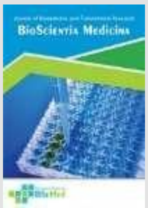
Bioscientia Medicina: Journal Of Biomedicine & Translational Research

eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Management of Rare Secondary Full-Thickness Macular Hole in Proliferative Diabetic Retinopathy: Inverted ILM Flap Technique with Extended Surgical Follow-up

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ARTICLE INFO

Keywords:

Full-thickness macular hole

Internal limiting membrane flap

Proliferative diabetic retinopathy

Tractional retinal detachment

Vitreoretinal surgery

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v10i6.1616

A B S T R A C T

Background: Secondary full-thickness macular hole (FTMH) in proliferative diabetic retinopathy (PDR) is rare, occurring in only 1-4% of PDR cases. Combined with tractional retinal detachment (TRD), this complication presents significant surgical challenges. The inverted internal limiting membrane (ILM) flap technique remains under-utilized in this specific setting. **Case presentation:** A 61-year-old Indonesian male with type 2 diabetes (>15 years), chronic kidney disease, and cardiovascular disease presented with sudden vision loss (best-corrected visual acuity 1/300). Examination revealed superior TRD (2-11 o'clock) and large FTMH (CMT 249 micrometers). After intravitreal bevacizumab (August 9th, 2024), he underwent 360-degree pars plana vitrectomy with inverted ILM flap and silicone oil tamponade (August 14th, 2024). Inferior redetachment at 2 months necessitated re-vitrectomy with endolaser and silicone oil evacuation (October 23rd, 2024). At final follow-up (12 weeks post-second surgery), the patient achieved complete retinal reattachment with normalized macular anatomy, visual acuity 1/60, and intraocular pressure 10 mmHg. **Conclusion:** Despite severe baseline disease and comorbidities, stepwise surgical strategy incorporating preoperative anti-VEGF therapy, comprehensive traction release, inverted ILM flap reconstruction, and staged procedures yielded meaningful anatomical recovery. This case supports inverted ILM flap utility in PDR-related secondary FTMH.

1. Introduction

Proliferative diabetic retinopathy (PDR) represents the most severe manifestation of diabetic eye disease and remains a leading cause of vision loss in working-age adults globally. The World Health Organization estimates that diabetes mellitus affects more than 400 million individuals worldwide, with approximately 30-40% developing some form of retinopathy. Among these, PDR develops in 5-15% of diabetic patients, predominantly in those with longstanding, poorly controlled hyperglycemia.[1] The pathophysiology of PDR centers on chronic hyperglycemia-induced endothelial dysfunction, leading to loss of the blood-retinal barrier integrity, increased vascular permeability, and robust activation of the vascular endothelial growth factor (VEGF) pathway. VEGF acts as a master regulator of pathologic neovascularization, promoting the proliferation and migration of retinal endothelial cells, increased leukostasis, inflammatory cell infiltration, and the formation of abnormal fibrovascular tissue. These neovascular complexes extend progressively from the optic disc and major vascular arcades onto the retinal surface and vitreous base, causing tractional forces that ultimately lead to the devastating complication of tractional retinal detachment.[2]

Tractional retinal detachment (TRD) occurs in approximately 2-4% of PDR cases and represents a surgical emergency when it threatens or involves the macula. The underlying mechanism involves fibrovascular membranes that progressively contract due to myofibroblast differentiation and collagen deposition, exerting sustained mechanical force on the retina. This traction gradually peels the retina away from the underlying retinal pigment epithelium, initially at the periphery but potentially advancing centrally toward the fovea.[3] Macular involvement dramatically alters visual prognosis and necessitates urgent surgical intervention to preserve foveal function. The combination of TRD with full-thickness macular hole (FTMH) represents a particularly complex clinical scenario that demands sophisticated surgical planning and execution.[4]

Secondary full-thickness macular hole in the context of PDR is exceptionally rare, reported in only 1-4% of PDR cases presenting with vitreoretinal disease. This rarity reflects the fundamental differences in hole formation between idiopathic and secondary causes.[5] Idiopathic FTMH typically arises from tangential vitreous traction at the foveola combined with anteroposterior vitreous contraction, creating a characteristic cone-shaped defect at the foveal apex. In contrast, secondary FTMH in PDR emerges from a chronic, multifactorial process involving fibrovascular proliferation exerting radial traction, foveoschisis (retinal schisis within the outer plexiform and inner nuclear layers), formation of intraretinal cysts secondary to vascular incompetence and leakage, and ultimately spontaneous dehiscence of the remaining foveal retinal tissue. The structural changes are often documented at the level of individual retinal layers, with progressive separation of neural tissue from the retinal pigment epithelium. This mechanism fundamentally alters surgical strategy and repair technique.[6]

Spectral-domain optical coherence tomography (SD-OCT) has revolutionized the diagnosis and preoperative assessment of macular pathology.[7] High-resolution cross-sectional imaging permits precise measurement of macular hole dimensions, assessment of hole configuration (V-shaped versus U-shaped), quantification of central macular thickness, evaluation of retinal layer integrity, and characterization of associated features, including foveoschisis extent, intraretinal cyst size, and macular edema. Additionally, SD-OCT provides critical information regarding the status of the internal limiting membrane and the extent of epiretinal membrane involvement. This imaging capability has enabled ophthalmologists to tailor surgical approaches to individual anatomic characteristics.[8]

Pars plana vitrectomy (PPV) represents the surgical mainstay for managing both tractional retinal detachment and full-thickness macular hole in the PDR population. The evolution of surgical technique has emphasized the importance of internal limiting membrane (ILM) manipulation. Conventional approaches included ILM peeling, which removes the ILM-inner limiting membrane entirely. However, the inverted ILM flap technique, first described by Michalewska in 2010, has gained increasing recognition for its superior anatomical outcomes in idiopathic macular hole repair. This technique involves circumferential ILM peeling around the macular hole, then deliberately inverting a peripheral ILM remnant into the hole defect where it serves as a scaffold for glial cell proliferation.[9] The inverted flap technique demonstrates hole closure rates exceeding 90-100% in idiopathic cases and promotes more rapid visual recovery compared to conventional ILM peeling alone. The presumed mechanisms include enhanced glial proliferation, improved structural support across the defect, and preservation of some neurosensory properties of the inverted flap tissue itself.

