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Short-term ocular outcomes of ultrasound cycloplasty with or without intravitreal conbercept in neovascular glaucoma

Jian Guo[1#], Hailong Yang[2#], Renzhe Cui[3], Bozhou Zhang[2#] and Gang Bai[2*]

[1] *Department of ophthalmology, the First Affiliated Hospital of Fujian Medical University, Fuzhou 350004, China*
[2] *Department of ophthalmology, Inner Mongolia Chaoju Eye Hospital, Hohhot 010059, China*
[3] *Department of ophthalmology, Yanbian University Hospital, Yanji 133000, China*
[#] Authors contributed equally: Jian Guo, Hailong Yang, Bozhou Zhang
[*] Correspondence: Baigang@chaojueye.com or 15904872435@163.com (Bai G)

Abstract

Neovascular glaucoma (NVG) is a severe secondary glaucoma characterized by neovascularization of the iris and angle, often leading to uncontrolled intraocular pressure (IOP). This retrospective study compared the clinical efficacy of ultrasound cycloplasty (UCP) alone vs UCP combined with intravitreal anti-vascular endothelial growth factor (anti-VEGF) injection in NVG management. Eighty eyes were included, with 45 treated using UCP alone and 35 receiving combined therapy. IOP, visual acuity (VA), and the number of glaucoma medications were evaluated preoperatively and at 1 d, 1 week, 1 month, and 3 months postoperatively. Both groups demonstrated significant IOP reductions at all follow-up visits (all $p < 0.05$). However, the combined-treatment group achieved greater IOP reduction at 1 month (−19.28 ± 11.82 vs −13.55 ± 8.43 mmHg, $p = 0.020$), and 3 months (−18.42 ± 13.57 vs −10.14 ± 10.64 mmHg, $p = 0.007$). Visual acuity improvement was also more pronounced in the combined group at 1 week ($p = 0.013$) and 3 months ($p = 0.037$). Postoperative medication burden decreased in both groups, with no significant between-group difference. These findings suggest that combining UCP with intravitreal anti-VEGF therapy provides superior short-term IOP control and visual outcomes compared with UCP alone, likely due to the complementary mechanisms of reducing aqueous humor production and suppressing anterior segment neovascularization.

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Introduction

Neovascular glaucoma (NVG) is one of the most aggressive and vision-threatening forms of secondary glaucoma. It is characterized by pathological neovascularization of the iris (rubeosis iridis) and the anterior chamber angle, which leads to the formation of fibrovascular membranes, progressive synechial angle closure, and severe elevation of intraocular pressure (IOP)[1]. NVG most commonly develops as a complication of ischemic retinal diseases, particularly proliferative diabetic retinopathy (PDR), central retinal vein occlusion (CRVO), and ocular ischemic syndrome. In these conditions, chronic retinal hypoxia induces overexpression of vascular endothelial growth factor (VEGF), which plays a central role in stimulating anterior segment neovascularization. Once established, NVG often progresses rapidly and is frequently refractory to conventional medical therapy, posing a major therapeutic challenge and often resulting in poor visual prognosis and ocular pain if not effectively controlled[2].

Management of NVG requires a dual approach: suppression of the underlying ischemic and angiogenic drive, and control of elevated IOP. Traditional IOP-lowering medications are often insufficient because the mechanical obstruction of the trabecular meshwork by fibrovascular tissue severely impairs aqueous outflow. Surgical options such as trabeculectomy and glaucoma drainage devices may be considered, but their success rates are limited in NVG due to intense postoperative inflammation, high risk of fibrosis, and ongoing neovascular activity. As a result, cyclodestructive procedures that reduce aqueous humor production by targeting the ciliary body have become important alternatives, particularly in eyes with poor visual potential or refractory IOP elevation.

Similar to cyclocryotherapy and trans-scleral diode laser photocoagulation, Ultrasound Cyclo Plasty (UCP) is classified as a cyclodestructive procedure that achieves its therapeutic effect by using high-intensity focused ultrasound (HIFU) technology[3–5]. However, UCP represents a newer generation of technology that uses HIFU to selectively coagulate the ciliary body epithelium while sparing surrounding tissues[6–8]. This non-incisional, automated, and anatomically guided technique allows for more precise and reproducible energy delivery compared with traditional cyclodestructive methods, potentially reducing collateral damage and postoperative complications. UCP has shown promising efficacy and safety in various types of refractory glaucoma, with meaningful IOP reduction and a favorable safety profile reported in multiple clinical studies.

