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Original Article

Comparison of Bleb Morphology Following Trabeculectomy with and Without Mitomycin-C in primary open-angle glaucoma or primary angle-closure glaucoma

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ABSTRACT

Introduction: Glaucoma is the second leading cause of blindness worldwide, mainly through primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PACG). Trabeculectomy is the standard surgery for reducing intraocular pressure (IOP), but scarring can cause bleb failure. Mitomycin-C (MMC) improves outcomes by inhibiting fibroblast growth. **Aim of this study:** To compare bleb morphology following trabeculectomy with and without MMC in POAG and PACG patients and to correlate morphological features with IOP control, surgical success, and complications. **Methods & Materials:** This study at the National Institute of Ophthalmology Hospital (NIOH) and Shaheed Suhrawardi Medical college and Hospital, Dhaka, Bangladesh, from April 2024 to March 2025 involved 120 patients with uncontrolled POAG or PACG undergoing trabeculectomy—60 in MMC group and 60 in non-MMC group. The MMC group received 0.4 mg/ml MMC for 3 minutes. Bleb morphology was assessed via slit-lamp and AS-OCT. Postoperative IOP, success, and complications were recorded at 12 months. **Results:** The MMC group showed better bleb morphology, with more diffuse avascular (63.3% vs 36.7%) and thin polycystic (33.3% vs 6.7%) blebs, while the non-MMC group had more flat vascularized (46.7% vs 3.3%) and encapsulated (10.0% vs 0%) blebs (p=0.004). AS-OCT revealed MMC blebs had thinner walls (80–120 µm vs 110–450 µm), greater height (1.89–2.34 mm vs 1.45–1.92 mm), lower reflectivity (0.7–0.9 vs 0.9–2.6), and larger fluid spaces (0.85–1.42 mm vs 0.04–1.15 mm). The MMC group achieved greater IOP reduction (57.1% vs 35.8%, p<0.001), higher success rates (70.0% vs 30.0%, p<0.001), and had lower bleb fibrosis (3.3% vs 36.7%, p<0.001). **Conclusion:** MMC-augmented trabeculectomy yields better bleb morphology, diffuse, avascular, thin, polycystic, leading to superior IOP control, higher success, and less fibrosis than conventional surgery. Low-dose, short MMC use is safe and effective in primary glaucoma.

Keywords: *Bleb morphology, trabeculectomy, mitomycin-C, POAG, PACG, intraocular pressure, anterior segment OCT*

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INTRODUCTION

Glaucoma is the second leading cause of blindness globally and the main cause of irreversible vision loss, marked by worsening optic nerve damage and visual field deficits [1,2]. The two most common types are primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PACG), with PACG being especially frequent in Asian populations [2]. Elevated intraocular pressure (IOP) is the key modifiable risk factor, and reducing IOP significantly has been proven to slow the disease's progression [3]. If medications and laser treatments do not lower IOP to the desired level, surgical intervention is necessary. Trabeculectomy, introduced by Cairns in 1968, remains the gold standard filtration procedure for lowering IOP [4]. The procedure creates a fistula allowing aqueous humor to drain from the anterior chamber to the subconjunctival space, forming a filtering bleb [5]. However, the natural wound healing process—characterized by fibroblast proliferation and subconjunctival scarring frequently leads to bleb failure and inadequate IOP control[6]. The degree of fibrotic response varies considerably and is influenced by factors including age, ethnicity, and duration of preoperative topical medication[7]. The introduction of mitomycin-C (MMC) as an adjunctive antifibrotic agent has significantly improved surgical outcomes since Chen and colleagues first reported its use in 1983[8]. MMC is an alkylating antibiotic that inhibits DNA synthesis and fibroblast proliferation, preventing excessive scarring at the surgical site [9]. A 2021 systematic review and meta-analysis demonstrated that intraoperative MMC reduces the relative risk of trabeculectomy failure in both high-risk and primary surgery settings [5]. The drug is typically applied intraoperatively at concentrations of 0.2 to 0.4 mg/ml for 2 to 5 minutes[10]. While MMC enhances success by maintaining bleb patency, it produces distinctive thin-walled, avascular, and often cystic blebs that facilitate low IOP but may predispose to late-onset complications, including bleb leakage and infection [11]. The evaluation of bleb morphology has evolved considerably with advances in imaging technology. The Indiana Bleb Appearance Grading Scale (IBAGS) provides a validated clinical system for assessing bleb height, horizontal extent, vascularity, and leakage [12]. A 2025 study comparing IBAGS with three-dimensional anterior segment OCT found that IBAGS variables explained approximately 16% of variance in IOP, with a significant negative relationship between bleb height and IOP (for each unit increase in bleb height, IOP decreased by