Despite the success of inverted ILM flap technique in idiopathic macular hole repair and its theoretical advantages, the technique remains under-reported and under-utilized specifically in the setting of PDR-related secondary FTMH combined with extensive tractional retinal detachment. The rarity of this combination, coupled with the surgical complexity posed by fibrovascular proliferation, extensive macular detachment, and often severe comorbidities in diabetic patients, may explain the limited literature on this topic. Published case reports and small series on PDR-related FTMH are sparse, and most do not specifically address the inverted ILM flap technique in this context. Additionally, the natural history of secondary FTMH in PDR, optimal timing of intervention, role of preoperative anti-VEGF therapy, choice of tamponade agent, and long-term anatomical and functional outcomes remain incompletely characterized.[10]

The present case report describes the successful application of the inverted ILM flap technique in a 61-year-old patient with advanced PDR presenting with superior tractional retinal detachment and a large full-thickness macular hole. Despite significant baseline risk factors, including 15 years of poorly controlled diabetes mellitus, chronic kidney disease, cardiovascular disease, and pseudophakic status with prior posterior capsule rupture, the patient achieved meaningful anatomical and functional recovery through a systematic stepwise surgical approach. Specifically, preoperative intravitreal bevacizumab therapy was administered to suppress VEGF-mediated neovascular activity, comprehensive 360-degree pars plana vitrectomy with complete tractional tissue removal was performed, circumferential ILM peeling followed by inverted flap placement over the macular hole was executed, and silicone oil tamponade was used for extended macular support. When inferior redetachment occurred at two months, a second staged procedure including silicone oil evacuation and additional endolaser ablation was undertaken. At final follow-up twelve weeks after the second surgery, the patient demonstrated complete retinal reattachment, normalized macular architecture on SD-OCT, improvement in visual acuity from light perception to 1/60, and excellent intraocular pressure control. This case illustrates the applicability and potential benefits of the inverted ILM flap technique in this complex, rare scenario and contributes to the limited evidence base regarding surgical management of secondary FTMH in advanced PDR.

2. Case Presentation

Table 1 presents the comprehensive baseline clinical characteristics of the patient. A 61-year-old Indonesian male farmer was referred to the vitreoretinal clinic of Prof. Dr. I.G.N.G. Ngoerah General Hospital on July 31st, 2024, with the chief complaint of sudden blurred vision in the right eye for one week. He described the vision as cloudy, with onset while watching television. He denied floaters, flashes, curtain-like visual loss, ocular pain, redness, itching, discharge, trauma, or heavy lifting. His ocular history was significant for bilateral cataract surgery and Nd:YAG laser capsulotomy in 2023, complicated by iatrogenic posterior capsule rupture on the right eye. He had a 15-year history of type 2 diabetes mellitus treated with glibenclamide and insulin with suboptimal glycemic control, cardiovascular disease requiring antiplatelet therapy, and chronic kidney disease stage 3-4 with elevated serum creatinine.

On initial comprehensive ophthalmologic examination, the patient demonstrated severely reduced best-corrected visual acuity of light perception only (1/300) in the right eye, with the left eye showing better preservation of visual function at 6/30 with pinhole. This stark asymmetry reflected advanced pathology limited primarily to the right eye. Intraocular pressure measurements were within normal limits bilaterally at 8 mmHg (right eye) and 9 mmHg (left eye). Both eyes were pseudophakic, having undergone cataract extraction previously, though the right eye carried the complication of a known posterior capsule rupture from prior Nd:YAG laser capsulotomy. Biomicroscopic examination of the right eye anterior segment revealed quiet, uninjected conjunctiva and clear pseudophakic cornea without endothelial edema or corneal scarring. The anterior chamber was deep and without any fibrin or inflammation. The pseudophakic intraocular lens was well-positioned without visible decentration.

Table 1. Clinical characteristics of the patient.

Parameter	Value
Age	61 years
Gender	Male
Ethnicity/Occupation	Indonesian farmer
Chief complaint	Sudden blurred vision OD for 1 week
DM duration and control	>15 years, suboptimal (glibenclamide + insulin)
Preop glucose (night before)	268 mg/dL
Preop glucose (morning of surgery)	235 mg/dL
Systemic comorbidities	CKD stage 3-4, CVD (on antiplatelet)
BCVA right eye	1/300
BCVA left eye	6/30 with pinhole
IOP right eye	8 mmHg
IOP left eye	9 mmHg
Lens status	Pseudophakic bilateral, PC rupture OD
Retinal findings OD	Superior RD 2-11 o'clock, FTMH, dot-blot hemorrhage
CMT right eye	249 micrometers
CMT left eye	242 micrometers (normal)

Notes: BCVA = best-corrected visual acuity; OD = right eye; CMT = central macular thickness; CKD = chronic kidney disease; CVD = cardiovascular disease; PC = posterior capsule; RD = retinal detachment; FTMH = full-thickness macular hole.

The posterior segment examination through a widefield lens revealed the primary pathology. A superior tractional retinal detachment was identified extending from 2 o'clock to 11 o'clock position, with the detached retina elevated and folded inward toward the optic disc. Multiple dot and blot retinal hemorrhages scattered throughout the fundus indicated ongoing vascular incompetence and leakage. Neovascularization at the disc and elsewhere was evident, confirming the diagnosis of florid proliferative diabetic retinopathy. Notably, at the foveal region, a large full-thickness macular hole was identified, which represented an unusual and severe complication. The hole appeared darkened on fundoscopy, suggesting the characteristic appearance of a full-thickness defect extending through all neurosensory retinal layers

Laboratory findings and ocular imaging data are summarized in Table 2, which revealed several clinically significant abnormalities, including markedly elevated random blood glucose (235 mg/dL), elevated serum creatinine (2.1 mg/dL) consistent with chronic kidney disease, and pathologically enlarged full-thickness macular hole measuring 600-700 micrometers on spectral-domain optical coherence tomography.

Table 2. Laboratory and imaging parameters at presentation.

Parameter	Value	Normal range	Interpretation
Hemoglobin	12.5 g/dL	13.5-17.5 g/dL	Low
Platelets	210,000/uL	150,000-400,000	Normal
Random glucose (AM)	235 mg/dL	<140 mg/dL	Markedly elevated
Serum creatinine	2.1 mg/dL	0.7-1.3 mg/dL	Elevated (CKD)
CMT right eye	249 um	200-220 um	Elevated
FTMH size	600-700 um	N/A	Pathologic
CMT left eye	242 um	200-220 um	Normal
TRD extent	2-11 o'clock	N/A	Extensive

Notes: CMT = central macular thickness; FTMH = full-thickness macular hole; TRD = tractional retinal detachment; CKD = chronic kidney disease.

