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GLAUCOMA

IOP-lowering and drug-sparing effects of trabectome surgery with or without cyclodialysis ab interno

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Abstract

Purpose To compare the postoperative intraocular pressure (IOP) after ab interno trabeculectomy (AIT; trabectome surgery) alone or combined with cyclodialysis ab interno (AITC).

Patients and methods Forty-three eyes with insufficiently controlled open-angle glaucoma were included in this consecutive case series. All eyes received AIT, combined with phacoemulsification and IOL-implantation in phakic instances, with or without additional cyclodialysis ab interno. Postoperative visual acuity, IOP, number of IOP-lowering medications and complications were registered over 12 months.

Results A total of 19 eyes (14 patients) received AIT and 24 (19 patients) received AITC. Both groups were comparable for baseline IOP (AIT: 19.7 ± 8.2 mmHg; AITC: 19.4 ± 6.8 mmHg; $p = 0.96$), there was a comparable IOP reduction after 6 months (AIT: − 3.8 ± 12.3, median (interquartile range (IQR)): − 3.8 (− 7.8–4.8) mmHg; AITC: − 4.9 ± 8.3, median (IQR): − 2.0 (− 10.8–2.0) mmHg; $p = 0.95$) and 12 months (AIT: − 4.3 ± 6.6, median (IQR): − 4.0 (− 8.0 to − 1.0) mmHg; AITC: − 3.7 ± 6.7, median (IQR): − 1.5 (− 5.5 to − 0.5) mmHg; $p = 0.49$). While final visual acuity was similar between the groups, they differed regarding topical IOP-lowering medications (baseline: AIT 2.9 ± 1.2 and AITC 2.9 ± 1.2; 1 year after surgery: AIT 2.6 ± 1.5 ($p = 0.16$) and AITC 1.3 ± 1.3; $p < 0.001$)). Depending on the definition, a complete or qualified success of 33.4–45.8% was achieved in AITC compared to 15.8–21.1% in AIT.

Conclusion The additional suprachoroidal outflow when AIT is combined with cyclodialysis ab interno (AITC) seems to result in an additional drug sparing effect for at least 1 year without critical safety signals. Thus, AITC might be further investigated prospectively prior to advocating its use in routine minimally invasive glaucoma surgery.

Keywords Glaucoma · Ab interno trabeculectomy · Trabectome · Minimally invasive glaucoma surgery · MIGS · Combined cataract and glaucoma surgery · Cyclodialysis · Trabecular meshwork surgery

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Key messages

What is kown:

- The IOP-lowering effect of minimally-invasive anti-glaucoma surgery is generally moderate with success rates of roughly 50%. This also accounts for the Schlemm channel opening trabectome surgery.
- Due to their limited increased intraocular pressure-lowering potential, the main clinical field for their application are eyes with mild-to-moderately increased IOP with or without intolerance to anti-glaucoma medication.

What is new:

- In this proof-of-concept study, we observed an additional drug-sparing effect and no disadvantages with the combination of trabectome surgery and cyclodialysis ab interno with a success of 33.4-45.8% compared to 15.8-21.1% for trabectome surgery alone.
- Critical safety signals were not encountered with combined trabectome surgery and cyclodialysis ab interno, though this study was not sufficiently powered to detect such.

Introduction

Despite their limited intraocular pressure (IOP) lowering effect, minimally invasive glaucoma surgeries (MIGS) have constantly increased their share of all glaucoma surgeries because they appear to be generally safe and reasonably efficacious, as far as can be concluded from the limited number of sufficiently controlled studies for the different techniques [1–5]. Beyond the advantages of the heterogenous range of available MIGS options is the chance to tailor therapy in an individualised manner. The predictability of surgical success, however, has remained low [6–8]. The most relevant underlying reasons in favour of MIGS are a typically short outpatient procedure with a short learning curve in experienced hands, the ease of combining it with cataract surgery, a low adverse event rate as well as low demands during the early postoperative course [1].

Many new techniques and implant devices have been developed and marketed in the last 10–15 years, with several already evolving to second- and third-generation models [1]. Nevertheless, failure rates are generally high, so that a substantial portion of patients still suffer unsatisfying IOP control, even after a second MIGS, despite several topical glaucoma medications with increasing ocular surface problems resulting from topical glaucoma medications, topical corticosteroid therapy and surgical trauma [9]. The relatively high failure rate of primary MIGS may argue against the implantation of IOP-lowering implant devices, thereby leading to local problems including dislocation, migration and corneal damage. Consequently, these implants may have to be removed in the context of revision surgeries [10–12]. MIGS without implants are therefore gaining ground. One of these techniques, ab interno trabeculectomy (AIT) or trabectome surgery, is relatively well established in the USA and has also raised increasing interest in European countries in the last 15 years [13].

