Original Article

Effects of Trabeculectomy with Mitomycin-C (MMC) and without MMC in Primary Open Angle Glaucoma and Primary Angle Closure Glaucoma on 50 Cases A: Multicenter Study

Tussie R[1], Sharif AQMO[2], Sharmee TH[3], Shipu ZR[4], Ferdous J[5], Sarkar S[6], Alam MR[7]

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ABSTRACT:

Background: *Glaucoma is a leading cause of irreversible blindness worldwide. Trabeculectomy is the standard surgical procedure for controlling raised intraocular pressure (IOP) when medical treatment fails. Mitomycin-C (MMC) is used as an adjunct to improve surgical success by reducing postoperative fibrosis.*

Objective: *To evaluate the effects of trabeculectomy with MMC and without MMC in Primary Open Angle Glaucoma (POAG) and Primary Angle Closure Glaucoma (PACG) patients.*

Methods: *This prospective interventional study was conducted at National Institute of Ophthalmology and Hospital & Shaheed Suhrawardy Medical College and Hospital from January 2023 to December 2023. A total of 50 patients were included by purposive sampling. Among them, 30 patients underwent trabeculectomy with MMC and 20 underwent trabeculectomy without MMC. Patients were grouped as POAG and PACG cases. Preoperative and postoperative IOP, bleb morphology, surgical success, and complications were assessed during follow-up.*

Results: *In the MMC group (n=30), 14 (46.67%) were male and 16 (53.33%) were female, with mean age 54.7 years. In the non-MMC group (n=20), 6 (30%) were male and 14 (70%) were female, with mean age 51.05 years. In POAG patients, complete success (IOP <21 mmHg) was achieved in 100% of MMC-treated cases versus 44.44% in non-MMC cases (p<0.006). In PACG patients, complete success was achieved in 93.75% of MMC-treated cases compared with 36.36% in non-MMC cases (p<0.007).*

Conclusion: *Trabeculectomy with MMC was more effective than conventional trabeculectomy in maintaining bleb patency and reducing IOP in both POAG and PACG patients. MMC-augmented trabeculectomy is a safe and effective option for glaucoma surgery.*

Key Words:
Trabeculectomy, Mitomycin-C, Filtering Bleb.

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Authors:

1. Rumana Tussie; Assistant Professor, Department of Ophthalmology, Shaheed Suhrawardy Medical College, Dhaka.
2. AQM Omar Sharif; Associate Professor, Department of Ophthalmology, Shaheed Suhrawardy Medical College, Dhaka
3. Tania Hussain Sharmee; Associate Professor, Department of Ophthalmology, Shaheed Suhrawardy Medical College, Dhaka
4. Zinat Rehana Shipu; Assistant Professor, Department of Ophthalmology, Shaheed Suhrawardy Medical College, Dhaka.
5. Jannatul Ferdous; Assistant Professor, Department of Ophthalmology, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh
6. Suprokash Sarkar; Assistant Professor, Department of Ophthalmology, Shaheed Suhrawardy Medical College, Dhaka,
7. Md. Raqibul Alam; Associate Professor, Department of Otolaryngology, Tangail Medical College, Tangail.

Correspondence:
Dr. Rumana Tussie, Assistant Professor, Department of Ophthalmology, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh;
Email: rumanaalam1977@gmail.com. Mobile: 01716497487

Introduction

Glaucoma is one of the leading causes of blindness worldwide and is also an important cause of preventable blindness. Visual impairment due to glaucoma presents a major challenge to ophthalmologists and public health planners because the disease is usually chronic, progressive, and irreversible once optic nerve damage has occurred. Since glaucoma commonly remains asymptomatic until advanced stages, it is often described as the "sneak thief of sight". Patients may remain unaware of the disease until marked peripheral visual loss develops, making early diagnosis and timely treatment essential [1-3].

Unlike many ocular disorders, glaucoma is a lifelong disease that can be controlled but not cured. Successful management requires regular follow-up, adherence to medication, and sometimes repeated interventions. Similar to chronic systemic diseases such as diabetes mellitus or hypertension, glaucoma demands long-term patient compliance and continuous monitoring to prevent progression of visual disability [2,3].