1.9 mmHg; p=0.03)[13]. This suggests that clinical grading may be more relevant for predicting surgical success than quantitative imaging alone[13]. Anterior segment optical coherence tomography (AS-OCT) allows non-invasive, high-resolution assessment of bleb architecture, including wall thickness, fluid spaces, and reflectivity[14,15]. A systematic review of 52 studies confirmed that AS-OCT bleb parameters such as height, wall thickness, fluid cavity size, and reflectivity are significantly linked to IOP control after trabeculectomy [16]. Chelerkar et al. showed that successful blebs have multiform reflectivity and large cystic spaces on AS-OCT, while fibrosed blebs show very high reflectivity with no hyporeflective areas [17]. AS-OCT can detect changes in encapsulation weeks before clinical signs, enabling timely postoperative intervention[18]. Limited studies have compared bleb morphology between POAG and PACG after trabeculectomy. PACG involves angle crowding and pupillary block, which may affect wound healing and bleb development differently than POAG [3]. Data indicate both subtypes achieve significant IOP reduction with MMC-augmented surgery, with similar bleb outcomes at 12 months [17]. The aim of this study was to compare bleb morphology with and without MMC in POAG and PACG, and correlate features with IOP control, success, and complications. groups.

Materials and Methods

This cross-sectional study was carried out at the National Institute of Ophthalmology and Hospital NIOH and Shaheed Suhrawardi Medical college and Hospital, Sher-E-Bangla Nagar, Dhaka, Bangladesh, from April 2024 to March 2025. A total of 120 patients diagnosed with primary open-angle glaucoma (POAG) or primary angle-closure glaucoma (PACG) were enrolled through non-random purposive sampling, with 60 assigned to the MMC group and 60 to the non-MMC group. All underwent trabeculectomy as the primary surgical method for medically uncontrolled glaucoma. Patients were divided into two groups: those in the MMC group received intraoperative mitomycin-C (0.4 mg/ml applied for 3 minutes under the scleral flap with a soaked sponge), while the non-MMC group underwent standard trabeculectomy without antifibrotic agents.

RESULTS

A total of of 120 patients, 60 in the MMC group and 60 in the non-MMC group, completed the 12-month follow-up. Baseline traits, including age, gender, glaucoma subtype, preoperative IOP, and medications, showed no significant differences (p>0.05), ensuring comparable groups. Bleb morphology was classified into four types: diffuse avascular, thin polycystic, flat vascularized, and encapsulated, assessed via slit-lamp. Anterior segment OCT measured bleb wall thickness, height, intrableb reflectivity, and subconjunctival fluid. Postoperative IOP, success rates—complete (IOP ≤21 mmHg without meds), qualified (with meds), failure (IOP >21), and complications were compared.

Table 1

Baseline Characteristics (*n*=120).

Parameter		MMC Group (n=60)	Non-MMC Group (n=60)	P Value
Demographic Profile	Mean Age (years)	58.4 ± 11.2	55.7 ± 10.8	0.18
	Age Range (years)	40–79	41–78	–
	Male	35 (58.3%)	32 (53.3%)	0.58
	Female	25 (41.7%)	28 (46.7%)	0.58
Glaucoma Type	POAG	28 (46.7%)	26 (43.3%)	0.71
	PACG	32 (53.3%)	34 (56.7%)	0.71
Ocular Parameters	Preoperative IOP (mmHg)	27.5 ± 8.3	26.8 ± 7.9	0.42
	Preoperative Medications (n)	2.4 ± 0.9	2.3 ± 0.8	0.56
	Mean Glaucoma Duration (years)	4.2 ± 2.1	3.9 ± 1.9	0.32

Table I shows that the baseline characteristics were comparable between the MMC and non-MMC groups with no statistically significant differences (p>0.05 for all parameters). Both groups had similar age distributions, gender ratios, glaucoma subtype distributions, preoperative IOPs, and medication use, ensuring a valid comparison of outcomes.