The trabectome is a device with a curved, relatively blunt footblade in combination with a bipolar cauterisation, infusion and active suction of removed tissue, thereby reducing the risk of intraoperative chamber angle haemorrhage interfering with the surgical performance [14]. Opening of the Schlemm canal is achieved over 90–120° under optical control, and can easily be combined with cataract surgery, which significantly contributes to its IOP-lowering effect; surprisingly, the degree of Schlemm's canal opening has no relevant impact [15]. Based on a definition of surgical success as a postoperative IOP of ≤ 18 mmHg and/or reduction of the topical treatment demand after 1 year, we found similar success rates in our own patients in eyes with preoperatively uncontrolled IOP and those with controlled IOP, but intolerance to topical glaucoma medication, i.e. a surgical success rate of 35–48% and a reduction of 0.7–0.8 topical medications [16].

Given the duration of this intervention of usually less than 10 min under topical and intracameral anaesthesia, and given that this surgical technique does not require foreign materials and does not impair further surgical options, namely for filtering surgical techniques, this technique might have its place in MIGS, while the predictive preoperative factors for success have as yet to be identified [15, 17]. Since we were not fully satisfied with the outcomes of this technique in our hands [16], we felt that a combination with another MIGS procedure with a different mechanism of action might add to its effect by further reducing the IOP and/or treatment demand [18]. For this, we considered classical cyclodialysis ab interno, used for decades as a technique namely for the treatment of congenital glaucoma [19], as a useful adjunct to trabectome surgery, possibly adding to its IOP-lowering effect by opening a suprachoroidal outflow. In the underlying hypothesis-generating proof-of-concept study, we consequently compared the outcomes of trabectome surgery (AIT) alone and in combination with cyclodialysis ab interno (AITC).

Methods

In this retrospective explorative consecutive case series, we included 43 eyes from 33 patients requiring IOP-lowering surgery for the treatment of their insufficiently controlled open angle glaucoma (Shaffer grade ≥ 3 in all quadrants of the study eye without any gonioscopic abnormalities in the angle) who received either AIT or AITC between January 2018 and October 2021. Until May 2020, standard AIT was performed with opening of the nasal 3–4 clock hours of Schlemm's canal. Following that, it was combined with a cyclodialysis ab interno (AITC) over 2–3 clock hours at the same position under optic control using a handheld prisma gonioscope and topical and intracameral anaesthesia (unconserved Lidocaine 0.5%) using the same limbal access. None of these eyes had a history of glaucoma surgery while two AIT eyes had had selective laser trabeculoplasty (SLT), one argon laser trabeculoplasty, and two YAG laser iridotomy. Four eyes undergoing AITC had received SLT. In phakic instances, the procedure was combined with clear cornea phacoemulsification and IOL implantation. At the end of the surgery, patients received Carbachol (Miostat®) intracamerally and were instructed to strictly use Pilocarpine 2% three times daily for 4 weeks in addition to their anti-glaucoma medication, which was postoperatively adopted according to the IOP regulation.

The primary aim of this study was to compare the effect of both procedures on the reduction of IOP and topical glaucoma medication. All eyes were operated by a single surgeon and required to have a follow-up of at least 12 months.

Best-corrected visual acuity (BCVA) was measured on a Snellen decimal scale and converted to Early Treatment of Diabetic Retinopathy Study (ETDRS) letter scores, where a Snellen decimal BCVA of 1.0 is defined as 85 ETDRS letters for the statistical analysis. IOP (Goldmann applanation tonometry) was recorded along with the number of (topical and systemic) IOP-lowering medications prior to surgery and for the following postoperative timepoints: 1 day, 1 week, and 1, 3, 6, and 12 months, along with intra- and postoperative complications and revision surgeries.

To test our hypothesis, the following surgical success criteria according to the World Glaucoma association (WGA) [20] were applied:

1. Complete surgical success defined as an IOP between 6 and 18 mmHg and a reduction of the IOP of ≥ 20% from baseline without the need for glaucoma medication. Qualified success defined as achievement of the target IOP (6–18 mmHg and a reduction of the IOP of ≥ 20% from baseline) with a reduction in ≥ 1 glaucoma medication and no need for revision surgeries within the first year after the intervention.
2. Complete surgical success defined as an IOP between 6 and 15 mmHg without the need for glaucoma medication. Qualified success defined as achievement of the target IOP (between 6 and 15 mmHg) with a reduction in ≥ 1 glaucoma medication and no need for revision surgeries within the first year after the intervention [20].

