, which activates the intrinsic coagulation cascade, culminating in blood clot formation and hemostasis. The production of numerous growth factors (e.g., vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and fibroblast growth factor (FGF)) and cytokines occur as a result of platelet activation and the blood-clotting cascade (e.g., interleukins). Inflammatory cells are chemotactic.[12]

Hemostasis, inflammatory, proliferative, and remodelling phases are the four phases of postoperative wound healing in the eye (Table 1). Blood cells, platelets, and plasma proteins such as fibrin, fibronectin, and plasminogen will leak due to the initial vascularization. Histamine, serotonin, prostaglandins, and leukotrienes are released in the early aftermath of surgical trauma. These substances can increase vascular permeability, intensify the inflammatory response, and influence fibroblast activity later on. Granulation tissue is formed when activated fibroblasts interact with a growing epithelium. Through wound contraction, manipulation of fibrotic tissue migration, modulation of angiogenesis, and apoptosis of cells that are no longer functional, this tissue will promote tissue remodeling.[12,13]

Tabel 1. Timecourse of the scleral wound healing (modified from Orsted HL, 2009, Seibold *et al*, 2012) [12,13]

Stage of Wound Healing	**Onset**	**Mechanism Involved**
Hemostatic Phase	5 – 10 minutes	Due to the exposure of subendothelial collagen and von Willebrand factor to circulating platelets and clotting factors, the coagulation process is activated.
Inflammatory Phase	6 – 8 hours	The presence of neutrophils and monocytes distinguishes this condition. Neutrophils can be identified at the trauma site in minutes and reach their peak within 48 hours. In around 5 days after the trauma, T cells can be identified at the trauma site.
Proloferation Phase	4 – 7 days, until 21 days	Proliferation of epithelial cells Within hours of the trauma, epithelial growth begins along the wound's angle. As early as 24 hours after a trauma, fibroblasts can be identified at the trauma site.
Remodelling Phase	21 days – 2 years	The transformation of thick, hypocellular tissue into granulation tissue abundant in cells. It's possible that this phase

	will overlap with others that came before it.

Generally, there are aggravating factors and alleviating factors in healing scleral wounds. Tears and optimal lubrication, high glucocorticoid concentrations on the eye surface, high oxygen permeability on the eye surface, the presence of growth factors such as EGF, IGF, and HGF, glycoproteins in the form of optimal fibronectin, and the presence of glycosaminoglycans in the extracellular matrix are all aggravating factors. Heparin-sulfate and other extracellular substance, the blink reflex and excessive eyelid movement, the poisonous ingredient benzalkonium chloride in eye drops, the excessive angiogenesis process, the inflammatory reaction, excessive fibrosis, and overexpression of gap-junction proteins, can all hinder scleral wound healing.[14]

Scleral Wound Healing on Suture Pars Planar Vitrectomy

Healing of sclerotomy wounds after pars plana vitrectomy with sutures is generally achieved 6-8 weeks after the procedure. Keshavamurty et al. (2006) reported a case of a patient diagnosed with Eales' disease and nonresolving vitreous hemorrhage using 25 G TSV and standard 20 G vitrectomy with sutures in the same eye. After a 2-week follow-up using Ultrasound Biomicroscopy to measure the gap at the sclerotomy site, it was found that on the 14th postoperative day there was still a gap observed in the PPV sclerotomy wound with sutures.[15]

Sclerotomy wound healing can also be observed from the cicatricial image on Ultrasound Biomicroscopy examination. In the study of Avitabile et al., scleral wound healing in 30 eyes receiving 20 G conventional PPV compared to 30 eyes receiving 25 G TSV by observing scars on Ultrasound Biomicroscopy. It was seen that the healing of the scleral wound at 20 G PPV was only achieved at 8 weeks postoperatively based on the cicatricial image on Ultrasound Biomicroscopy. This is relatively slow compared to scleral wound healing at 25 G TSV achieved at 4 weeks postoperatively.[16]