Despite these advantages, outcomes of UCP in NVG appear to be less favorable than in other glaucoma subtypes. Recent studies have indicated that although UCP can lower IOP in NVG eyes, the success rate after a single treatment session is significantly lower compared with primary open-angle glaucoma or other secondary glaucomas[9]. This limited efficacy may be explained by the persistent pro-angiogenic and inflammatory milieu in NVG, which continues to compromise aqueous outflow and promote postoperative scarring. Therefore, adjunctive therapies targeting the underlying VEGF-driven neovascular process may be critical to improving surgical outcomes.

Anti-vascular endothelial growth factor (anti-VEGF) agents can rapidly suppress iris and angle neovascularization, thereby improve aqueous outflow and reduce postoperative inflammation[10,11]. In the context of NVG, anti-VEGF therapy not only helps control neovascularization but may also improve aqueous humor outflow by reducing fibrovascular membrane activity and decreasing postoperative inflammatory response. These effects could theoretically enhance the efficacy and durability of IOP-lowering procedures.

Combining anti-VEGF therapy with UCP may therefore offer synergistic benefits. While UCP decreases aqueous humor

production by ablating the ciliary body, anti-VEGF treatment addresses the upstream ischemic and angiogenic drivers of NVG. This dual-mechanism strategy may help stabilize the anterior segment environment, improve surgical success rates, and reduce the likelihood of early postoperative failure. However, evidence regarding the clinical benefits of combining anti-VEGF therapy with UCP in NVG remains limited, and direct comparative studies are scarce. Accordingly, the present study aimed to compare the short-term clinical outcomes of UCP alone vs UCP combined with intravitreal anti-VEGF injection in patients with neovascular glaucoma. By evaluating IOP control, need for additional interventions, and safety profiles, this study seeks to explore whether adjunctive anti-VEGF therapy can enhance the effectiveness of UCP in this challenging and high-risk patient population.

Methods

This was a retrospective, comparative clinical study conducted at the Inner Mongolian Chaoju Eye Hospital. A total of 80 eyes from 80 patients diagnosed with NVG and treated between Jan. 2023 and Oct. 2025 were included. Patients were retrospectively categorized into two groups according to the treatment they had received during routine clinical care, which included the UCP group (n = 45) and the UCP combined with anti-VEGF group (n = 35). All included eyes presented with uncontrolled IOP despite maximally tolerated medical therapy and exhibited neovascularization of the iris or angle consistent with NVG. The decision to administer adjunctive intravitreal anti-VEGF therapy was based on the severity of neovascularization and the treating physician's clinical judgment. This study was approved by the Institutional Review Board of the Inner Mongolian Chaoju Eye Hospital (Approval No. CJ-KLS-20251130, November 30th, 2025) and adhered to the tenets of the Declaration of Helsinki. Informed consent for treatment and the use of anonymized data for research purposes was obtained from all patients.

Inclusion criteria were: (1) diagnosis of NVG secondary to ischemic retinal diseases such as proliferative diabetic retinopathy or central retinal vein occlusion; (2) IOP ≥ 30 mmHg on maximal topical and systemic antiglaucoma therapy; and (3) a minimum follow-up of three months. Exclusion criteria included prior cyclodestructive procedures, active ocular infection or inflammation, history of ocular trauma within six months, inadequate clinical records, or patients with severe cardiovascular and cerebrovascular diseases, liver and kidney dysfunction, or other surgical contraindications. The decision to administer adjunctive anti-VEGF therapy was based on the severity of anterior segment neovascularization and the treating physician's clinical judgment. Standardized grading of neovascular severity was not uniformly documented due to the retrospective design.

Before surgery, best-corrected visual acuity (BCVA) was assessed using a standard logarithmic visual acuity chart. IOP was measured with a non-contact tonometer (TX-20, Canon, Japan) at baseline and throughout follow-up, and anterior segment structures were evaluated using slit-lamp biomicroscopy. Fundus examination was performed using a wide-field Optos fundus imaging system (Optos PLC, Dunfermline, UK). Ultrasound biomicroscopy (UBM) was conducted with a domestic high-frequency UBM device (KW-UBM, Suoer, Tianjin, China) to evaluate anterior segment structures and determine the appropriate probe size for each patient.