This analysis was approved by the Ethics Committee of the canton Berne (registration number 2021–01341) based on the informed consent of all included patients to use their coded data for this retrospective analysis and performed in accordance with the International Council for Harmonisation E6 Good Clinical Practice Guideline, the Declaration of Helsinki, and federal laws.

Statistical analyses were performed using the SPSS software package V.23 (SPSS, Inc., Chicago, Illinois, USA) and R (version 3.2.4; R: A language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria, 2016).

The Shapiro–Wilk test was applied to check for distribution patterns and revealed that the data were not normally distributed. The non-parametric Mann–Whitney *U* test was used for the intergroup comparisons of continuous variables. For intragroup changes, the Wilcoxon signed-rank test was applied. To test whether two categorical variables are associated, we used the chi-square test for association. The level

Table 1 Baseline epidemiologic characteristics of the study population

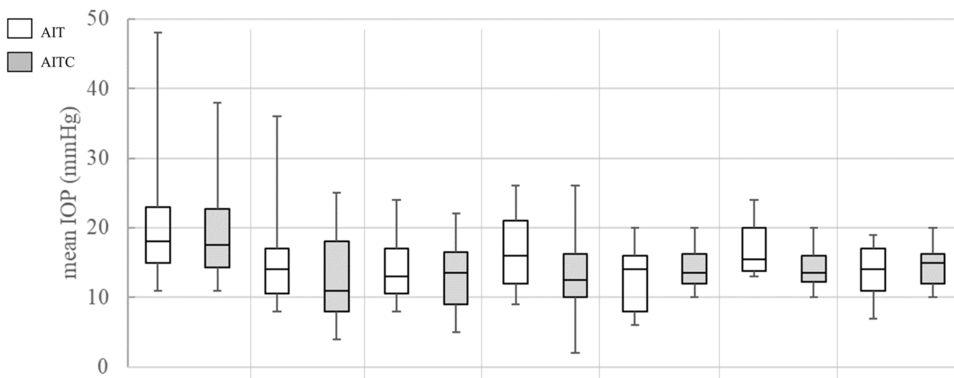
	AIT (n = 19)	AITC (n = 24)	*p* value
Age (years: mean ± SD)	76.7 ± 6.1 75.6; 71.9–75.6	75.5 ± 12.8 76.3; 74.6–81.6	0.60
Gender (% females)	71.4	57.9	0.49
IOP (mmHg; mean ± SD)	19.7 ± 8.2 18.0; 15.0–23.0	19.4 ± 6.8 17.5; 14.3–22.8	0.96
Best-corrected visual acuity (ETDRS letter score; mean ± SD; median and IQR)	61.3 ± 22.8 69.9; 54.9–75.0	69.2 ± 18.2 75.0; 62.7–80.2	0.16
Number of IOP-lowering drugs (mean ± SD; median and IQR)	2.9 ± 1.2 3.0; 2.0–4.0	2.9 ± 1.2 3.0; 2.0–4.0	0.90
Nr. and % of PEX glaucoma	9 (47.4%)	12 (50%)	0.47

AIT, ab interno trabeculectomy; *AITC*, AIT combined with ab interno cyclodialysis; *IOP*, intraocular pressure; *ETDRS*, Early Treatment of Diabetic Retinopathy Study

Table 2 Intraocular pressure (IOP) comparison between the groups and changes over time

Mean ± SD median, IQR	Group 1 (AIT) n = 19	Group 2 (AITC) n = 24	*p*-value group comparison	Effect size	Confidence interval	*p*-value change within the group	Effect size	Confidence interval
Baseline IOP	19.7 ± 8.2 18.0, 15.0 – 23.0	19.4 ± 6.8 17.5, 14.3 – 22.8	0.96	0.51	-0.64 – 0.56	n.a		
Change in IOP after 6 months	-3.8 ± 12.3 -3.8, -7.8 – 4.8	-4.9 ± 8.3 -2.0, -10.8 – 2.0	0.95	0.53	-0.87 – 0.65	g1: 0.36 g2: **0.03**	g1: -0.61 g2: -0.75	g1: -1.15 – 0.39 g2: -1.59 – -0.34
Change in IOP after 1 year	-4.3 ± 6.6 -4.0, -8.0 – -1.0	-3.7 ± 6.7 -1.5, -5.5 – -0.5	0.49	0.53	-0.60 – 0.78	g1: **0.017** g2: **0.016**	g1: -0.74 g2: -0.74	g1: -1.61 – -0.19 g2: -1.53 – -0.25