According to the World Health Organization, glaucoma is the second leading cause of blindness globally. In Bangladesh, glaucoma is an emerging public health concern. A population-based survey conducted in Dhaka division reported that among people aged 40 years and above, the prevalence of definite and probable glaucoma was 2.1%, with an estimated 5,86,000 affected individuals in this age group [4]. These findings indicate a substantial burden of undiagnosed and untreated glaucoma in the country.

Glaucoma refers to a group of diseases characterized by progressive optic neuropathy associated with loss of retinal ganglion cells, optic disc cupping, and corresponding visual field defects. Although multiple mechanisms are involved in its pathogenesis, elevated intraocular pressure (IOP) remains the most important and only modifiable risk factor. Reduction of IOP has been proven to slow the progression of optic nerve damage and preserve visual function in most patients [5-7]. Therefore, the principal aim of glaucoma treatment is too lower IOP to a level at which further damage is minimized.

Medical therapy with topical anti-glaucoma drugs is usually the first line of treatment. However, some patients continue to show progressive visual field loss or uncontrolled IOP despite maximum tolerated medical therapy and laser procedures. In such cases, surgical intervention becomes necessary. Bringing IOP into the low normal range, often 17 mmHg or less, can arrest or significantly slow disease progression in the majority of cases [8,9].

Trabeculectomy, first introduced by John Cairns, remains the gold standard filtering surgery for medically uncontrolled glaucoma. The procedure lowers IOP by creating a fistula that allows aqueous humor to drain into the subconjunctival space, forming a filtering bleb. However, postoperative wound healing and subconjunctival fibrosis may obstruct the fistula and cause surgical failure [8,9].

To improve surgical success, antimetabolites have been used as adjuncts during trabeculectomy. Since 1983, intraoperative antimetabolites such as 5-fluorouracil (5-FU) and Mitomycin-C (MMC) have significantly increased filtration success rates, especially in eyes at high risk of scarring [10,11]. MMC is an alkylating agent that inhibits DNA replication, mitosis, and protein synthesis. It suppresses fibroblast proliferation and vascular ingrowth, thereby reducing postoperative subconjunctival scarring and maintaining bleb function. MMC is considered more potent than 5-FU [9,11].

The indications for MMC include previous failed filtration surgery, prior intraocular operations, prolonged topical anti-glaucoma medication use, young age, secondary glaucoma, and eyes with excessive healing response. Long-term use of topical anti-glaucoma medications has been associated with increased inflammatory cells and fibroblasts in conjunctival tissues, which may reduce the success rate of future filtering surgery [12-14]. Intraoperative application of MMC has also been shown to improve the success rate of initial trabeculectomy in primary glaucoma [15].

Despite its benefits, MMC may be associated with complications such as corneal epithelial defects, thin cystic bleb formation, ocular hypotony, late bleb leakage, scleral melting, hypotony maculopathy, ciliary body toxicity, and endophthalmitis [7]. Therefore, the dose and duration of exposure must be carefully selected. Commonly used concentrations range from 0.2 to 0.4 mg/ml for 2 to 5 minutes depending on risk factors such as age, prior surgery, duration of medical treatment, and tendency toward wound scarring [16,18].

In the present study, the outcomes of trabeculectomy with Mitomycin-C and without MMC were evaluated in patients with Primary Open Angle Glaucoma and Primary Angle Closure Glaucoma treated at National Institute of Ophthalmology and Hospital. The study was designed to compare postoperative IOP control, visual outcomes, and complications in order to determine the effectiveness and safety of MMC use in our population.

Objectives

The main objective was to evaluate the effects of trabeculectomy with and without Mitomycin-C (MMC) in Primary Open Angle Glaucoma and Primary Angle Closure Glaucoma patients.

Methodology & Materials

This prospective interventional study was conducted at National Institute of Ophthalmology and Hospital & Shaheed Suhrawardy Medical College and Hospital from January 2023 to December 2023 to evaluate the effects of trabeculectomy with Mitomycin-C (MMC) and without MMC in patients with Primary Open Angle Glaucoma (POAG) and Primary Angle Closure Glaucoma (PACG). A total of 50 consecutive patients diagnosed with POAG or PACG who fulfilled the selection criteria were enrolled by non-random purposive sampling. All patients were selected for first-time trabeculectomy after failure of adequate medical treatment.