Table II

Comparison of Bleb Morphology Distribution (*n*=120).

Bleb Type	MMC Group (n=60)	Non-MMC Group (n=60)	P Value
Diffuse Avascular	38 (63.3%)	22 (36.7%)	0.004*
Thin Polycystic	20 (33.3%)	4 (6.7%)	
Flat Vascularized	2 (3.3%)	28 (46.7%)	
Encapsulated	0 (0%)	6 (10.0%)	

**Statistically significant (χ^2=18.45, DF=3)*

Table II shows bleb morphology via slit-lamp, classified as diffuse avascular, thin polycystic, flat vascularized, or encapsulated. The MMC group had more diffuse avascular (63.3% vs 36.7%) and thin polycystic (33.3% vs 6.7%) blebs; the non-MMC group had flat vascularized (46.7% vs 3.3%) and encapsulated (10.0% vs 0%) blebs. Morphology differed significantly (p=0.004).

Table III
Comparison of AS-OCT Parameters by Bleb Type (*n*=120).

Bleb Type	Group	Wall Thickness (µm)	Bleb Height (mm)	Reflectivity (0-3)	Fluid Space (mm)
Diffuse Avascular	MMC	120 ± 40	1.89 ± 0.51	0.9 ± 0.4	0.85 ± 0.32
	Non-MMC	180 ± 50	1.45 ± 0.42	1.2 ± 0.5	0.52 ± 0.24
Thin Polycystic	MMC	80 ± 30	2.34 ± 0.62	0.7 ± 0.3	1.42 ± 0.56
	Non-MMC	110 ± 40	1.92 ± 0.48	0.9 ± 0.4	1.15 ± 0.48
Flat Vascularized	MMC	250 ± 60	0.52 ± 0.18	2.1 ± 0.5	0.12 ± 0.08
	Non-MMC	320 ± 80	0.48 ± 0.15	2.3 ± 0.6	0.08 ± 0.05
Encapsulated	MMC	–	–	–	–
	Non-MMC	450 ± 100	0.56 ± 0.20	2.6 ± 0.5	0.04 ± 0.02

Table III shows AS-OCT measurements of bleb wall thickness, height, reflectivity, and fluid space, highlighting differences between MMC and non-MMC groups across bleb types. MMC-treated blebs had thinner walls (30–70 µm), greater height (0.04–0.44 mm), lower reflectivity (0.2–0.3), and larger fluid spaces (0.04–0.33 mm) than non-MMC blebs of the same type. Thin polycystic blebs in the MMC group had the thinnest walls (80 µm) and largest fluid spaces (1.42 mm), while encapsulated blebs in the non-MMC group had the thickest walls (450 µm) and highest reflectivity (2.6).

Table IV
Comparison of Postoperative IOP and Success Rate by Bleb Type (*n*=120).

Bleb Type	Group	Postop IOP (mmHg)	Complete Success	Qualified Success	Failure
Diffuse Avascular	MMC	10.8 ± 3.2	28 (73.7%)	10 (26.3%)	0
	Non-MMC	14.8 ± 4.5	12 (54.5%)	8 (36.4%)	2 (9.1%)
Thin Polycystic	MMC	11.2 ± 3.8	14 (70.0%)	6 (30.0%)	0
	Non-MMC	15.2 ± 4.8	2 (50.0%)	1 (25.0%)	1 (25.0%)
Flat Vascularized	MMC	16.5 ± 4.1	0	1 (50.0%)	1 (50.0%)
	Non-MMC	19.6 ± 5.2	4 (14.3%)	8 (28.6%)	16 (57.1%)
Encapsulated	MMC	–	–	–	–
	Non-MMC	22.4 ± 5.8	0	1 (16.7%)	5 (83.3%)

Table IV compares postoperative IOP and success rates between the MMC and non-MMC groups for each bleb type. For each bleb type, the MMC group achieved lower postoperative IOP (by 3.1–4.0 mmHg) and higher complete success rates compared to the non-MMC group. Diffuse avascular blebs in the MMC group had the best outcomes (IOP 10.8 mmHg, 73.7% complete success), while encapsulated blebs in the non-MMC group had the worst (IOP 22.4 mmHg, 83.3% failure).

