27-Gauge vitrectomy vs. 25-gauge vitrectomy in the management of proliferative diabetic retinopathy with preoperative intravitreal injection of conbercept

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Abstract. Small-gauge vitrectomy has become popular due to its notable advantages, including less trauma, shortened convalescence and improved manoeuvrability. The aim of the present study was to compare the surgical outcomes of 27-gauge (27-G) vitrectomy with those of 25-gauge (25-G) vitrectomy in the management of proliferative diabetic retinopathy (PDR) with preoperative intravitreal injection of conbercept. The data of 48 consecutive patients with PDR (48 eyes) were retrospectively collected. The patients underwent conbercept intravitreal injection and pars plana vitrectomy with a 27-G group (23 eyes) or 25-G group (25 eyes) vitrectomy system. The operating time, suturing rate, endodiathermy rate, postoperative best-corrected visual acuity (BCVA), intraocular pressure (IOP) and complications were recorded. The mean postoperative BCVA at final follow-up was significantly improved compared with that at the baseline in both groups (P<0.001 for both). The differences in the mean BCVA changes between the two groups were not significant (P>0.99), and no differences were observed in the final central foveal thickness (P=0.51) between the two groups. The final IOP remained stable compared with that at the baseline in the 27-G group (P=0.36) and the 25-G group (P=0.05). The suturing rate was significantly decreased in the 27-G group compared with the 25-G group (P=0.04). There were no significant differences between the two groups in terms of the operating time (P=0.18), rate of endodiathermy use (P>0.99), iatrogenic retinal breaks (P=0.42) or postoperative recurrent vitreous haemorrhage (P>0.99). In addition, no case of ocular hypotony was observed in either group. In conclusion, 27-G vitrectomy was as efficient and safe as 25-G vitrectomy in the management of PDR in terms of operating time and complications. With reference to the literature, preoperative conbercept injection appears to assist in decreasing the incidence of intraoperative and postoperative complications.

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Introduction

Proliferative diabetic retinopathy (PDR) continues to be a major cause of vision loss, and it has been reported that there were >90 million adults with diabetes in China as of 2010, and patients with PDR accounted for 2.8% of those with diabetes (1). Although panretinal photocoagulation (PRP) has been the treatment of choice for delaying the diabetic retinopathy process and preventing visual loss, there remains a high number of patients progressing to the advanced stages, such as vitreous hemorrhage and tractional retinal detachment, and subsequently requiring pars plana vitrectomy (PPV) to clear vitreous haemorrhage (VH) and reattach the retina. However, PPV for patients with PDR can often be challenging (2). Vitreous removal, membrane peeling and membrane delamination can be difficult procedures due to the tight adhesions formed between the fibrovascular membrane and the retina, which can lead to intraoperative haemorrhages and iatrogenic breaks (3). Furthermore, surgery-related complications, such as recurrent VH and postoperative reproliferation, represent a major concern for patients with PDR, resulting in poorer anatomic and functional visual outcomes (4,5).

Since the introduction of the 25-gauge (25-G) sutureless transconjunctival system in 2002 by Fujii *et al* (6), microincision vitrectomy surgery (MIVS) has progressively developed towards the use of smaller gauge instruments. In 2010, Oshima *et al* (7) first reported 100% anatomic success and 65% visual improvement of ≥3 lines using a novel

27-gauge (27-G) PPV system in patients with vitreoretinal diseases. Small-gauge vitrectomy has become popular due to its notable advantages, including less trauma, shortened convalescence, reduced inflammatory response and improved manoeuvrability (8). As a result, the use of 27-G PPV has expanded from simple macular diseases to complicated cases, including rhegmatogenous retinal detachment (RRD) (9). With the improvement of instruments, 25-G and 27-G PPV have been widely used in the management of different vitreoretinal diseases such as VH, retinal detachment, macular hole and PDR (10). Smaller gauge vitrectomy cutters may offer a smaller sphere of influence compared with larger gauge vitrectomy probes (11,12). Furthermore, the shortened port-tip distance improves access to surgical tissue planes and facilitates aspiration of preretinal and subretinal materials (7). Consequently, 27-G instruments with smaller gauge and shorter port-tip distance are considered safer compared with 25-G instruments. However, whether a 27-G system can be used to perform complex intraocular manipulations, such as fibrovascular membrane dissection and haemostasis in diabetic vitrectomy, is still a concern.