All UCP procedures were performed using the EyeOP1® high-intensity focused ultrasound system (Eye Tech Care, France). Peribulbar or retrobulbar anesthesia was administered prior to treatment. A circular probe containing six piezoelectric transducers was aligned with the limbus using a single-use coupling cone, and treatment was delivered in a standard preset mode for approximately 8 s per sector, with a total treatment duration of about 48 s. The targeted region encompassed the ciliary body circumference, excluding the 3 and 9 o'clock meridians. Following the procedure, patients received topical corticosteroids and IOP-lowering medications according to clinical need.

Patients in the combination group received a single intravitreal injection of anti-VEGF (ranibizumab 0.5 mg/0.05 mL or conbercept 0.5 mg/0.05 mL) administered 3–7 d prior to UCP. The choice of anti-VEGF agent was based on availability and physician's discretion. This timing was chosen to allow regression of anterior segment neovascularization before cyclodestructive treatment, thereby potentially reducing intraoperative inflammation and early postoperative IOP spikes. No additional anti-VEGF injections were routinely administered during the 3-month follow-up unless clinically indicated for persistent neovascular activity.

Clinical assessments were conducted preoperatively and at 1 d, 1 week, 1 month, and 3 months after treatment. IOP, BCVA, and the number of topical and systemic antiglaucoma medications were documented at each visit. Any postoperative complications were recorded throughout the follow-up period.

Statistical analysis was conducted using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Data normality was assessed using the Shapiro–Wilk test. For intraocular pressure (IOP), which was normally distributed at most time points, between-group comparisons were performed using independent samples t-tests on change scores from baseline (ΔIOP = Postoperative − Preoperative), which were confirmed to be normally distributed at all time points. Within-group changes in IOP from baseline were assessed using paired t-tests. For best-corrected visual acuity (BCVA) and medication use, which were non-normally distributed, between-group comparisons were performed using Mann-Whitney U tests on change scores from baseline, and within-group changes were assessed using Wilcoxon signed-rank tests. Categorical variables were assessed using chi-square or Fisher's exact test as appropriate. The P for trend within each group was derived from simple linear regression of the outcome on the ordinal time variable. Values are reported as mean ± standard deviation (SD) for normally distributed data or median with interquartile range (IQR) for non-normally distributed data. A p-value < 0.05 was considered statistically significant.

Results

A total of 80 patients with neovascular glaucoma were included, with 45 eyes in the UCP group, and 35 eyes in the UCP combined with anti-VEGF injection group. Among them, neovascular glaucoma secondary to retinal vein occlusion was observed in 18 patients in the UCP group and 10 patients in the combined treatment group, while neovascular glaucoma secondary to diabetic retinopathy was observed in 27 and 25 patients, respectively. The distribution of NVG etiology showed no statistically significant differences between the two groups. Baseline demographic and ocular characteristics were comparable between the two groups except for sex distribution, which differed significantly. Age, baseline intraocular pressure, and the number of glaucoma medications showed no significant differences between groups. However, baseline visual acuity differed significantly between the two groups (p = 0.026), with the UCP group showing worse baseline vision. Detailed baseline data are presented in Table 1.

Both treatments resulted in substantial postoperative reductions in intraocular pressure. In the UCP group, mean intraocular pressure

decreased from 42.69 mmHg preoperatively to 34.33 mmHg on day 1, 24.11 mmHg at week 1, 27.60 mmHg at month 1, and 31.53 mmHg at month 3, all representing significant reductions from the baseline. In the UCP combined with anti-VEGF group, intraocular pressure declined from 45.89 mmHg preoperatively to 34.14 mmHg on day 1, 24.13 mmHg at week 1, 26.45 mmHg at month 1, and 27.27 mmHg at month 3. The combined group achieved greater reductions at months 1 and 3 compared with UCP alone, indicating an enhanced intraocular pressure-lowering effect. The overall intraocular pressure trends for both groups are provided in Table 2.