IOP, intraocular pressure; *SD*, standard deviation; *IQR*, interquartile ranges; *AIT*, ab interno trabeculectomy; *AITC*, ab interno trabeculectomy combined with cyclodialysis ab interno; *n.a.*, not applicable; *g1*, group 1; *g2*, group 2. Significant *p*-values are marked in bold



	Baseline	1 day	1 week	1 month	3 months	6 months	1 year
AIT	19.7±8.2 18.0;15.0-23.0	14.9±7.3 14.0;10.5-14.0	14.3±4.7 13.0;10.5-14.0	16.3±5.2 16.0;12.0-21.0	13.0±4.7 14.0;8.0-16.0	17.0±4.0 15.5;13.8-20.0	13.7±3.8 14.0;11.0-17.0
AITC	19.4±6.8 17.5;14.3-22.8	12.7±5.8 11.0;8.0-18.0	13.3±4.9 13.5;9.0-16.5	13.8±5.3 12.5;10.0-16.3	14.3±2.9 13.5;12.0-16.3	14.2±2.9 13.5;12.3-16.0	14.5±2.9 15.0;12.0-16.3
Mann-Whitney U test	*p*=0.96	*p*=0.25	*p*=0.73	*p*=0.18	*p*=0.78	*p*=0.06	*p*=0.61

Fig. 1 Box plots representing change in intraocular pressure (IOP, in mmHg) over time. Mean ± SD as well as median and IQR are reported in the table within the figure

of significance was set at $p < 0.05$. Data are presented as mean ± standard deviation (SD) as well as median and interquartile ranges (IQR 25 and 75). Effect sizes and 95% confidence intervals are also reported for group comparisons.

Results

Forty-three eyes of 33 patients were included in this study. Nineteen eyes (14 patients) received AIT alone and 24 (19 patients) AITC (85.7% and 89.5% with phacoemulsification and IOL implantation). The mean age of the AIT group was 76.7 ± 6.1 years and 71.4% of the sample was female, which was comparable to the AITC group (mean age 75.5 ± 12.8, 57.9% female; Table 1).

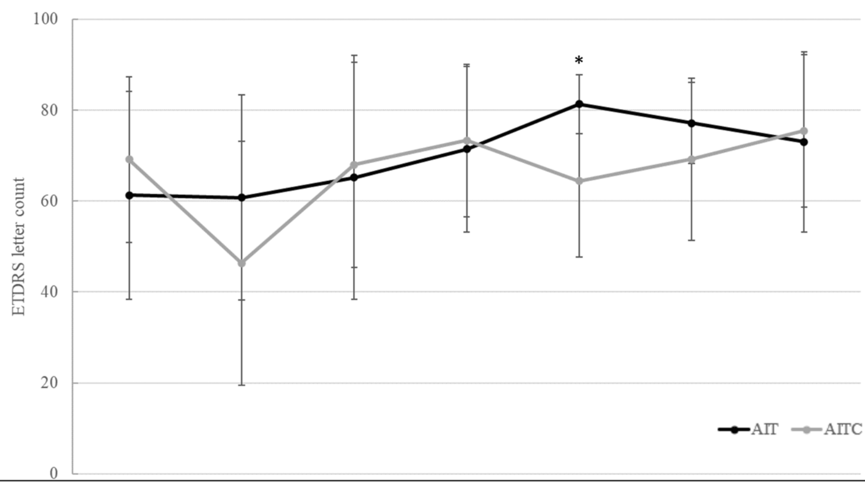
Both groups showed a similar baseline IOP (AIT: 19.7 ± 8.2 mmHg; AITC: 19.4 ± 6.8 mmHg; $p = 0.96$) as well as a comparable IOP reduction after 6 months [AIT: − 3.8 ± 12.3, median and IQR: − 3.8 (− 7.8–4.8) mmHg; Wilcoxon signed rank test: $p = 0.36$; AITC: − 4.9 ± 8.3; median and IQR: − 2.0 (− 10.8–2.0) mmHg; $p = 0.030$) and 12 months (AIT: − 4.3 ± 6.6, median and IQR: − 4.0 (− 8.0 to − 1.0) mmHg; $p = 0.017$; AITC: − 3.7 ± 6.7, median and IQR: − 1.5 (− 5.5 to − 0.5) mmHg; $p = 0.016$; Mann–Whitney *U* test for the comparison between groups: $p = 0.49$; Table 2; Fig. 1).