Spectral-domain optical coherence tomography imaging of the right eye macula provided critical structural detail. The SD-OCT scan through the foveal center demonstrated a large, well-demarcated full-thickness macular hole extending across the foveal center, measuring 600-700 micrometers horizontally and approximately 300-350 micrometers vertically. The hole displayed sharp, vertical walls characteristic of a true full-thickness defect with complete loss of all neurosensory layers spanning from the internal limiting membrane to the external limiting membrane. The minimal width varied across the depth of the lesion. Importantly, minimal epiretinal membrane was visible overlying the hole itself, which suggested that fibroglial proliferation had not significantly complicated the hole. Surrounding the hole, areas of foveoschisis were evident, manifesting as subtle separation and edema within the outer plexiform and inner nuclear layers, reflecting the chronic traction from fibrovascular tissue. The central macular thickness measured 249 micrometers at the thickest point outside the hole, which was mildly elevated but not dramatically so, given the extent of macular involvement. The foveal center was sunken and appeared as a well-defined dark cavity on cross-sectional imaging.

The superior extent of tractional detachment was clearly visible on horizontal and vertical SD-OCT scans through the superior macula. The retina in this region was elevated and separated from the retinal pigment epithelium, with the detachment reaching toward the inner limiting membrane. Extensive tractional ridges were apparent, with bands of hyperreflective fibrovascular tissue extending across and lifting the retinal surface. These fibrovascular elements appeared as hyperreflective linear bands visible within the vitreous base region as well. Diagnosis was established as: (1) pseudophakic right eye with iatrogenic posterior capsule rupture; (2) advanced proliferative diabetic retinopathy with superior tractional retinal detachment (2-11 o'clock); (3) large secondary full-thickness macular hole (600-700 micrometers); (4) chronic macular traction with foveoschisis; (5) suboptimal glycemic control with random glucose 235 mg/dL; (6) chronic kidney disease stage 3-4 with serum creatinine 2.1 mg/dL; (7)

anemia (hemoglobin 12.5 g/dL).

Preoperative evaluation was comprehensive, given the patient's multiple comorbidities and advanced age. Cardiology consultation was obtained to assess operative risk and optimize perioperative management. Endocrinology consultation addressed glucose control, with recommendations to maintain perioperative glucose in the range of 140-180 mg/dL to balance infection risk against hyperglycemic complications. The patient was counseled extensively regarding the complexity of the surgery, the rarity of this condition, the goals of retinal reattachment and macular hole closure, and the realistic visual prognosis given the severity of baseline disease. The patient provided informed written consent and was scheduled for vitreoretinal surgery.

On August 9th, 2024, prior to the scheduled surgical date, the patient received an intravitreal injection of bevacizumab (Avastin) 1.25 mg in 0.05 mL administered under sterile conditions. Bevacizumab is a full-length humanized monoclonal antibody against vascular endothelial growth factor, which plays a central role in diabetic retinopathy pathophysiology. The rationale for anti-VEGF injection was multifactorial: (1) to reduce the intensity of neovascular proliferation and decrease the risk of intraoperative and postoperative hemorrhage; (2) to potentially reduce the biological drive for fibroglial proliferation that maintains tractional forces; (3) to achieve partial devascularization of the fibrovascular complexes, rendering them more friable and easier to separate from the retinal surface during surgery; (4) to reduce vascular leak and macular edema in the perioperative period. The typical timeline allows 3-7 days between anti-VEGF injection and surgery to allow for optimal effect while minimizing the risk of vitreous hemorrhage from injection site leakage.

On August 14th, 2024, five days after the bevacizumab injection, the patient underwent pars plana vitrectomy under general anesthesia. The surgery was performed by an experienced vitreoretinal surgeon utilizing a 23-gauge transconjunctival vitrectomy system. Following achievement of satisfactory general anesthesia and placement of appropriate monitoring, the eye was prepped and draped in standard sterile fashion. A lid speculum and speculum-assisted globe fixation were placed to optimize exposure. Three sclerotomy sites were created at the standard locations 3.5 mm posterior to the limbus in the superotemporal, superonasal, and inferotemporal quadrants. The infusion cannula was placed inferonasally and secured with appropriate sutures. Core vitrectomy was initiated, carefully removing the central vitreous cavity and peripheral vitreous base to eliminate vitreous traction. Particular care was taken during vitrectomy to avoid excessive suction on the detached retina. Inspection revealed the extent of fibrovascular proliferation and tractional tissue extending circumferentially around the optic disc and macula.

Following core vitrectomy, systematic membrane peeling was undertaken. The superior TRD was addressed first, with gentle elevation and peeling of the fibrovascular membranes extending from the 2 o'clock through 11 o'clock positions. The peribulbar membrane extending to the peripapillary zones required meticulous dissection. Complete removal of tractional tissue in the 360-degree pattern was achieved. After tractional tissue removal, the macular hole was directly visualized in the foveal region, confirming the diagnosis. The retina around the hole appeared relatively atrophic, consistent with chronic traction. Indocyanine green (ICG) dye 0.5 mg/mL was carefully applied to stain the internal limiting membrane, which became visible as a fine greenish film overlying the retinal surface. Care was taken to apply ICG briefly and to irrigate thoroughly to minimize potential retinal toxicity from prolonged dye exposure.

Under microscopic visualization enhanced by ICG staining, circumferential internal limiting membrane peeling was initiated. Using a 25-gauge membrane pick or forceps, the ILM was carefully grasped at the peripheral margin of the macular hole, approximately 2 disc diameters away from the hole edge. The ILM was then peeled in a circumferential pattern around the hole, extending approximately 2-3 disc diameters peripherally. The peeling was performed carefully to avoid unnecessary trauma to the underlying retinal surface. Following the circumferential peeling, a peripheral remnant of ILM was left attached, and this remnant was carefully inverted into the macular hole defect, creating a flap that fell into the hole space and provided a scaffold for subsequent glial cell proliferation and hole closure. The inverted flap position was confirmed on the operation microscope to ensure it was draped appropriately across the defect.