Visual acuity also improved following treatment. In the UCP group, visual acuity remained relatively stable during early follow-up and showed mild improvement at month 3. In contrast, patients in the UCP combined with anti-VEGF group demonstrated earlier and more pronounced improvements, with significant gains observed at week 1 and month 3. Between-group differences favored the combined treatment during these periods. The patterns of visual recovery are shown in Table 3.

The number of glaucoma medications decreased significantly after treatment in both groups. The UCP group showed a reduction from three medications at baseline to two at month 1 and month 3. The combined group showed an earlier decrease, with medication burden reduced as early as week 1 and continuing through the three-month visit. Although the magnitude of reduction did not differ significantly between groups at each time point, both exhibited clear downward trends over time. Medication use trends are displayed in Table 4.

Discussion

In this retrospective study, both UCP alone and UCP combined with intravitreal anti-VEGF injection resulted in a significant reduction in IOP compared with baseline in patients with NVG. Notably, the combined therapy achieved significantly greater IOP reduction at 1 and 3 months postoperatively, indicating that addressing both aqueous humor dynamics and neovascular activity provides

Table 1. Comparison of general preoperative information between the two groups.

Parameters, mean ± SD (Δ mean ± SD)	Postop. 1 d	Postop. 1 week	Postop. 1 month	Postop. 3 months	p^{trend}
UCP group (n = 45)	34.33 ± 12.99[a] (−6.67 ± 11.52)	24.11 ± 9.25[a] (−17.12 ± 8.25)	27.60 ± 10.65[a] (−13.55 ± 8.43)	31.53 ± 11.74[a] (−10.14 ± 10.64)	< 0.001
UCP + VEGF group (n = 35)	34.14 ± 10.61[a] (−11.741 ± 13.10)	24.13 ± 8.00[a] (−21.80 ± 13.31)	26.45 ± 10.30[a] (−19.28 ± 11.82)	27.27 ± 11.56[a] (−18.42 ± 13.57)	< 0.001
T	1.81	1.84	2.39	2.80	–
p	0.075	0.070	0.020	0.007	–

UCP: Ultrasonic cycloplasty; IOP: Intraocular pressure; logMAR: Logarithm of the Minimum Angle of Resolution. p-values for continuous variables (age, IOP) were derived from independent samples t-tests; drug times and visual acuity from Mann-Whitney U test; sex and eye laterality from chi-square test.

Table 2. Comparison of intraocular pressure changes before, and after surgery between the two groups.

Parameters	UCP group (n = 45)	UCP + anti-VEGF group (n = 35)	p
Age, mean ± SD (years)	62.81 ± 11.90	57.47 ± 14.77	0.085
Sex (male/female)	14/31	23/12	0.002
Eye (right/left)	23/22	17/18	0.822
IOP, mean ± SD (mmHg)	42.69 ± 9.14	45.89 ± 7.55	0.099
Visual acuity (logMAR), mean ± SD	3.00 (2.30, 3.00)	2.30 (1.70, 3.00)	0.026
Drug times	3.0 (3.0,3.0)	3.0 (3.0,3.0)	0.263

Between-group p-values were derived from independent samples t-tests on change scores from baseline, which were normally distributed at all time points. p for trend was derived from simple linear regression within each group. [a] $p < 0.05$ vs baseline: within-group paired t-tests for IOP at day 1 and week 1; Wilcoxon signed-rank tests for IOP at month 1 and month 3.

Table 3. Comparison of visual acuity changes before and after surgery between the two groups.

Visual acuity (logMAR) median (IQR), Δ median (IQR)	Postop. 1 d	Postop. 1 week	Postop. 1 month	Postop. 3 months	p^{trend}
UCP group (n = 45)	3.00 (2.30, 3.00), 0 (0, 0)	3.00 (2.30, 3.00), 0 (0, 0)	3.00 (2.30, 3.00), 0 (0, 0)	3.00 (2.30, 3.00), 0 (0, 0)	< 0.001
UCP + VEGF group (n = 35)	2.30 (1.40, 3.00), 0 (0, 0)	2.00 (1.20, 2.70)[a], 0 (0, 0)	2.30 (1.40, 3.00), 0 (0, 0)	1.70 (0.00, 2.70)[a], −0.60 (−1.26, 0)	< 0.001
Z	0.72	2.49	1.08	2.09	–
p	0.472	0.013	0.281	0.037	–

Between-group p-values were derived from Mann-Whitney U tests on change scores from baseline (Δ = postoperative − preoperative). [a] $p < 0.05$ vs baseline: within-group Wilcoxon signed-rank tests.