The study population was divided into two major groups. Group A included POAG patients who underwent trabeculectomy and was further subdivided into Group A1 (trabeculectomy with MMC) and Group A2 (trabeculectomy without MMC). Group B included PACG patients who underwent trabeculectomy and was further subdivided into Group B1 (trabeculectomy with MMC) and Group B2 (trabeculectomy without MMC).

Patients of both sexes aged 40 to 80 years having Primary Open Angle Glaucoma or Primary Angle Closure Glaucoma with inadequate control on medical therapy were included. Patients with concomitant corneal or retinal disease, previous intraocular or filtration surgery, secondary glaucoma, use of immunosuppressive drugs, and age below 40 years or above 80 years were excluded from the study.

Detailed history, physical examination, complete ophthalmic evaluation, and relevant laboratory investigations were performed in all cases. Baseline assessment included age, sex, visual acuity, slit lamp examination, fundus examination, intraocular pressure measurement, gonioscopy, and optic disc evaluation. All relevant information was recorded in a predesigned data collection sheet.

Trabeculectomy was performed under peribulbar anesthesia using standard aseptic precautions. A fornix-based conjunctival flap was created followed by haemostasis and preparation of a partial thickness scleral flap. In MMC groups, surgical sponges soaked with Mitomycin-C solution (0.4 mg/ml) were applied beneath the conjunctiva and over the scleral bed for 3 minutes, followed by thorough irrigation with Ringer's lactate solution. A trabecular block was excised, peripheral iridectomy was performed, and the scleral flap was closed with interrupted 10-0 nylon sutures. Tenon capsule and conjunctiva were closed in separate layers. In non-MMC groups, the same surgical steps were followed except application of Mitomycin-C.

Postoperatively, all patients received standard antibiotic, steroid, cycloplegic medication, eye padding, and scheduled follow-up visits. Patients were evaluated during follow-up for intraocular pressure control, bleb status, visual outcome, and postoperative complications.

Statistical Analysis: All data were recorded systematically in preformed data collection form and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was carried out by using Statistical analysis was done by using SPSS (Statistical Package for Social Science) Version 20. A p-value of less than 0.05 was considered statistically significant. Confidentially was strictly maintained.

Results

Table 1: Demographic characteristics of study subjects (n = 50)

Study group	Mean Age ± SD (years)	P-value
POAG		
Group A1	59.07± 13.37	0.17*
Group A2	52.44± 8.82	
PACG		
Group B1	51.19±9.28	0.75*
Group B2	49.91 ± 11.30	

Table 1 shows the demographic characteristics of the study subjects. Among POAG patients, the mean age was 59.07±13.37 years in Group A1 and 52.44±8.82 years in Group A2, with no statistically significant difference (p=0.17). Among PACG patients, the mean age was 51.19±9.28 years in Group B1 and 49.91±11.30 years in Group B2, also without significant difference (p=0.75).

Figure 1: Sex distribution of study subjects (n = 50)

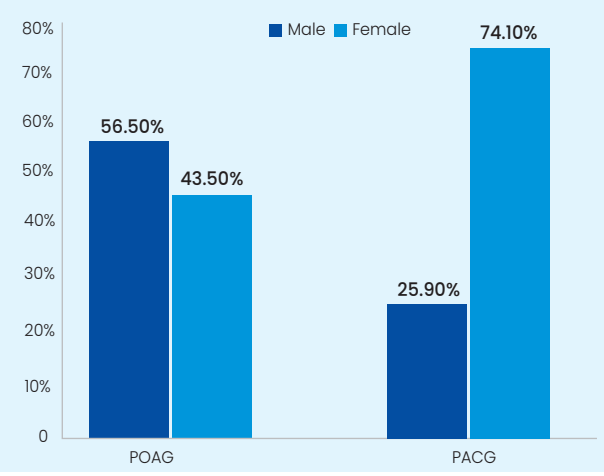

Figure 2 shows distribution of sex among study subjects. Out of 23 cases of group A (POAG patients) male were 13 (56.5%) and female were10 (43.5%). In group B (PACG patients) male were 7(25.9%) and female were20 (74.1%). Sex distribution was statistically significant.