The increase in visual acuity from baseline to 6 months did not differ significantly between the groups [AIT: + 17.7 ± 28.0, median and IQR: + 6.8 (− 0.7–30.1), Early Treatment of Diabetic Retinopathy Study (ETDRS)

Table 3 Visual acuity (ETDRS letters) comparison between the groups and changes over time

Mean ± SD median, IQR	Group 1 (AIT) n = 19	Group 2 (AITC) n = 24	*p*-value group comparison	Effect size	Confidence interval	*p*-value change within the group	Effect size	Confidence interval
Baseline VA	61.3 ± 22.8 69.9, 54.9 – 75.0	69.2 ± 18.2 75.0, 62.7 – 80.2	0.16	0.61	-0.22 – 1.00	n.a		
Change in VA after 6 months	+ 17.7 ± 28.0 6.8, -0.7 – 30.1	+ 2.3 ± 11.3 4.8, -9.9 – 10.2	0.31	0.70	-1.62 – 0.15	g1: **0.050** g2: 0.59	g1: 0.72 g2: 0.50	g1: -0.024 – 1.61 g2: -0.71 – 0.71
Change in VA after 1 year	+ 10.8 ± 16.0 8.7, -4.9 – 16.3	+ 2.9 ± 2.7 4.8, 0 – 5.2	0.12	0.67	-1.47 – 0.20	g1: **0.013** g2: **0.026**	g1: 0.65 g2: 0.60	g1: -0.16 – 1.24 g2: -0.39 – 1.09

VA, visual acuity; *SD*, standard deviation; *IQR*, interquartile ranges; *AIT*, ab interno trabeculectomy; *AITC*, ab interno trabeculectomy combined with cyclodialysis ab interno; *n.a.*, not applicable; *g1*, group 1; *g2*, group 2. Significant *p*-values are marked in bold



	Baseline	1 day	1 week	1 month	3 months	6 months	1 year
AIT	61.3±22.8 69.9;54.9-75.0	60.8±22.6 65.1;54.9-75.5	65.2±26.9 75.0;65.1-82.6	71.4±18.2 69.9;69.9-85.0	81.3±6.5 82.6;73.9-86.2	77.1±8.9 78.7;74.7-85.0	73.0±19.8 77.6;74.7-82.7
AITC	69.2±18.2 75.0;62.7-80.2	46.4±26.8 52.5;19.9-66.3	68.0±22.5 75.0;65.1-80.2	73.3±16.8 80.2;65.1-85.0	64.4±16.8 69.9;53.8-77.6	69.2±17.8 80.2;60.3-85.0	75.4±16.7 80.2;72.9-85.0
Mann-Whitney U test	*p*=0.16	*p*=0.12	*p*=0.98	*p*=0.60	*p*=0.013	*p*=0.56	*p*=0.55

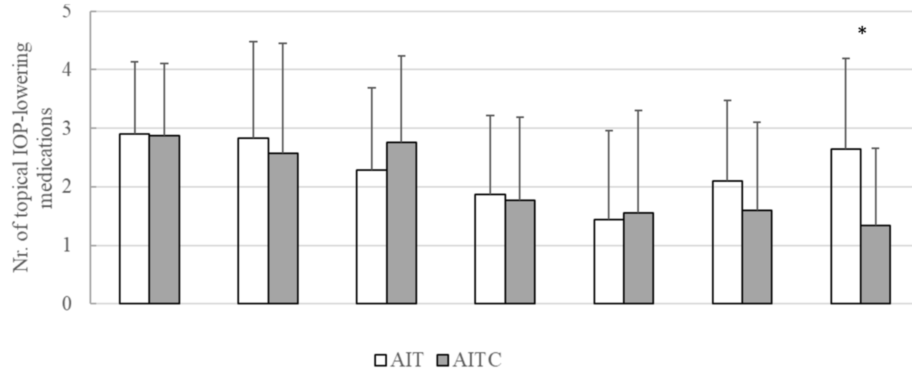
Fig. 2 Change in best-corrected visual acuity (BCVA in ETDRS letters) over time. Black line: AIT; grey line: AITC. Mean ± SD as well as median and IQR are reported in the table within the figure

letters, $p = 0.050$; AITC: + 2.3 ± 11.3 median and IQR: + 4.8 (− 9.9–10.2) letters, $p = 0.59$. Mann–Whitney *U* test for the comparison between groups: $p = 0.31$] and 12 months [AIT: + 10.8 ± 16.0, median and IQR: 8.7 (− 4.9–16.3) letters; $p = 0.013$; AITC: + 2.9 ± 2.7, median and IQR: + 4.8 (0–5.2) letters; $p = 0.026$; Mann–Whitney *U* test for the comparison between groups: $p = 0.12$; Table 3, Fig. 2].