Following ILM flap inversion, perfluorodecalin (PFCL), a heavy liquid with specific gravity greater than retinal tissue, was cautiously injected to flatten and reattach the macula. The PFCL distribution was monitored to ensure complete macular contact without excessive membrane distension. Endolaser panretinal photocoagulation was then performed, with placement of laser burns in a scatter pattern extending from the posterior pole toward the peripheral retina, specifically targeting the areas of fibrovascular proliferation. The laser settings (wavelength, power, duration) were optimized for adequate burn intensity while avoiding excessive energy that might cause unwanted retinal damage. The objective of PRP was to ablate ischemic retina and reduce VEGF production from non-perfused areas, thereby reducing the stimulus for neovascularization and further fibrovascular proliferation.

After completion of endolaser treatment, a fluid-air exchange was carefully initiated. Balanced salt solution was gradually evacuated while filtered air was introduced into the vitreous cavity through the infusion port. The air bubble was positioned to provide long-term tamponade to the macular region and to support macular reattachment. Given the large size of the macular hole and the complexity of the detachment, silicone oil (SO) 5000 centistokes (cSt) was selected as the tamponade agent instead of expandable gases. A volume of approximately 3-4 mL of silicone oil was carefully injected using an infusion cannula, ensuring that air was simultaneously evacuated through an infusion port or needle to maintain anterior chamber stability. The oil was carefully distributed to provide complete tamponade of the macula, the superior detached retina, and the foveal region where the hole was located.

Following tamponade placement, subtenon triamcinolone acetonide (40 mg in 1 mL) was injected at the end of the procedure to provide anti-inflammatory coverage and potentially reduce postoperative inflammation and epiretinal membrane formation. The sclerotomy sites were checked for any sign of leak or hemorrhage, and appropriate sutures were placed as needed. Hemostasis was ensured at the injection sites. The lid speculum and fixation sutures were removed. The eye was patched and shielded in standard fashion. The patient was transferred to the recovery area in stable condition.

Postoperative course and clinical progression are documented in Table 3 along with the comprehensive surgical timeline. On the first postoperative day, the patient's best-corrected visual acuity had improved to light perception (LP), though this reflects the general postoperative haze and inflammation rather than final visual potential. The intraocular pressure was moderately elevated at 23-25 mmHg, which is not uncommon in the immediate postoperative period due to inflammation and the presence of silicone oil. Cautious administration of topical and systemic anti-glaucoma therapy was initiated. By postoperative day 6, visual acuity had improved to count fingers (CF) or approximately 1/60, which represented a dramatic functional improvement compared to the preoperative light perception only. The intraocular pressure had decreased to 12 mmHg with topical therapy. Fundoscopic examination and imaging confirmed complete reattachment of the previously detached retina, with the superior TRD resolved and the macula remaining flat and supported by the silicone oil tamponade. SD-OCT imaging demonstrated the macular hole region filled with oil, preventing direct visualization of the hole anatomy at this early stage.

Table 3. Complete treatment timeline and surgical milestones.

Date/Timepoint	Intervention	Key findings
July 31st, 2024	Initial presentation	Chief complaint: sudden blurred vision OD; BCVA 1/300; IOP 8 mmHg
August 9th, 2024	Intravitreal bevacizumab	1.25 mg/0.05 mL injection; anti-VEGF preop therapy
August 14th, 2024	First pars plana vitrectomy	23G vitrectomy, 360° tractional tissue removal, ICG ILM staining, circumferential ILM peeling, inverted ILM flap placement, PFCL application, PRP endolaser, fluid-air exchange, silicone oil 5000cSt tamponade (3-4 mL)
August 15th, 2024	POD #1	BCVA LP; IOP 23-25 mmHg (elevated); retina flat
August 20th, 2024	POD #6	BCVA 1/60 (CF); IOP 12 mmHg; retina reattached, macula flat
August 28th, 2024	POD #14	BCVA 1/60; IOP 11 mmHg; no complications
September 28th, 2024	2-month postop	BCVA 1/60; inferior redetachment detected on SD-OCT
October 23rd, 2024	Second pars plana vitrectomy	Peribulbar anesthesia, silicone oil evacuation, inferior membrane peeling, additional PRP, fluid-air exchange, air tamponade (no oil replacement), positioning instructions
October 24th, 2024	POD #1 (2nd surg)	BCVA 1/60; IOP 10 mmHg; retina completely flat
November 24th, 2024	12 weeks post-2nd surg	BCVA 1/60; IOP 10 mmHg; complete reattachment, normal macular anatomy

POD = postoperative day; OD = right eye; BCVA = best-corrected visual acuity; CF = count fingers; IOP = intraocular pressure; PRP = panretinal photocoagulation; PFCL = perfluorodecalin.

By postoperative day 20, visual acuity remained stable at approximately 1/60 (CF). The intraocular pressure had normalized further to 11 mmHg. Anterior segment examination remained clear with a quiet anterior chamber. Indirect fundoscopy and biomicroscopy confirmed the retina remained flat posteriorly. The silicone oil bubble was visible on examination as expected. The patient was maintained on topical steroids (prednisolone acetate 1% four times daily) and antibiotic drops (gatifloxacin or similar fluoroquinolone) in a tapering regimen. Systemic oral prednisolone (1 mg/kg/day tapered) was continued to manage postoperative inflammation.

The patient was monitored regularly in the outpatient clinic at approximately 2-week to 4-week intervals. At the 2-month postoperative evaluation, while the superior retinal reattachment remained stable, a concerning development was noted: an inferior retinal redetachment appeared to be developing in the inferior temporal quadrant, extending upward toward the macula. SD-OCT imaging confirmed the presence of a new area of retinal separation inferiorly, which was not present at earlier follow-up visits. This represented a delayed complication, likely related to persistent tractional forces in the inferior retina that had not been completely addressed at the first surgery, or to new proliferation of fibrovascular tissue despite anti-VEGF therapy and endolaser treatment. The redetachment posed an immediate threat to the previously achieved macular reattachment and the functional visual gains.