Table 2: Overview of ranges and mean of Preoperative and postoperative IOP in POAG and PACG patients

Parameter	POAG		PACG	
	Group A1	Group A2	Group B1	Group B2
Preoperative IOP (mmHg)	27.17 ± 4.10 (22–36)	25.44 ± 6.10 (22–32)	38.36 ± 7.10 (24–50)	32.36 ± 6.30 (24–36)
Postoperative IOP (mmHg)	11.29 ± 4.03 (8–16)	15.78 ± 4.60 (10–24)	11.88 ± 5.04 (8–18)	17.82 ± 5.20 (10–32)

Table 2 shows the comparison of preoperative and postoperative intraocular pressure (IOP). In POAG patients, mean IOP decreased from 27.17±4.10 mmHg to 11.29±4.03 mmHg in Group A1 and from 25.44±6.10 mmHg to 15.78±4.60 mmHg in Group A2. In PACG patients, mean IOP reduced from 38.36±7.10 mmHg to 11.88±5.04 mmHg in Group B1 and from 32.36±6.30 mmHg to 17.82±5.20 mmHg in Group B2. Greater postoperative IOP reduction was observed in MMC-treated groups.

Table 3: Distribution of IOP status in POAG and PACG patients

IOP (mmHg)	POAG				PACG			
	Group A1 n (%)		Group A2 n (%)		Group B1 n (%)		Group B2 n (%)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
>40	0	0	0	0	5 (31.25%)	0	0	0
31–40	3 (21.43%)	0	2 (22.22%)	0	9 (56.25%)	0	7 (63.64%)	1 (9.09%)
21–30	11 (78.57%)	0	7 (77.78%)	4 (44.45%)	2 (12.5%)	0	4 (36.36%)	4 (36.36%)
11–20	0	9 (64.29%)	0	5 (55.55%)	0	11 (68.75%)	0	6 (55.55%)
6–10	0	5 (35.71%)	0	0	0	5 (31.25%)	0	0

Table 3 shows the distribution of IOP levels before and after surgery. Most patients had preoperative IOP above 21 mmHg, whereas postoperative IOP shifted mainly to the 11–20 mmHg and 6–10 mmHg ranges, especially in MMC-treated groups.

Table 4: Postoperative bleb morphology among study groups

Bleb Type	POAG		P-value	POAG		P-value
	Group A1 n (%)	Group A2 n (%)		Group B1 n (%)	Group B2 n (%)	
Diffuse avascular	9 (64.3%)	6 (66.7%)	0.127	11 (68.8%)	6 (54.5%)	0.05
Thin polycystic	5 (35.7%)	1 (11.1%)		5 (31.3%)	1 (9.1%)	
Flat vascularized	0	2 (22.2%)		0	3 (27.3%)	
Encapsulated	0	0		0	1 (9.1%)	

Table 4 shows postoperative bleb morphology. Diffuse avascular bleb was the commonest finding in all groups. Flat vascularized and encapsulated blebs were more frequent in non-MMC groups. The difference was not significant in POAG (p=0.127) but significant in PACG patients (p=0.05).

Table 5: Early postoperative complications (0–4 weeks)

Complication	POAG		PACG	
	Group A1 n (%)	Group A2 n (%)	Group B1 n (%)	Group B2 n (%)
Shallow anterior chamber	4(28.57%)	3(33.33%)	6 (37.5%)	2 (18.18%)
Anterior uveitis	6 (42.86%)	1(11.11%)	7 (43.75%)	5 (45.45%)
Hyphaema	2 (14.29%)	0	2 (12.5%)	2 (18.18%)
Mild corneal edema	9 (64.28%)	4 (44.44%)	7 (43.75%)	3 (27.27%)
Nonformation of bleb	0	0	0	0
Wound leakage	0	0	0	0
Bleb necrosis	0	0	0	0
Ocular hypotony	0	0	0	0

Table 5 shows early postoperative complications within 4 weeks. Mild corneal edema, anterior uveitis, shallow anterior chamber, and hyphaema were the most common complications. No wound leakage, bleb necrosis, nonformation of bleb, or ocular hypotony was observed.