While the IOP reduction and increase in visual acuity were similar between the groups, a difference was observed in the number of topical IOP-lowering medications over 1 year: From baseline to 6 months (AIT: − 0.5 ± 1.0, median and IQR: 0 (− 1.3–0), $p = 0.13$; AITC: − 1.3 ± 1.9, median and IQR: − 2.0 (− 2.0 – − 0.3); $p < 0.008$; Mann–Whitney *U* test for the comparison between groups: $p = 0.12$) and 12 months (AIT: − 0.4 ± 1.2, median and IQR: 0 (− 1.0–0); $p = 0.16$; AITC: − 1.7 ± 1.2, median and IQR: − 2.0 (− 2.0 to − 1.0); $p < 0.001$; Mann–Whitney *U* test for the comparison between groups: $p = 0.001$; Fig. 3).

Surgical success over 12 months is displayed in Tables 4, 5, 6 and 7. The 12-month follow-up information for IOP and the number of IOP lowering medications was not available for 6 and 5 eyes, respectively (13.9% and 11.6%). To determine surgical success after 12 months for those eyes, the 6 months information was used.

While no complications were recorded in the AIT group, one larger hyphema was encountered in the AITC group which spontaneously resolved within 1 week, and two



	Baseline	1 day	1 week	1 month	3 months	6 months	1 year
AIT	2.9±1.2 3.0;2.0-4.0	2.8±1.6 4.0;1.3-4.0	2.3±1.4 2.5;1.0-3.3	1.9±1.4 2.0;0-3.0	1.4±1.5 2.0;0-2.5	2.1±1.4 2.0;1.5-3.3	2.6±1.5 3.0;2.0-4.0
AITC	2.9±1.2 3.0;2.0-4.0	2.6±1.9 3.0;1.0-4.0	2.8±1.5 3.0;1.0-4.0	1.8±1.4 2.0;0.8-3.0	1.5±1.8 2.0;0-2.0	1.6±1.5 2.0;0-2.0	1.3±1.3 1.5;0-2.0
Mann-Whitney U test	p=0.90	p=0.75	p=0.36	p=0.80	p=1.0	p=0.33	p=0.017

Fig. 3 Number of topical IOP-lowering medications over time. Black line: AIT; grey line: AITC. Mean ± SD as well as median and IQR are repsorted in the table within the figure

Table 4 Surgical success of AIT and AITC according to two different World Glaucoma Association definitions. Complete surgical success defined as an IOP between 6 and 18 mmHg and a reduction of the IOP of ≥ 20% from baseline without the need for glaucoma medication. Qualified success defined as achievement of the target IOP (6–18 mmHg and a reduction of the IOP of ≥ 20% from baseline) with a reduction in ≥ 1 glaucoma medication and no need for revision surgeries within the first year after the intervention. Chi^2 test was applied to determine if there is a significant difference in the portion of success rates between AIT and AITC

	Complete success	Qualified success	Failure
AIT	3 (15.8%)	0	16 (84.2%)
AITC	4 (16.7%)	4 (16.7%)	16 (66.7%)
p	0.16		

AIT, ab interno trabectome surgery; *AITC*, ab interno trabectome surgery combined with cyclodialysis ab interno

Table 5 Surgical success of AIT and AITC according to two different World Glaucoma Association definitions. Complete surgical success defined as an IOP between 6 and 15 mmHg without the need for glaucoma medication. Qualified success defined as achievement of the target IOP (between 6 and 15 mmHg) with a reduction in ≥ 1 glaucoma medication and no need for revision surgeries within the first year after the intervention. Chi^2 test was applied to determine if there is a significant difference in the portion of success rates between AIT and AITC

	Complete success	Qualified success	Failure
AIT	3 (15.8%)	1 (5.3%)	15 (78.9%)
AITC	5(20.8%)	6 (25.0%)	13 (54.2%)
p	0.16		

AIT, ab interno trabectome surgery; *AITC*, ab interno trabectome surgery combined with cyclodialysis ab interno

instances of hypotony, which resolved spontaneously within 1 week and 1 month, respectively. No revision surgery was required in any case during the observation period.