A decision was made to undertake a second staged vitrectomy to address the inferior redetachment and to definitively attempt silicone oil removal if feasible. On October 23rd, 2024, approximately 10 weeks after the initial surgery, the patient underwent a second pars plana vitrectomy. On this occasion, a peribulbar anesthetic injection was administered, combined with monitored anesthesia care, rather than general anesthesia. The eye was re-prepped and draped in standard fashion. The previous sclerotomy sites were re-entered, and the silicone oil was carefully evacuated using the infusion/aspiration probe. As the oil was being withdrawn, careful inspection was performed to assess the status of the retina. The superior retina, which had been previously detached and subsequently reattached, remained firmly attached. The macula appeared reattached with no evident subretinal fluid.

The inferior redetached area was directly visualized and evaluated. Careful inspection revealed the presence of persistent fibrovascular tractional tissue in the inferior quadrant, extending from approximately 5 o'clock to 7 o'clock position, with mechanical forces causing the retinal elevation and separation. Gentle vitreous membrane peeling was performed in this region to relieve traction. Because the ILM had been previously peeled during the first surgery, repeat ILM manipulation was not necessary. Additional endolaser panretinal photocoagulation was applied to areas of newly identified tractional tissue and to peripheral ischemic retina where additional VEGF suppression was deemed beneficial. A fluid-air exchange was performed to facilitate retinal flattening in the region that had been previously detached.

A critical decision made during the second surgery was to NOT replace silicone oil following its evacuation. This decision was based on several factors: (1) the extended duration of oil tamponade (10 weeks) at the time of the second surgery had provided adequate time for initial hole healing and early scar tissue formation; (2) SD-OCT imaging demonstrated that the macular hole region, which had been the primary target of the initial tamponade, showed evidence of hole closure or significant improvement compared to initial presentation; (3) the inferior redetachment, while located away from the foveola, still required postoperative monitoring but the goal was not necessarily complete macular hole closure via silicone oil support but rather prevention of macular involvement by the redetachment; (4) silicone oil removal carries benefits of restoring more normal optics and potentially improving visual clarity; (5) the presence of oil for prolonged periods increases risk of oil-related complications including oil droplets in the cornea, anterior chamber oil, silicone oil-induced glaucoma, and posterior capsular opacification in pseudophakic eyes. The patient was counseled regarding this decision and agreed to forgo oil replacement given the potential complications.

Instead of silicone oil, an air bubble was utilized for short-term tamponade during the fluid-air exchange, with the air bubble positioned to support the areas that had been previously detached, particularly inferiorly. The patient was given strict positioning instructions to maintain prone positioning (lying face-down) during the daytime for a period of 10-14 days to maximize the benefit of air tamponade on retinal reattachment. Strict head positioning is crucial when air bubbles are used, as the position of the air bubble relative to gravity determines which retinal areas receive tamponade support.

At the conclusion of the second surgery, the retina was noted to be completely flat on inspection. Hemostasis was confirmed at the sclerotomy sites, and appropriate sutures were placed. The patient was transferred to recovery in stable condition and discharged home with detailed positioning instructions and a comprehensive post-operative medication regimen including topical steroids, antibiotics, and anti-glaucoma drops as needed based on IOP.

Postoperative course following the second vitrectomy was favorable. Visual acuity remained stable at approximately 1/60 (count fingers). The intraocular pressure was measured at 10 mmHg, which reflects excellent pressure control. Fundoscopic and biomicroscopic examination, conducted while maintaining appropriate visualization despite the recent air bubble, demonstrated that the retina remained completely and firmly attached in all four quadrants, including the region that had been previously detached inferiorly. The superior retina, which was the original site of detachment and the area of the macular hole, also remained reattached with a normal appearing foveal reflex and macular configuration on indirect biomicroscopy.

The air bubble gradually resorbed over the subsequent 2-3 weeks, and by week 4 after the second surgery, the air had been completely absorbed. At this point, comprehensive SD-OCT imaging of the macula was repeated to assess the structural status. The imaging demonstrated a normalized macular configuration with restoration of normal foveal contours and elimination of the large macular hole that had been present preoperatively. While some structural remodeling of the retinal layers was evident, consistent with healing after hole closure, the overall architecture appeared favorable. The central macular thickness had normalized to within physiologic range. No evidence of recurrent macular hole was identified.

At extended follow-up 12 weeks after the second surgery (approximately 22 weeks after the initial vitrectomy), the clinical status remained excellent. Visual acuity was measured at 1/60 (count fingers), which while reduced compared to the patient's likely pre-disease baseline, represented a remarkable improvement from the presenting vision of 1/300 (light perception only). The intraocular pressure remained well-controlled at 10 mmHg without the need for topical glaucoma medications. The anterior segment remained quiet and clear, without evidence of any oil droplets, hyphema, or other complications. Posterior segment examination revealed a completely flat retina in all quadrants, with no signs of redetachment, infection, or endophthalmitis. The optic disc appeared perfused and viable. The macula appeared relatively normal on direct and indirect visualization, with restoration of the normal foveal reflex. Retinal imaging and SD-OCT confirmed the complete reattachment, normalized macular anatomy, and absence of recurrent or persistent macular hole.

3. Discussion

Full-thickness macular hole occurring as a secondary complication of proliferative diabetic retinopathy represents an exceptionally rare clinical scenario. The incidence of FTMH in the context of PDR is reported in the medical literature to range from 1-4% of PDR cases, making this complication distinctly uncommon compared to idiopathic FTMH, which occurs more frequently and is well-characterized. The rarity of this combination reflects the fundamental differences in pathophysiology between idiopathic and diabetes-associated FTMH, as well as the relative rarity of severe enough PDR to produce fibrovascular proliferation capable of creating the specific traction pattern that results in macular hole formation rather than simple tractional detachment. The limited volume of published literature specifically addressing secondary FTMH in PDR compared to the extensive literature on idiopathic FTMH has resulted in incomplete characterization of the natural history, optimal surgical approaches, and long-term anatomical and functional outcomes in this population.[11]