Scleral Wound Healing on Sutureless Pars Planar Vitrectomy

Wound healing in PPV sutureless relies on the self-sealing properties of the sclera itself. A study combining ultrasound biomicroscopy and histological investigation revealed the mechanism of self-sealing scleral wound closure. Fibrous tissue expands to cover the wound gap on the second day, and wound healing begins. The connective tissue was then extended to span the entire thickness of the wound on the third day. The connective tissue thickens and begins to align with the lamellae of the surrounding normal connective tissue on the fifth day. On the seventh day, the wound had healed and appeared to have normal tissue formation.[17]

Intraoperative and non-operative factors can both contribute to scleral self-sealing. Even with appropriate intraocular pressure, intraoperative variables such as a scleral incision size greater than 3.0 mm can cause spontaneous scleral leakage. To ensure excellent scleral self-sealing without producing scleral leaking even when stimulated, incisions smaller than 2.0 mm are necessary.[18] Multiple intraocular manipulation treatments can distort the sclerotomy wound, reducing the architecture of the sclerotomy valve and causing self-sealing to be delayed.[19,20] The creation of vitreous imprisonment can help cure scleral lesions by completing the process of correcting the configuration of the self-sealing sclerotomy valve.[20,21] Although this contradicts the findings of other studies, the relatively long period of surgery can cause scleral leaking due to tissue exhaustion.[20,22]

Other intraoperative factors that play a role in the self-sealing nature of the sclera are the incision technique, and the instrument used. The oblique incision technique was superior in terms of the lower conjunctival bleb formed compared to the straight incision technique, although there was no difference in the wound healing process during the 30-day observation.[23] The microvitreoretinal (MVR) blade instrument has a weakness where the wound angle is wider than the bevelled trochar. However, there is no significant difference in scleral wound closure and complications of hypotony and scleral wound leakage during 14 days of observation.[24] Hagemann et al. also showed that a sclerotomy wound could close promptly following a scleral tunnel incision using their method. A self-sealing tunnel incision is made by making an oblique incision with a sharp inserter and gripping the inferior rectus muscle to give ocular fixation. The muscle serves as a fixation point for the eye, providing the necessary counterforce to avoid the rotational movement caused by this type of cannula implantation.[25]

Non-operative factors that contribute to self-sealing sclerotomy are age and length of the axial axis of the eyeball. The higher the age, the easier it is to close the self-sealing sclerotomy wound. This correlation is because ageing is associated with stiffening of the sclera, which can facilitate the restoration of wound valve architecture through scleral massage.[20,25] The length of the eyeball's axial axis and myopia is related to the thin sclera and the irregular direction of the collagen fibres, which can adversely affect wound closure and postoperative hypotonia.[27,28] However, the length of the axial axis of the eye may only relate to sclerotomy wounds for cataract surgery, not TSV surgery.[20]

Scleral Wound Healing on Pars Planar Vitrectomy with Various Vitreous Substitutes

Vitrectomy is based on various techniques using air, perfluorooctane (PFO) or silicone oil in the eye. Vitrectomy, membrane forceps, segmentation/delamination scissors, diathermy, laser, and retinectomy all work well with these agents in the eye. Air and Silicone Oil float in the vitreous, but the PFO sinks; It is very important to understand that a fluid layer is always present on the surface of the retina and that the retina is made up of more than 90% water and is immiscible in air, PFO, or oil.[23] In the use of Silicone Oil, although no sutures were performed, no oil migrated through the sclerotomy and no hypotony was found postoperatively. To avoid leakage of Silicone Oil, the incision must be made sure to close itself, by making an incision with a maximum angle of 30° through the eye wall. This puts pressure on the sclera, flattening the walls of the eye and creating a slightly longer tunnel effect for better closure.[5] At the end of the operation, when the trocar was withdrawn, some eyes showed a slight accumulation of Silicone Oil from under the conjunctiva. However, the fact that the intraocular pressure did not decrease postoperatively meant that closure occurred well.[24]