Table 6 Surgical success of AIT and AITC according to two different World Glaucoma Association definitions in phakic eyes undergoing combined phacoemulsification, trabectome surgery and cyclodialysis ab interno (after exclusion of preoperatively pseudophakic eyes, 2 in the AIT and 3 in the AITC group). Complete surgical success defined as an IOP between 6 and 18 mmHg and a reduction of the IOP of ≥ 20% from baseline without the need for glaucoma medication. Qualified success defined as achievement of the target IOP (6–18 mmHg and a reduction of the IOP of ≥ 20% from baseline) with a reduction in ≥ 1 glaucoma medication and no need for revision surgeries within the first year after the intervention. Chi^2 test was applied to determine if there is a significant difference in the portion of success rates between AIT and AITC

	Complete success	Qualified success	Failure
AIT	3 (17.6%)	0	14 (82.4%)
AITC	4 (19.0%)	3 (14.3%)	14 (66.7%)
p	0.25		

AIT, ab interno trabectome surgery; *AITC*, ab interno trabectome surgery combined with cyclodialysis ab interno

Discussion

In this hypothesis-generating pilot study, we demonstrated a potential benefit of the combination of cyclodialysis and AIT with respect to its drug-sparing effect compared to AIT alone. AITC is performed under topical and intracameral anaesthesia and combines AIT and cyclodialysis, two MIGS techniques with the aim of tackling two independent outflow mechanisms via Schlemm's canal and the suprachoroidal space to reduce the ciliary aqueous production. It does, moreover, not touch the conjunctiva, nor does it rely on the implantation of any costly filtration device, facilitating later revision surgery. It has to be kept in mind that 87% of all eyes in our series received a combined procedure including phakoemulsification. On

Table 7 Surgical success of AIT and AITC according to two different World Glaucoma Association definitions in phakic eyes undergoing combined phacoemulsification, trabectome surgery and cyclodialysis ab interno (after exclusion of preoperatively pseudophakic eyes, 2 in the AIT and 3 in the AITC group). Complete surgical success defined as an IOP between 6 and 15 mmHg without the need for glaucoma medication. Qualified success defined as achievement of the target IOP (between 6 and 15 mmHg) with a reduction in ≥ 1 glaucoma medication and no need for revision surgeries within the first year after the intervention. Chi^2 test was applied to determine if there is a significant difference in the portion of success rates between AIT and AITC

	Complete success	Qualified success	Failure
AIT	3 (17.6%)	1 (5.9%)	13 (76.5%)
AITC	5(23.8%)	5(23.8%)	11 (52.4%)
p	0.23		

AIT, ab interno trabectome surgery; *AITC*, ab interno trabectome surgery combined with cyclodialysis ab interno

the one hand, this limits the predictive value for the IOP-lowering effect of AIT without phacoemulsification, but, on the other hand, the majority of MIGS surgeries are considered in the context of a planned cataract surgery in eyes with advanced nerve fibre damage and insufficient or borderline IOP and surface problems or intolerance to their IOP-lowering medication [21], as in our series. This is explained by the fact that a combined procedure seems to have a possibly over-additive IOP-lowering effect compared to MIGS and cataract surgery alone [5, 22].

Cyclodialysis was introduced more than 100 years ago by Leopold Heine (1905), mainly for treating open angle glaucoma and glaucoma in aphakic eyes. Presumably, the success of cyclodialysis is based on an increased aqueous outflow via the suprachoroidal space and a reduced aqueous production [23]. Since the late eighties, cyclodialysis was widely replaced by laser-trabeculoplasty and by trabeculectomy [23], although it had been used successfully, namely in combination with cataract surgery in open angle glaucoma [24]. It may be speculated, that this was linked to a high intraoperative complication rate (namely intraocular haemorrhage), and a high spontaneous closure rate of the cyclodialysis space along with a relatively high surgical failure rate, namely in the early postoperative period. A correlation between the persistence of a suprachoroidal space and the IOP-lowering effect, on the other hand, is not convincing [25]. Based on these experiences, we tried to escape this problem in a preventive strategy via the application of acetylcholine at the end of surgery and the strict use of Pilocarpine 2% three times daily over 4 weeks in all cases; this was in addition to the adaptation of anti-glaucoma medication in response to the postoperative IOP.