Among the various factors involved in the pathogenesis of PDR, vascular endothelial growth factor (VEGF) appears to serve an important role (13). Previous reports have indicated high levels of VEGFs are present in both animal models of diabetes and patients with diabetes (14,15). Inhibition of VEGF receptors by anti-VEGF agents has been reported to induce endothelial cell apoptosis in blood vessels with vascular regression and to induce normalisation of premature vessels by increasing pericyte coverage and reducing vessel fenestration in PDR (16). It has also been reported that the application of intravitreal anti-VEGF before PPV in PDR has the effect of reducing operating times, potentially as a result of facilitating the surgery by reducing the incidence of intra-operative bleeding (17). Therefore, anti-VEGF agents have been widely adopted as adjunctive therapy in patients requiring vitrectomy for PDR with VH and tractional retinal detachment (18). Conbercept, also known as KH902, a novel drug that can bind to all isoforms of VEGF-A, placental growth factor and VEGF-B, has been demonstrated to serve an active role in treating ocular diseases with choroidal neovascularisation (19). Previous studies have reported the efficacy and safety of conbercept for accelerating postoperative vitreous recovery in 23-gauge (23-G) PPV for PDR (20,21).

To the best of our knowledge, there has been no research concerning the difference between 27-G and 25-G PPV in diabetic retinopathy with preoperative intravitreal injection of conbercept. Therefore, the purpose of the present study was to investigate the feasibility, efficiency and safety of 27-G vitrectomy with preoperative intravitreal conbercept injection for PDR treatment compared with those of 25-G vitrectomy.

Materials and methods

Ethical approval. The present study was an interventional, comparative and ambispective longitudinal study. The study was approved by the Institutional Review Board of Zhongshan Ophthalmic Center at Sun Yat-sen University (approval no. 2018KYPJ144; Guangzhou, China) and performed in accordance with the World Medical Association's Declaration of Helsinki. Written informed consent was obtained from each subject.

Patient inclusion. A total of 48 consecutive patients (48 eyes) were included in the present study. The inclusion criteria were as follows: Patients who were diagnosed with PDR and had been administered a conbercept intravitreal injection followed by 27-G or 25-G vitrectomy at the Zhongshan Ophthalmic Center at Sun Yat-sen University (Guangzhou, China) between March 2016 and February 2017. The exclusion criteria were as follows: i) A history of previous PPV; and ii) eyes that had <6 months of follow-up after PPV. In addition, as the diameter of 27-G is smaller than 25-G, more time is needed to complete silicone oil tamponade with 27-G (22). The operating time of the two groups (25-G and 27-G) would therefore not be comparable if silicone oil injection is used. Consequently, patients who needed silicone oil tamponade were also excluded from the present study. Preoperative data, including the age, sex, course of the disease and history of laser photocoagulation of the patient, were recorded. Preoperative ophthalmologic evaluations included measurements of the best-corrected visual acuity (BCVA) and intraocular pressure (IOP), biomicroscopic examination, B-scan, indirect ophthalmoscopy, and optical coherence tomography.

Patient treatment. The diagnosis, operation and monitoring in both groups were conducted by one experienced vitreoretinal surgeon. All patients received an intravitreal injection of conbercept (0.5 mg; 0.05 ml; 10 mg/ml; KH902; Chengdu Kanghong Pharmaceutical Group Co., Ltd.) in the superior temporal sector 3.5-4.0 mm from the sclerocorneal limbus 7-14 days before vitrectomy. Patients underwent a standard three-port PPV using a 27-G or 25-G system (Constellation Vitrectomy System; Alcon Inc.) under retrobulbar anaesthesia. After displacement of the conjunctiva, three cannulas were inserted 4.0 mm posterior to the limbus with the following method: The trocar-cannula was inserted parallel to the limbus in a tangential orientation at an angle of 30-40˚ to the sclera. After insertion of the beveled trocar to the level of the beginning of the cannula, the trocar-cannula was redirected such that the cannula entered perpendicular to the sclera. The surgical parameters were set as follows: i) Cutting rate of 6,000 cuts per min (cpm) in the 27-G group and 5,000 cpm in the 25-G group; ii) linear aspiration of 600 mmHg in the 27-G group and 500 mmHg in the 25-G group; iii) duty cycle of 50/50; and iv) shave mode set as the horizontal mode. Procedures such as fibrovascular membrane dissection, endodiathermy and PRP were performed as required. Endolaser photocoagulation was performed for sealing retinal holes if iatrogenic retinal breaks occurred. For patients with tractional retinal detachment (TRD), intraoperative perfluorocarbon liquid injection, gas-fluid exchange and gas tamponade were selectively performed according to the extent of retinal detachment and surgeon's experience. After surgery, all sclerotomy sites were inspected and, if required, a suture was placed to prevent leakage. Patients who received intraocular tamponade were instructed to remain face down for 7-10 days. When the follow-up schedule was adhered to, the patients were followed up at 1 day, 1 week, 1 month, 3 months and 6 months postoperatively.