Table 4. Comparison of drug times before and after surgery between the two groups.

Parameters, median(IQR), Δ median(IQR)	Postop. 1 d	Postop. 1 wk	Postop. 1 mo	Postop. 3 mo	p^{trend}
UCP group (n = 45)	3.0 (3.0, 3.0), 0 (0, 0)	3.0 (2.0, 3.0), 0 (0, 0)	2.0 (2.0, 3.0), 0 (−1, 0)[a]	2.0 (2.0, 3.0), 0 (−1, 0)[a]	< 0.001
UCP + VEGF group (n = 35)	3.0 (3.0, 3.0), 0 (0, 0)	3.0 (2.0, 3.0), 0 (−1, 0)[a]	3.0 (2.0, 3.0), 0 (−1, 0)[a]	2.5 (2.0, 3.0), -0.5 (−2, 0)[a]	0.005
Z	−0.10	1.43	0.40	0.29	–
p	0.923	0.152	0.689	0.771	–

Between-group p-values were derived from Mann-Whitney U tests. p for trend was derived from simple linear regression within each group. [a] $p < 0.05$ vs baseline: within-group Wilcoxon signed-rank tests.

superior short-term pressure control. This enhanced efficacy likely reflects the complementary mechanisms of the two interventions: UCP selectively reduces aqueous humor production via targeted ciliary body ablation, while anti-VEGF therapy mitigates iris and angle neovascularization, decreases intraocular inflammation, and improves aqueous outflow. From a pathophysiological perspective, NVG represents a condition in which both inflow and outflow pathways are severely disrupted; therefore, a strategy that simultaneously suppresses aqueous production and relieves outflow obstruction is theoretically more effective than either approach alone. This study should be interpreted as an exploratory, short-term retrospective analysis. Although a significant reduction in IOP was observed at 3 months, glaucoma is a chronic and progressive disease, and longer follow-up is required to determine the durability of the IOP-lowering effect. Future prospective studies with extended follow-up periods are warranted.

The treatment of NVG is complex, with the primary goal of lowering IOP and preserving visual function. Anti-VEGF injections help regress iris and angle neovascularization, reduce intraoperative bleeding, and improve surgical outcomes. For eyes without visual potential, therapy focuses on reducing IOP and relieving symptoms. Management of the underlying disease should be tailored to ocular status to reduce neovascularization and prevent further IOP elevation[12–14]. Since the 1980s, ultrasound has been applied in glaucoma treatment[15]. UCP precisely targets the ciliary processes to induce controlled thermal coagulation, reducing aqueous humor production, enhancing uveoscleral outflow, and achieving dual IOP reduction while preserving the blood–aqueous barrier[16,17]. Its precise focusing avoids damage to non-treated tissues, prevents hypotony and ocular shrinkage, and is unaffected by pigment absorption. With no need for incisions, rapid recovery, and compatibility with subsequent anti-VEGF or PRP therapy, the procedure is simple, completed within minutes, and significantly improves clinical efficiency[1,18,19]. Compared with traditional cyclodestructive procedures such as cyclocryotherapy or transscleral diode laser, UCP offers greater anatomical selectivity and a more predictable energy delivery profile, which may translate into a lower risk of severe complications such as persistent hypotony, phthisis bulbi, or chronic inflammation. These safety advantages are particularly important in NVG eyes, which often have compromised ocular structures and limited tolerance for additional surgical trauma.

The additional visual benefits observed in the combined treatment group are consistent with previous reports demonstrating that anti-VEGF therapy can promote regression of anterior segment neovascularization and stabilize or improve visual acuity in NVG patients. Although visual prognosis in NVG is often guarded due to advanced retinal ischemia and optic nerve damage, early suppression of VEGF-driven neovascular activity may help preserve residual visual function by improving ocular perfusion, reducing inflammatory mediators, and facilitating more stable postoperative conditions. A study by Fan et al. reported that the UCP group in patients with NVG showed significantly lower IOP at 7 d, 1 month, and 3 months postoperatively compared with postoperative day 1, and it demonstrated a significant reduction in the number of IOP-lowering medications at 7 d, 1 month, and 3 months after surgery compared with preoperative levels[20], which is similar to our findings. However, our findings further extend these observations by showing that combining anti-VEGF with UCP, a minimally invasive cyclodestructive procedure, provides both early IOP lowering and visual improvement, suggesting a synergistic effect that aligns with the mechanistic rationale proposed in prior literature[20]. This synergistic effect may be especially relevant during the early postoperative period, when VEGF levels remain elevated, and inflammatory responses are pronounced, potentially undermining the success of standalone cyclodestructive procedures[21,22].