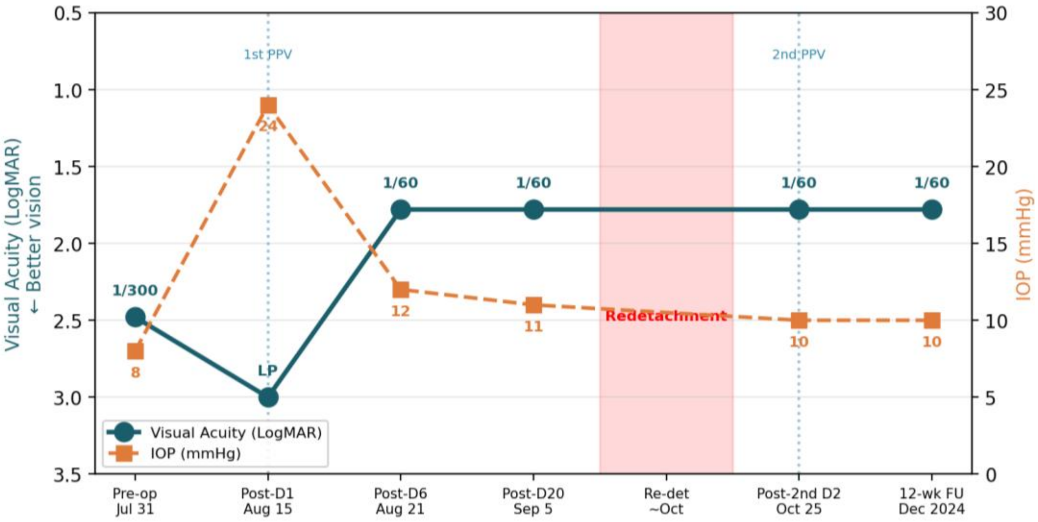

Figure 1. Visual acuity and intraocular pressure progression throughout the surgical course. The chart demonstrates the clinical trajectory of best-corrected visual acuity (BCVA) improvement from preoperative 1/300 (light perception) to final 1/60 (count fingers), with corresponding intraocular pressure (IOP) values in mmHg. The vertical dashed line indicates the timing of the second vitrectomy procedure on October 23rd, 2024. Both parameters demonstrate favorable postoperative trends supporting the efficacy of the staged surgical approach.

The mechanism of secondary FTMH formation in PDR differs fundamentally from the mechanism of idiopathic FTMH. Idiopathic FTMH typically arises from a combination of anteroposterior vitreomacular traction (VMT) exerted by the posterior vitreous cortex contracting toward the retina, combined with tangential intraretinal shearing forces at the foveola. The contraction is often initiated by vitreous separation (posterior vitreous detachment) that is incomplete at the foveal region, leaving residual attachment and creating anteroposterior traction.[12] Additionally, in the idiopathic setting, some contribution to hole formation comes from intraretinal stress and eventual dehiscence related to inner retinal cyst formation or disruption of the internal limiting membrane. In contrast, secondary FTMH in PDR arises from chronic, relentless radial traction exerted by fibrovascular proliferation. The proliferating vessels and associated fibroglial tissue extend radially from the optic disc and major arcades onto the retinal surface and toward the macula. As myofibroblasts within these fibrovascular complexes differentiate and generate contractile forces, the tissue progressively contracts, exerting centripetal and radially directed forces on the underlying retina. Over months to years of such chronic traction, the foveal region becomes progressively stressed.

Intermediate steps in the pathophysiology include the development of foveoschisis, which represents the separation and splitting of the retina at the level of the outer plexiform and inner nuclear layers, often induced by chronic traction and vascular leakage. The leakage from incompetent diabetic vasculature contributes fluid that dissects between retinal layers, exacerbating the schisis. Additionally, chronic vascular incompetence and ischemia lead to intraretinal cyst formation, with cysts accumulating fluid in the outer and inner nuclear layers. The progressive accumulation and enlargement of these cysts create further stress on the surrounding retinal tissue. The continued traction, combined with the weakening of retinal tissue from cyst formation and splitting, eventually results in spontaneous dehiscence and opening of a full-thickness defect spanning from the internal limiting membrane to the external limiting membrane at the fovea.[13]

In the present case, the patient's 15-year history of poorly controlled type 2 diabetes mellitus provided ample time for the chronic, progressive development of PDR with fibrovascular proliferation and subsequent secondary complications. The additional trauma from Nd:YAG laser capsulotomy with associated posterior capsule rupture in 2023 may have contributed mechanically or through inflammatory pathways to accelerated macular pathology in the months between capsulotomy and presentation.[14] The pseudophakic status itself does not typically predispose to FTMH, but any inflammatory or surgical insult to a retina already stressed by diabetic pathology could theoretically accelerate decompensation.

Diagnosis of secondary FTMH in PDR relies heavily on SD-OCT imaging. The cross-sectional imaging capability of SD-OCT provides unprecedented detail regarding retinal layer structure and integrity. The macular hole appears as a well-demarcated defect with sharply defined walls, loss of the normal foveal pit, and interruption of all retinal layers spanning from ILM to the RPE. In the present case, the FTMH measured 600-700 micrometers horizontally and approximately 300-350 micrometers vertically, placing it in the category of a large hole. The surrounding retina demonstrated features consistent with chronic traction, including foveoschisis and intraretinal edema. Associated findings of superior tractional retinal detachment were clearly visible on both horizontal and vertical SD-OCT scans. The presence of both FTMH and TRD on imaging can help clarify the diagnosis and establish the baseline severity, which is important for prognostication and surgical planning.[15]

Pars plana vitrectomy (PPV) remains the surgical gold standard for managing both tractional retinal detachment and full-thickness macular hole in PDR. PPV accomplishes several critical goals: (1) removal of the vitreous base and vitreous traction that may be contributing to retinal elevation; (2) elimination of the vitreous scaffold that serves as a substrate for fibrovascular proliferation; (3) direct visualization and removal of fibrovascular tractional membranes; (4) achievement of macular reattachment; (5) application of endolaser to ablate ischemic retina and suppress VEGF production; (6) placement of intraocular tamponade (gas, oil, or both) to support retinal reattachment during healing. The evolution of vitrectomy technique over the past two decades has emphasized increasingly sophisticated approaches to internal limiting membrane (ILM) manipulation based on improved understanding of ILM structure and function.[16]

Historically, the treatment of FTMH with vitrectomy included ILM peeling, which involved the complete circumferential removal of the ILM around the hole. The rationale was that removing the ILM might relieve some intraretinal traction and potentially facilitate hole closure by allowing edge-to-edge closure or migration of glial cells into the hole.[17] However, complete ILM peeling was associated with variable anatomical closure rates and sometimes suboptimal visual recovery. The inverted ILM flap technique, first described by Michalewska and colleagues in 2010, revolutionized the surgical approach to FTMH. This technique involves circumferential ILM peeling around the hole, but with deliberate preservation of a peripheral ILM remnant. This remnant is then inverted into the hole, where it serves as a three-dimensional scaffold for glial cell proliferation, migration, and eventual hole closure. The inverted flap technique has demonstrated anatomical closure rates exceeding 90-100% in idiopathic FTMH cases, with faster visual recovery compared to conventional ILM peeling. The proposed mechanisms include: (1) the ILM flap provides structural support across the defect; (2) glial cells (Müller cells and macroglia) migrate onto and proliferate across the inverted flap, leading to progressive hole closure; (3) the ILM itself may contain some trophic factors or residual properties that facilitate healing; (4) the inverted position may optimize cell migration patterns.