Table V
Comparison of IOP Reduction by Bleb Type (*n*=120).

Bleb Type	Group	Preop IOP (mmHg)	Postop IOP (mmHg)	IOP Reduction (mmHg)	IOP Reduction (%)
Diffuse Avascular	MMC	27.2 ± 8.1	10.8 ± 3.2	16.4 ± 4.9	60.30%
	Non-MMC	26.5 ± 7.6	14.8 ± 4.5	11.7 ± 3.1	44.20%
Thin Polycystic	MMC	27.8 ± 8.5	11.2 ± 3.8	16.6 ± 4.7	59.70%
	Non-MMC	27.2 ± 8.2	15.2 ± 4.8	12.0 ± 3.4	44.10%
Flat Vascularized	MMC	28.1 ± 7.9	16.5 ± 4.1	11.6 ± 3.8	41.30%
	Non-MMC	27.0 ± 7.8	19.6 ± 5.2	7.4 ± 2.6	27.40%
Encapsulated	MMC	–	–	–	–
	Non-MMC	26.8 ± 8.0	22.4 ± 5.8	4.4 ± 2.2	16.40%
Overall	MMC	27.5 ± 8.3	11.8 ± 3.6	15.7 ± 4.5	57.1%
	Non-MMC	26.8 ± 7.9	17.2 ± 5.1	9.6 ± 3.3	35.8%

($p<0.001$ for overall comparison, significant)

Table V presents the IOP reduction comparisons between the MMC and non-MMC groups for each bleb type. MMC group achieved a significantly greater overall IOP reduction (57.1% vs 35.8%). For each bleb type, the MMC group achieved a higher IOP reduction (13.9–16.1%). Diffuse avascular and thin polycystic blebs in the MMC group had the best IOP reduction (59.7–60.3%), while encapsulated blebs in the non-MMC group had the poorest (16.4%).

Table VI
Comparison of Complications by Bleb Morphology (n=120).

Complication	Diffuse Avascular		Thin Polycystic		Flat Vascularized		Encapsulated	
	MMC (n=38)	Non-MMC (n=22)	MMC (n=20)	Non-MMC (n=4)	MMC (n=2)	Non-MMC (n=28)	MMC (n=0)	Non-MMC (n=6)
Bleb Fibrosis	2 (5.3%)	2 (9.1%)	0	0	0	16 (57.1%)	0	4 (66.7%)
Encapsulated Bleb	0	0	0	0	0	6 (21.4%)	0	0
Anterior Uveitis	8 (21.1%)	6 (27.3%)	6 (30.0%)	2 (50.0%)	0	8 (28.6%)	0	2 (33.3%)
Corneal Edema	10 (26.3%)	8 (36.4%)	8 (40.0%)	2 (50.0%)	0	10 (35.7%)	0	2 (33.3%)
Cataract Formation	5 (13.2%)	3 (13.6%)	5 (25.0%)	1 (25.0%)	0	4 (14.3%)	0	1 (16.7%)
Patients ≥1 Complication	25 (65.8%)	17 (77.3%)	16 (80.0%)	4 (100%)	0	26 (92.9%)	0	6 (100%)

Table VI demonstrates that the overall complication rate was higher in the non-MMC group across all bleb types. Complications in diffuse avascular blebs occurred in 65.8% of MMC patients compared to 77.3% of non-MMC patients. For thin polycystic blebs, 80.0% of MMC patients experienced complications, while 100% of non-MMC patients did. In the non-MMC group, flat vascularized blebs had a 92.9% complication rate, and encapsulated blebs reached 100%. Bleb fibrosis was notably the most significant difference between groups, affecting 5.3% of MMC patients with diffuse avascular blebs and none of the other MMC blebs. Non-MMC patients with flat, vascularized, and encapsulated blebs had fibrosis rates of 57.1% and 66.7%, respectively. Encapsulated bleb formation was exclusive to non-MMC patients (21.4% in flat vascularized). Anterior uveitis and corneal edema were more frequent in non-MMC, especially among those with thin polycystic blebs (50.0%). Cataract formation was similar between groups, with a slight increase in MMC patients with thin polycystic blebs (25.0%).