In PPV that uses Silicone Oil substitution, generally there is no postop silicone oil leak. In a study by Oliveira and Reiss (2007) on 20 patients with complex retinal detachment who received 23 G TSV with silicon oil tamponade, no hypotony or silicon oil leakage was found at a follow-up period of 3-14 months.[24] In a study by Siquierra et al. (2007) in 31 patients with retinal detachment who received 23 G TSV with silicon oil tamponade, it was found that 3 patients (9.67%) had subconjunctival silicone oil leakage.[29] In PPV using gas/liquid tamponade, no gas leak was found in the subconjunctiva. In the study, 41 eyes with a diagnosis of macular pucker (n-=12), macular hole (n=11), PDR/NPDR (n=9), RRD (n=8), and CRVO (n=1) received 23 G TSV with gas/liquid tamponade, no hypotonic eyes were found (IOP < 12 mmHg). Similarly, no subconjunctival gas leak was found.[30]

Scleral Wound Healing on Pars Planar Vitrectomy with Various Trochar and Incision Technique

Vitrectomy with small trocar provides more advantages than vitrectomy with large trocar, and provides better anatomy and function in various retinal diseases.[31] One study reported that 25G trocar was more effective than 20G trocar to reduce the risk of complications from vitrectomy such as retinal detachment and vitreous hemorrhage.[32] The 25G trocar produced less postoperative inflammatory processes than the 20G and 23G trocars.[33] Sclerotomy wounds heal faster and cause less changes in corneal shape with a 25G trocar compared to a 20G trocar.[16]

Sclerotomy construction is key to the success of minimally invasive sutures in vitrectomy. A

23G (gauge) one-step system was developed which is similar to the 25G trocar but allows for a faster run. To achieve a tunnel-like effect, the incision construction should be as slanted and as long as possible. In achieving optimal watertight/airtight sclerotomy, the first step is to change the angle of the incision. With an angle of 45° it can reach a tunnel of 1,154 mm. By reducing the angle of incision by 15° and using an angle of 30°, the length of the tunnel is increased by 30% while the length of the tunnel becomes 1,415 mm which is more airtight. Another way is with the "Zorro" incision where the direction of the incision is inserted at an angle without being straightened. The blade is inserted 3.2 mm from the limbus at an angle of 10º to 15º where it can enter the vitreous without having to straighten. On day 1 on ultrasound biomicroscopy, the incision appeared to be completely closed and barely detectable. In the endoscopic view, the Zorro incision is smaller and narrower than the standard incision where it is airtight and secure. In all previous oblique incisions, the blade was positioned perpendicular to the cornea and directed to the 12 o'clock position. This resulted in an airtight sclerotomy, but caused the scleral fibers to be cut and thus slowed the wound closure process.[34]

In addition, incisions that run parallel to the scleral fibers can close more quickly, because most of the fibers are separated and not cut. Taking into account the structural arrangement of the sclera, incisions can be made parallel to the limbus and for the scleral fibers using the same modality as the 20G incision. The trocar is inserted at a 30° tangential oblique angle to the scleral surface. The blade is then positioned parallel to the cornea, enters the sclera towards the posterior pole and exits into the vitreous space at 4 mm. In this system of insertion, the scleral fibers are scattered but not completely torn. The sclera is closed with a fibrin plug within 6 to 12 hours, so it is important to assess whether the incision is closed early postoperatively. Ultrasound biomicroscopy performed 3 hours postoperatively showed a 23G parallel oblique incision was closed in this case.[34]

CONCLUSION

The process of scleral wound healing due to sclerotomy in PPV procedures varies depending on several factors. In general, TSV has a faster wound healing rate than conventional PPV methods. Vitrectomy with silicone oil has a relatively faster healing rate than conventional methods although it is not significant. The direction of the oblique incision also affects the post-PPV scleral wound healing process.

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