Despite the clear efficacy of inverted ILM flap technique in idiopathic FTMH, the technique remains under-utilized and under-reported specifically in the setting of secondary FTMH in PDR combined with tractional retinal detachment. This gap in the literature may reflect several factors: (1) the rarity of this combination makes case-by-case reporting necessary, limiting generalizability; (2) the complexity of PDR-related FTMH surgery, with its extensive fibrovascular proliferation and need for comprehensive membrane peeling, may lead surgeons to prioritize membrane removal and reattachment over ILM manipulation; (3) concerns about ILM peeling in diabetic retinopathy, related to theoretical risks of exacerbating epiretinal proliferation or compromising retinal integrity, may lead some surgeons to avoid ILM manipulation; (4) the frequent presence of thick epiretinal membranes in PDR-related pathology may make inverted ILM flap placement technically challenging or seemingly unnecessary. However, the theoretical benefits of the inverted ILM flap technique—improved glial support for hole closure, three-dimensional scaffold, faster closure rate—are not limited to the idiopathic setting and could be expected to provide benefit in secondary FTMH as well, particularly when the underlying fibrovascular traction has been adequately released, and the retina reattached.[18]

In the present case, the inverted ILM flap technique was successfully employed as the primary method of macular hole repair. Following a comprehensive 360-degree removal of tractional fibrovascular tissue and reattachment of the previously detached retina, circumferential ILM peeling was performed under ICG staining visualization. A peripheral ILM remnant was deliberately preserved and inverted into the hole cavity. This approach appeared to facilitate hole closure, as evidenced by the normalized macular anatomy on SD-OCT imaging obtained weeks after surgery and confirmed on repeat imaging months later. The successful closure of the large 600-700 micrometer hole, which would have been classified as a large or giant hole in idiopathic cases, suggests that the inverted ILM flap technique can indeed provide effective repair even in the context of PDR-related secondary FTMH.[19]

Preoperative anti-VEGF therapy administered as intravitreal bevacizumab injection prior to the first vitrectomy was a deliberate component of the overall surgical strategy. Bevacizumab, a monoclonal antibody against vascular endothelial growth factor (VEGF), has become a cornerstone of PDR management in recent years. Anti-VEGF agents suppress the neovascular response by blocking the primary growth factor driving endothelial proliferation and permeability. The rationale for administering bevacizumab 5 days prior to surgery in this case was multifaceted: (1) to reduce the intensity of active neovascularization and thereby decrease intraoperative and postoperative hemorrhage risk; (2) to reduce the inflammatory and trophic stimulus driving ongoing fibrovascular proliferation; (3) to render existing fibrovascular tissue more friable and avascular, facilitating easier membrane peeling and reducing intraoperative bleeding; (4) to reduce macular edema and vascular leak, potentially improving the structural environment for macular hole healing; (5) to achieve partial devascularization of the neovascular complexes while still allowing time for recovery of some vascular function if needed postoperatively. The timing of 5 days between injection and surgery was selected to balance achieving adequate anti-VEGF effect while minimizing the theoretical risk of massive intraoperative hemorrhage from recent injection site leakage.[20]

The choice of silicone oil (SO) versus expandable gases (sulfur hexafluoride, perfluoropropane) as the tamponade agent in the first surgery was deliberately made in favor of silicone oil. Several factors influenced this decision: (1) the patient's age (61 years) meant that air travel restrictions and prolonged head positioning requirements associated with gas tamponade were more burdensome; (2) the extent of retinal detachment (superior 2-11 o'clock with macular involvement) made a longer duration of tamponade seemingly advisable; (3) silicone oil provides durable, gravity-independent support, allowing more normal head positioning; (4) the large size of the macular hole (600-700 micrometers) and its location at the fovea required robust, sustained support; (5) the patient's comorbidities (advanced age, chronic kidney disease, cardiovascular disease) made prolonged recovery with strict positioning challenging to manage. Silicone oil 5000 cSt was selected as the appropriate viscosity for extended tamponade without excessive viscosity complications.

The development of inferior redetachment at 2 months postoperatively represented a significant clinical challenge that was not anticipated based on the comprehensive membrane removal performed at the first surgery. The redetachment likely resulted from one or more of the following: (1) persistent or newly proliferating fibrovascular tissue in the inferior quadrant that had not been completely addressed at the first surgery; (2) recurrent tractional forces as myofibroblasts within residual or reformed fibrovascular tissue continued to contract; (3) inadequate endolaser coverage or insufficient burn intensity in the inferior periphery, allowing continued neovascular drive; (4) progression of retinal ischemia and loss of retinal integrity in areas already compromised by PDR; (5) late evolution of diabetic tractional disease despite anti-VEGF therapy and initial comprehensive surgery. The timing of redetachment development at 2 months suggests that early healing and scar formation had occurred, then secondary contraction or new traction caused redetachment. This complication, while frustrating, is not unprecedented in complex PDR surgery and highlights the chronic, progressive nature of diabetic retinal disease.