DISCUSSION

This study compared bleb morphology after trabeculectomy with or without mitomycin C (MMC) in patients with POAG and PACG. 120 patients were followed for 12 months. Results show MMC-augmented trabeculectomy yields better bleb morphology, improved IOP control, higher success rates, and less bleb fibrosis than conventional surgery.

The baseline characteristics of both groups were similar, with no significant differences in age, gender distribution, glaucoma subtype, preoperative IOP, or the number of anti-glaucoma medications ($p>0.05$ for all comparisons). This consistency suggests that any differences in outcomes are likely attributable to the intervention (MMC use), rather than to baseline disparities. The average age in our study (58.4 ± 11.2 years for the MMC group and 55.7 ± 10.8 years for the non-MMC group) aligns with other research on trabeculectomy outcomes in primary glaucoma patients, such as the 2021 study by Chelerkar et al., which reported mean ages of 64.26 years and 64.03 years in the MMC and Ologen groups, respectively[17]. The higher prevalence of PACG (53.3% in MMC, 56.7% in non-MMC) mirrors the greater occurrence of angle-closure glaucoma in Asian populations, as noted by Tham et al.[2].

Bleb morphology analysis with slit-lamp showed key differences. The MMC group had mainly diffuse avascular (63.3%) and thin polycystic (33.3%) blebs, while the non-MMC group showed flat vascularized (46.7%) and encapsulated (10.0%) blebs, a significant difference ($p=0.004$). These findings support that MMC promotes avascular, thin, cystic blebs by reducing fibroblast growth and vascular ingrowth [9,11]. The higher diffuse avascular bleb rate in the MMC group aligns with Kitazawa et al.'s report of these blebs' excellent IOP control [19]. The lack of encapsulated blebs in the MMC group and their 10.0% presence in the non-MMC group is notable. Encapsulated blebs or Tenon's cysts, which impair outflow, occur in 8-28% post-trabeculectomy [20], and our 10% rate in the non-MMC group fits this range. Their absence in the MMC group confirms its antifibrotic effect in preventing Tenon's cysts [21].

AS-OCT analysis showed morphological differences: MMC-treated blebs were thinner (30–70 µm), taller (0.04–0.44 mm), less reflectant, and had larger fluid spaces (0.04–0.33 mm) than non-MMC blebs. MMC blebs were thin, cystic with 80 µm walls and 1.42 mm fluid spaces; non-MMC blebs had thicker, more reflective walls (450 µm) and fewer fluid spaces. These findings align with prior studies. Chelerkar et al. noted 92% of MMC and 90% of Ologen patients had multiform reflectivity with cystic spaces, indicating functioning blebs [17]. Singh et al. described low reflectivity blebs with visible fluid [14]. Kallab et al. linked bleb size and shape to IOP control [16]. Lower reflectivity suggests aqueous humor and functioning blebs [22], while high reflectivity indicates fibrosis and failure [23]. Ahmadzadeh et al. found bleb height correlates with IOP reduction, supporting morphology's role in IOP control.[13]

The study found a strong link between bleb shape and intraocular pressure (IOP) control in both groups. In the MMC group, diffuse avascular and thin polycystic blebs had postoperative IOPs of 10.8 ± 3.2 mmHg and 11.2 ± 3.8 mmHg, with success rates of 73.7% and 70.0%. The non-MMC group showed diffuse avascular blebs with mean IOP of 14.8 ± 4.5 mmHg and a 54.5% success rate. Flat vascularized and encapsulated blebs had higher IOPs, with failure rates of 57.1% and 83.3%. Overall, IOP reduction was more significant in the MMC group (57.1% vs 35.8%) in the non-MMC group ($p<0.001$). These results align with Chelerkar et al., who reported postoperative IOPs of 14.09 ± 3.1 mmHg in MMC and 13.25 ± 2.5 mmHg in Ologen groups after 12 months, with no difference[17]. A 2021 study found that MMC 0.02% led to mean IOPs of 9.0 ± 3.6 mmHg versus 12.8 ± 4.0 mmHg with releasable versus fixed sutures[24]. Our MMC success rate of 70.0% matches Casson et al., who reported 80.9% at 3 years and 67% at 5 years with 0.02% MMC for 2 minutes[25]. A 2021 study showed success rates of 61.5% for trabeculectomy and 75.6% for drainage devices at 24 months[26]. The 30.0% success rate in our non-MMC group reflects typical trabeculectomy failure, where about 35% of blebs fail due to fibrosis within five years[7].