Table 6: Late postoperative complications (>4 weeks)

Complication	POAG		PACG	
	Group A1 n (%)	Group A2 n (%)	Group B1 n (%)	Group B2 n (%)
Bleb related Endophthalmitis	0	0	0	0
Corneal epithelial defect	0	0	0	0
Cataract formation	3 (21.4%)	1 (11.1%)	5 (31.3%)	2 (18.18%)
Bleb fibrosis	0	2 (22.2%)	0	3 (27.27%)
Encapsulated bleb	0	0	0	1 (9.09%)
Ocular hypotony	0	0	0	0
Scleral necrosis	0	0	0	0

Discussion

Glaucoma is characterized by a progressive optic neuropathy in which intraocular pressure (IOP) remains the most important modifiable risk factor, whether the presenting IOP is elevated or within statistically normal range. Therefore, the principal objective of treatment is to reduce IOP to a level that prevents further optic nerve damage and visual field loss. This may be achieved by medical, laser, or surgical methods, depending on disease severity and response to treatment [5,9]. Trabeculectomy remains the most widely practiced conventional filtration surgery for controlling raised IOP when medical therapy fails. The long-term success of trabeculectomy depends largely on the formation and maintenance of a functioning filtering bleb. Failure commonly occurs because of subconjunctival fibrosis and fibroblastic proliferation at the surgical site. The degree of healing response varies according to several factors such as age, race, previous surgery, inflammation, and tissue pigmentation [8,10,12,19]. The adjunctive use of antimetabolites, particularly Mitomycin-C (MMC), has significantly improved the success rate of trabeculectomy by inhibiting fibroblast proliferation and reducing scar formation at the bleb site [12]. In the present study, trabeculectomy with MMC was compared with conventional trabeculectomy without MMC in patients with Primary Open Angle Glaucoma (POAG) and Primary Angle Closure Glaucoma (PACG) treated at National Institute of Ophthalmology and Hospital & Shaheed Suhrawardy Medical College and Hospital. A total of 50 patients were included, of whom 30 underwent trabeculectomy with MMC and 20 underwent trabeculectomy without MMC. In this study, MMC was applied intraoperatively at a concentration of 0.4 mg/ml for 3 minutes. Similar concentrations and exposure times have been used by other investigators including Ramakrishnan et al. and Kitazawa et al., who reported favorable IOP control and improved bleb survival with MMC-augmented trabeculectomy [14,20]. Palmer also used a lower concentration of 0.2 mg/ml in both primary and repeat trabeculectomy cases [16]. Female predominance was observed in the study population, especially among PACG patients. This finding is consistent with the known higher frequency of angle closure glaucoma in women, likely related to anatomical predisposition such as shallower anterior chamber depth and shorter axial length. The present study demonstrated that trabeculectomy with MMC achieved superior postoperative IOP control compared with trabeculectomy without MMC in both POAG and PACG groups. In POAG patients treated with MMC, complete success was achieved in all eyes after follow-up, whereas non-MMC patients showed a substantially lower success rate and a considerable proportion of failures despite postoperative medication. Similarly, in PACG patients, complete success was markedly higher in the MMC-treated group than in the non-MMC group. These findings indicate that MMC significantly enhances surgical success by maintaining filtration function and preventing bleb scarring. Similar results have been reported by Kitazawa et al., V.P. Costa et al., Casson et al., and other authors [20]. The IOP-lowering effect was also greater in MMC-treated groups. In POAG patients, the percentage reduction of IOP was higher with MMC than without MMC. In PACG patients, postoperative reduction was even more pronounced in the MMC group. These findings suggest that MMC-augmented trabeculectomy is particularly beneficial in eyes with higher preoperative IOP or advanced disease where lower target pressure is required to prevent progression. Postoperative bleb morphology in the current study further supports the effectiveness of MMC. Most MMC-treated eyes developed diffuse avascular or thin functioning blebs, which are generally associated with satisfactory filtration. In contrast, non-MMC groups showed flatter vascularized and encapsulated blebs, reflecting failure due to fibrosis. Similar observations were reported by Kitazawa et al [20]. Tenon's cyst or encapsulated bleb was absent in MMC-treated eyes but present in some non-MMC eyes.