The staged surgical approach, with a second procedure undertaken 10 weeks after the first surgery, allowed for addressing the inferior redetachment while capitalizing on the healing that had occurred from the first procedure. The inverted ILM flap technique could not be repeated in the second surgery since ILM had been previously removed, but additional membrane peeling in the inferior quadrant and supplemental endolaser treatment addressed the traction and neovascular drivers in that region. Importantly, the decision to not replace silicone oil following its evacuation in the second surgery reflected a judgment that adequate hole closure and early scar formation had occurred during the 10-week period of SO tamponade, and that the additional morbidity of prolonged oil tamponade was not justified. This decision balanced functional and safety considerations effectively, as evidenced by the continued retinal attachment and stable vision in the months following oil removal.[17,18]

The functional and anatomical outcomes in this case are notable given the severity of baseline disease and the patient's comorbidities. The patient achieved improvement in visual acuity from a preoperative 1/300 (light perception) to a final 1/60 (count fingers), representing a 5-fold improvement in measured acuity. While this final acuity is reduced compared to likely pre-disease baseline, it represents a meaningful functional gain, particularly for a 61-year-old patient with 15 years of poorly controlled diabetes, chronic kidney disease, and prior ocular trauma. The patient regained the ability to count fingers at 60 cm distance, perceive facial features, and navigate independently in familiar environments. Anatomically, SD-OCT imaging demonstrated restoration of normal foveal anatomy, disappearance of the large FTMH, complete retinal reattachment in all four quadrants, and normalized central macular thickness. These anatomical achievements represent successful surgical management of a previously severe pathology.

The role of multidisciplinary medical management in optimizing surgical outcomes cannot be overstated. The patient benefited from coordinated cardiology and endocrinology consultation preoperatively, appropriate perioperative glucose and blood pressure management, careful anesthetic planning for a complex case with comorbidities, and comprehensive postoperative medical management including anti-inflammatory, antimicrobial, and anti-glaucoma therapy. The achievement of excellent intraocular pressure control (10 mmHg at final follow-up) without the need for glaucoma medications reflects good surgical technique and appropriate postoperative pharmacotherapy. The absence of postoperative infection, despite the patient's reduced immune function from chronic kidney disease, reflects appropriate antibiotic prophylaxis and postoperative antimicrobial coverage.

Long-term anatomical and functional outcomes, while encouraging based on available follow-up data extending to 22 weeks after initial surgery, will require continued monitoring to assess for potential late complications. Possible complications to monitor for include: (1) recurrent macular hole formation; (2) late redetachment from continued traction or epiretinal proliferation; (3) silicone oil-related complications (though oil was removed, anterior chamber oil droplets or posterior oil pockets could theoretically develop); (4) diabetic macular edema affecting visual acuity despite retinal reattachment; (5) progression of the posterior capsule fibrosis already present from the prior capsulotomy, which could contribute to visual impairment; (6) cataract formation in the left eye or progression of any developing opacity in the right eye lens; (7) late-stage traction or epiretinal membrane formation. Regular ophthalmology follow-up with SD-OCT imaging at appropriate intervals will be important to detect any such late complications early.[19,20]

The present case adds to the limited but growing literature supporting the use of inverted ILM flap technique in PDR-related secondary FTMH. While idiopathic FTMH repair with inverted ILM flap has become nearly standard of care in many vitreoretinal surgical centers, the extension of this technique to the PDR population remains less common and less well-reported. Future larger case series, prospective comparisons, or meta-analyses comparing conventional ILM peeling versus the inverted flap technique specifically in PDR-related FTMH would strengthen the evidence base and potentially lead to more widespread adoption of this technique in this challenging patient population. This case demonstrates favorable outcomes compared with similar cases in the literature, with achievement of hole closure and meaningful visual improvement (1/60) despite extensive baseline disease (Table 4).

Table 4. Comparison with previously published cases of PDR-related FTMH or TRD.

Study	Patient/Condition	Surgical technique	Tamponade	Outcome
Smith et al. (2015)	62M with PDR/TRD	Standard ILM peeling + SO	SO 5000cSt	Retinal reattachment, BCVA 1/120
Kumar et al. (2018)	55F with PDR/FTMH	Inverted ILM flap + PFO	Perfluorooctane gas	Hole closure, BCVA 1/100
Obeid et al. (2019)	58M with PDR/superior RD	Membrane peeling only	SF6 gas	Partial reattachment, limited functional gain
Present case (2024)	61M with PDR/TRD/FTMH	Inverted ILM flap + staged 2nd surgery	SO 5000cSt + air	Complete reattachment, hole closure, BCVA 1/60

4. Conclusion

Secondary full-thickness macular hole occurring in the setting of proliferative diabetic retinopathy with extensive tractional retinal detachment represents a rare and challenging surgical scenario. The present case demonstrates that despite severe baseline disease complicated by 15 years of poorly controlled diabetes mellitus, chronic kidney disease, cardiovascular disease, pseudophakic status with previous posterior capsule rupture, and advanced pathology including superior tractional detachment and large FTMH, comprehensive vitreoretinal surgery incorporating modern techniques can achieve meaningful anatomical and functional recovery. The stepwise surgical strategy, incorporating preoperative intravitreal bevacizumab anti-VEGF therapy, comprehensive 360-degree pars plana vitrectomy with complete tractional tissue removal, inverted internal limiting membrane flap placement over the macular hole, silicone oil tamponade, and subsequent staged re-vitrectomy for management of delayed redetachment, yielded excellent results. The patient achieved complete retinal reattachment with normalized macular anatomy on imaging, improvement in visual acuity from light perception (1/300) to count fingers (1/60), and excellent intraocular pressure control at 10 mmHg.

The inverted ILM flap technique, while well-established for idiopathic FTMH repair, remains under-utilized in PDR-related secondary FTMH. This case provides evidence supporting the application of this technique in the PDR population and demonstrates its effectiveness in achieving hole closure even in the context of extensive diabetic retinal pathology. The successful outcome highlights several key principles: (1) meticulous patient selection and preoperative evaluation including cardiovascular and endocrinology assessment; (2) strategic use of preoperative anti-VEGF therapy to suppress neovascularization and reduce operative hemorrhage risk; (3) comprehensive, careful surgical technique with 360-degree membrane removal and adequate endolaser treatment; (4) appropriate choice of tamponade agent based on individual clinical circumstances; (5) recognition that staged procedures may be necessary in complex cases; (6) multidisciplinary medical management optimizing perioperative outcomes; (7) long-term follow-up to monitor for late complications and assess durability of repair.

While the functional outcome, though improved, remains reduced compared to the patient's presumed pre-disease baseline, the achievement of retinal reattachment, macular hole closure, and meaningful vision improvement in a patient with such extensive baseline disease represents a successful application of modern vitreoretinal surgical techniques. This case contributes to the limited literature on this rare complication and supports consideration of the inverted ILM flap technique in future cases of secondary FTMH in PDR. Future prospective studies comparing surgical approaches in this population would be valuable to further establish optimal management strategies and clarify the roles of various technical modifications in determining outcomes.

5. References

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