In the MMC group, no significant bleb morphology difference was found between POAG and PACG patients ($p=0.63$). In contrast, PACG patients in the non-MMC group had more encapsulated blebs (11.8%) compared to POAG patients (7.7%) ($p=0.05$). This suggests PACG eyes may have a stronger wound healing response due to inflammation or anatomy, aligning with Chelerkar et al., who noted greater bleb thinning with higher MMC concentrations[17]. The tendency for encapsulation in PACG could relate to longer medication use or inflammation from angle-closure episodes[7].

The complication profile varied between groups. Bleb fibrosis was higher in the non-MMC group (36.7% vs 3.3%, $p<0.001$), and encapsulated bleb formation occurred only there (10.0%, $p=0.01$). These confirm MMC's role in preventing fibrotic complications[9,21]. Thin polycystic blebs in the MMC group linked to higher rates of anterior uveitis (33.3%), corneal edema (41.7%), and cataract (25.0%), with an overall complication rate of 83.3%. This aligns with known MMC-related issues like epithelial defects and thin cystic blebs[11]. No ocular hypotony or bleb-related endophthalmitis cases were seen, likely due to low MMC (0.4 mg/ml), short application (3 mins), and careful technique[27]. The higher cataract rate in MMC patients (16.7% vs 15.0%) matches prior findings, possibly from MMC toxicity or increased inflammation[28]. Vahedian et al. found triamcinolone improves bleb morphology safely by reducing vascularity and height, and increasing extent, suggesting postoperative management can be optimized[29].

Our findings align with previous studies on MMC-augmented and conventional trabeculectomy. The 70% success rate in the MMC group is similar to Beatty et al.'s 72.2% and Palmer's 84%[10,30]. The absence of encapsulated blebs supports Kitazawa et al.'s observation that MMC prevents Tenon's cysts[21]. The 57.1% IOP reduction mirrors V.P. Costa et al.'s 65.5%, reducing from 28.4 mmHg to 9.8 mmHg[31]. The non-MMC group's 35.8% reduction aligns with literature[7,32]. Our complication rates are lower; Zacharia et al. reported 32.7% ocular hypotony after MMC[28]. The absence in our study (0%) may result from shorter exposure (3 min) and thorough irrigation, lowering tissue concentration 5–15 fold[9].

LIMITATIONS

A sample of 60 patients per group is adequate for detecting significant differences but may miss rare complications like endophthalmitis. A 12-month follow-up is short for assessing long-term bleb survival and late complications. Longer follow-up is needed for durable IOP control and infection risk. Non-random purposive sampling could introduce bias, but similar baseline traits suggest minimal effect. Different surgeons performed surgeries, possibly causing variability, though all were experienced and followed a standard protocol.

CONCLUSION

MMC-augmented trabeculectomy produces superior bleb morphology with diffuse, avascular, thin polycystic blebs, leading to significantly better IOP control (57.1% reduction), higher success rates (70.0%), and lower bleb fibrosis (3.3%) than conventional trabeculectomy. PACG patients in the non-MMC group showed more encapsulated bleb formation than POAG patients. AS-OCT offers quantitative bleb assessment correlating with success, while IBAGS better predicts IOP outcomes. MMC is a safe, effective adjunct with low-dose, short-duration use to minimize severe complications. Future larger, longer, randomized studies are needed, and comparisons with agents like 5-fluorouracil and Ologen are warranted. Further research should explore MMC's differential effects in POAG versus PACG, especially the higher encapsulation risk in PACG.

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