In cases of intractable glaucoma, cyclodialysis ab interno did not provide convincing evidence as a standalone technique to achieve a sufficient IOP lowering effect. Nevertheless, the technique is easy to perform and offers safe and atraumatic access to the resorptive capability of the choroid while conjunctival manipulation is avoided [26]. Therefore, Krieglstein and colleagues combined goniocurettage combined with cyclodialysis which achieved a similar success as goniotomy and cyclodialsis ab interno, namely in instances of uncontrolled goniodysplasic congenital and paediatric glaucoma [27]. While Erb and colleagues compared this technique (goniotomy in combination with cyclodialysis) to trabectome surgery and found them to be equally effective in reducing IOP in open angle glaucoma, we added cyclodialysis to conventional trabectome surgery with the hope of an additional IOP-lowering effect. This was achieved independently of the persistence of the cleft, which in fact was closed in the majority of eyes between 1 and 3 months postoperatively, despite consequent pilocarpine therapy for 1 month [28], and closely compares to our results.

Based on the definition of surgical success used here, we experienced a twofold higher surgical success rate in eyes receiving AITC (depending on the definition, a success of 33.4–45.8% in AITC compared to 15.8–21.1% for AIT) which did, however, not reach statistical significance because of the limited sample size. In the setting of our hypothesis-generating pilot study, a comparison to possibly similar studies would be very helpful. The fact that there is no generally accepted definition for success in glaucoma surgery makes a comparison of the different studies virtually impossible [29]. We tried to apply robust criteria for surgical success: IOP < 18 or IOP reduction of ≥ 20%, along with a reduction of IOP-lowering medication and no revision surgery within 12 months of surgery. Therefore, we assume that the outcomes presented here are comparable to previous reports [30, 31] and in line with our previous report [16]. The hypothesised additional effect of cyclodialysis to AIT reported here may be explained by the fact that AIT is assumed to increase the trabecular outflow capacity while the addition of cyclodialysis generates a suprachoroidal outflow and reduces ciliary fluid production [18], which shows that AITC is more effective in reducing the IOP or medication burden than AIT.

The selection of patients for AIT and AITC may be biased by the observation that the highest success rates can be seen in eyes with a baseline IOP of 18–26 mmHg [16, 22, 31, 32]. Consequently, this baseline IOP group was overrepresented in this series, which could have contributed to the robust success rate in AITC, while patients with higher baseline IOP were more likely scheduled for filtering glaucoma surgery.

Besides the small sample size of this study, the inclusion of both eyes might be considered as a weakness, while the number of patients operated on in both eyes was symmetrically distributed. Furthermore, in a recent report, no significant difference was observed between the outcomes of the first and second eyes. The frequency of success in the second eye after effective surgery in the first eye significantly exceeded that after prior failure [29]. A strength of this technique is that no additional machines or devices are needed to add cyclodialysis to AIT, which was shown in our series in one run with the trabectome, and the option to combine it with cataract surgery. Another strength is that AITC seems to be a relatively safe method as far as can be concluded from this small case series: We experienced early hypotony in two instances in the AITC but not the AIT eyes, in one case persisting over 4 weeks before spontaneous recovery to stable and normal IOP values thereafter. Few incidental cases of unintended cyclodialysis have been reported in the context of AIT and cyclodialysis, all of which recovered spontaneously within a few weeks [33, 34]. What remains to be mentioned is a higher degree of early postoperative hyphema, which spontaneously recovered anyway, but can be worrying for the uninformed patient. Luckily, this was not treated in any case and is not a negative predictor [35, 36]. One eye demonstrated advanced zonular instability due to late stage PEX, which required the implantation of an iris clip IOL, which was performed without problems after AITC. No further complications were encountered.

In conclusion, AITC, without or with phacoemulsification, provided an additional drug-sparing effect over 12 months postoperatively, resulting in a surgical success rate of 33.4–45.8% compared to 15.8–21.1% for AIT alone without critical safety signals. AITC might thus be preferable to AIT in eyes with moderate OAG to reduce IOP or medication burden if confirmed prospectively.

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Data availability Data are available on request by contact of the corresponding author.

Declarations

Ethical approval This study was approved by the Ethics Committee of the canton Berne (registration number 2021–01341) based on the informed consent of all included patients to use their coded data for this retrospective analysis and performed in accordance with the International Council for Harmonisation E6 Good Clinical Practice Guideline, the 1964 Declaration of Helsinki and its later amendments, and federal laws.

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript. JGG acts as advisor and speaker for several pharmaceutical companies and contributes to several international industry-sponsored clinical studies in the fields of retinal disease and uveitis (AbbVie, Bayer, Novartis, Roche) which had no bearing on the underlying work. None of the authors have conflicting interests with the data that are presented herein.

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