Ophir reported the incidence of encapsulated bleb after routine trabeculectomy to be 8–28%, which is comparable with the present findings [21]. MMC likely reduces such complications through its antifibrotic action. Early postoperative complications such as shallow anterior chamber, anterior uveitis, hyphaema, and mild corneal edema were observed in both groups. These complications were generally mild, responded to conservative management, and had no serious effect on final outcome. No patient required surgical reformation of the anterior chamber. No early wound leakage, severe infection, or corneal epithelial defect was observed. This indicates that trabeculectomy with careful surgical technique and appropriate postoperative care is relatively safe. Late postoperative complications included cataract formation, bleb fibrosis, and occasional encapsulated bleb. Cataract formation was somewhat more frequent in MMC-treated groups, although most cases were visually insignificant. Casson et al. suggested that MMC use may be associated with increased risk of cataract after trabeculectomy, which supports the present observation. Ocular hypotony is one of the most concerning complications after MMC-augmented trabeculectomy. Hypotony may occur because of excessive aqueous outflow or toxic suppression of ciliary body function. However, no case of ocular hypotony was found in this study. Zacharia et al. reported that hypotony occurred more frequently when MMC was used at 0.4 mg/ml for prolonged exposure of 5–7 minutes, but not when exposure time was 3 minutes or less [22]. The absence of hypotony in the present series may therefore be related to controlled exposure time and meticulous surgical technique. No delayed endophthalmitis, scleral necrosis, wound leakage, or bleb necrosis was observed during follow-up. Although thin cystic blebs may carry lifelong risk of blebitis or endophthalmitis, none occurred in this study. Careful handling of conjunctiva, avoidance of excessive tissue damage, separate closure of Tenon's capsule and conjunctiva, and proper postoperative surveillance likely contributed to this favorable outcome [9]. The present study population consisted predominantly of dark-skinned individuals with pigmented eyes. In such patients, increased fibroblastic activity has been suggested as a cause of higher filtration failure. Despite this, excellent success rates were achieved with MMC. Ramakrishnan et al. also reported high success rates with intraoperative MMC in darkly pigmented Southern Indian populations, which correlates with the current findings [14]. Overall, the study demonstrates that trabeculectomy with Mitomycin-C provides better postoperative IOP control, higher surgical success, and more favorable bleb morphology than trabeculectomy without MMC in both POAG and PACG patients. When used in appropriate concentration and exposure time, MMC appears to be a safe and effective adjunct to filtration surgery. Therefore, MMC-augmented trabeculectomy may be considered a preferable surgical option, especially in patients at risk of bleb failure or requiring low target intraocular pressure.

Limitations of the study

This study had a short follow-up period and relatively small sample size with unequal group distribution (30 in MMC group and 20 in non-MMC group), which may limit the generalizability of the findings. Irregular follow-up visits by some patients also affected postoperative assessment. Surgeries were performed by different surgeons, which might have caused minor variation in surgical outcomes. Limited financial support and lack of long-term evaluation of late complications were additional limitations. Larger studies with longer follow-up are recommended.

Conclusion

Mitomycin-C (MMC) has significantly improved the outcome of trabeculectomy by increasing bleb survival and enhancing postoperative intraocular pressure (IOP) control. In this study, trabeculectomy with MMC showed a higher success rate than conventional trabeculectomy without MMC in both Primary Open Angle Glaucoma (POAG) and Primary Angle Closure Glaucoma (PACG) patients. MMC-treated cases demonstrated better maintenance of filtering bleb patency and greater reduction of IOP.

Therefore, primary trabeculectomy with MMC may be considered a preferable option over conventional trabeculectomy in selected POAG and PACG patients to achieve effective long-term IOP control, reduce the need for postoperative anti-glaucoma medication, and minimize the need for repeat surgery. MMC-augmented trabeculectomy appears to be a safe and effective surgical approach for glaucoma management.

Recommendation

A larger randomized clinical trial with longer follow-up duration is recommended to further evaluate the long-term efficacy and complications of MMC in our

population. Future studies should determine the optimum concentration, duration, and method of MMC application for best surgical outcomes. The IOP-lowering benefits of MMC should always be balanced against potential complications such as corneal epithelial defect, ocular hypotony, hypotony maculopathy, bleb necrosis, and cataract formation. For better uniformity of results, surgeries should preferably be performed by a single experienced surgeon or under standardized surgical protocol.

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