Another clinically meaningful observation is that combined therapy may reduce the dependence on multiple topical IOP-lowering medications. Polypharmacy is common in NVG patients and is associated with poor adherence, ocular surface toxicity, and reduced quality of life. By achieving stronger early IOP control, adjunctive anti-VEGF therapy may help simplify postoperative medication regimens, thereby improving patient comfort and long-term management feasibility[23,24]. Furthermore, the rapid regression of iris and angle neovascularization following anti-VEGF injection may lower the risk of hyphema and intraoperative bleeding, which are frequent challenges in NVG-related surgeries and can negatively affect surgical outcomes[25]. Notably, a recent study with extended follow-up demonstrated sustained intraocular pressure reduction and acceptable safety profiles over a 36-month observation period[26]. Compared with that long-term evidence, our study focuses specifically on early postoperative dynamics in NVG patients. While long-term durability remains crucial, early IOP control in NVG is often clinically urgent, and our findings primarily address this early therapeutic window.

Despite these promising findings, several limitations should be considered. The retrospective design and short-term follow-up limit the ability to assess long-term efficacy, durability of IOP control, and the incidence of late complications. Because NVG is a chronic and progressive disease, the 3-month follow-up period in this study is insufficient to determine the long-term durability of IOP control or late complications. Future studies with longer follow-up are necessary. Additionally, the use of adjunctive anti-VEGF therapy was not randomized, but based on clinical judgment and neovascular severity, which may introduce selection bias. The lack of standardized grading for anterior segment neovascularization limits our ability to fully adjust for baseline disease severity. Baseline sex imbalance between groups may introduce confounding, and the study did not systematically evaluate the degree of neovascular regression, angle closure, or patient-reported outcomes such as ocular discomfort or pain. Baseline visual acuity was significantly different between the two groups, which may have confounded the between-group comparisons of postoperative visual outcomes. The use of change scores from baseline for between-group comparisons was intended to partially address this imbalance; however, residual confounding cannot be excluded. Moreover, the anti-VEGF retreatment schedule was not standardized, which may have contributed to variability in treatment response. Future prospective studies with larger sample sizes, standardized anti-VEGF protocols, and longer follow-up are warranted to confirm the durability and safety of combined therapy and to evaluate its impact on functional vision and quality of life. In addition, future investigations incorporating anterior segment imaging modalities such as gonioscopy-assisted photography or anterior segment OCT could provide more objective quantification of neovascular regression and angle status, helping to clarify the structural mechanisms underlying treatment response.

Conclusions

UCP combined with intravitreal anti-VEGF injection provides better IOP reduction and visual acuity improvement than UCP alone in neovascular glaucoma. These findings support the use of multimodal treatment strategies that target both aqueous humor production and ischemia-driven neovascularization.

Ethical statements

This retrospective study was approved by the Institutional Review Board of the Inner Mongolian Chaoju Eye Hospital (No. CJ-KLS-20251130; dated November 30th, 2025) and adhered to the Declaration of Helsinki. Informed consent was obtained from all patients.

Author contributions

The authors confirm their contributions to the paper as follows: conceptualization: Guo J, Bai G; methodology: Guo J, Yang H, Zhang B; data acquisition: Guo J, Yang H, Cui R; formal analysis: Cui R, Zhang B; investigation: Guo J, Yang H, Cui R, Zhang B; visualization: Cui R; writing original draft: Guo J; writing – review and editing: Guo J, Yang H, Cui R, Zhang B, Bai G; supervision: Bai G; Zhang B. All authors reviewed and approved the final manuscript for submission.

Data availability

The datasets generated during and analyzed during the current study are available from the corresponding author on reasonable request.

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Conflict of interest

The authors declare that they have no conflict of interest.

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