Table I. Baseline characteristics, surgical procedures and complications.

Characteristic	27-Gauge vitrectomy	25-Gauge vitrectomy	P-value
Baseline characteristics			
Eyes, n	23	25	
Male patients, n (%)	13 (57)	13 (52)	0.75[a]
Age, years			
Mean ± SD	52.4±8.4	54.0±7.6	0.53[b]
Range	37-69	39-67	
Lens status, n (%)			
Phakic	23 (100)	25 (100)	
Primary indication, n (%)			
Vitreous hemorrhage	15 (65)	16 (64)	0.93[a]
Proliferative membrane	13 (57)	17 (68)	0.41[a]
Traction retinal detachment	5 (22)	8 (32)	0.42[a]
Preoperative panretinal photocoagulation, n (%)	11 (48)	13 (52)	0.77[a]
Follow-up, months			
Mean ± SD	9.8±3.3	9.1±2.7	0.45[b]
Range	6-15	6-15	
Surgical procedures			
Suturing rate, n (%)	3 (13)	10 (40)	0.04[a]
Operating time (min)	40.2±3.0	39.2±2.3	0.18[b]
Tamponade, n (%)			
Air	5 (22)	8 (32)	0.42[a]
Balanced salt solution	18 (78)	17 (68)	
Complications			
Intraoperative iatrogenic retinal breaks, n (%)	2 (9)	5 (20)	0.42[c]
Endodiathermy rate, n (%)	2 (9)	3 (12)	>0.99[c]
Postoperative VH, n (%)	1 (4)	2 (8)	>0.99[c]
Mean ± SD CFT, μm	258.17±46.44	266.88±45.13	0.51[b]

[a]Pearson χ^2 test. [b]Unpaired t-test. [c]Fisher's exact test. VH, vitreous hemorrhage; CFT, central foveal thickness.

The records of intraoperative findings focussed on the operating time, suturing rate and rate of endodiathermy use. Preoperative BCBA, postoperative BCVA at 1 month and the last date of follow up, central foveal thickness (CFT), preoperative IOP, postoperative IOP at 1 day, 1 week, 1 month, 3 months and the last date of follow up, and complications were also recorded at each follow-up visit.

Statistical analysis. Snellen visual acuities were recorded and converted to the logarithm of the minimum angle of resolution for subsequent analysis. An unpaired t-test was used for the analyses of age, operating time, CFT and follow-up duration. Pearson χ^2 test was used for the analyses of sex, primary indication, suturing rate, preoperative PRP and tamponade. Two-way mixed ANOVA and Bonferroni correction were used for the IOP and BCVA analysis between the two groups at different time points and within the same group pre- and post-operatively. Fisher's exact test was applied for the analyses of intraoperative iatrogenic retinal breaks, rate of endodiathermy use and postoperative VH. The parametric numerical data are presented as mean ± standard deviation, and the count data are shown as n (%). Analyses were conducted using the GraphPAD Prism 8.4.3 software (GraphPad Software; Dotmatics). P<0.05 was considered to indicate a statistically significant difference.

Results

Patient characteristics. The baseline demographic data of the patients are summarised in Table I. The differences in the demographic data were not significant between the groups. The data of 48 eyes from 48 patients with PDR were collected for the current study. Of the 48 eyes, 18 (37.5%) presented with VH, 8 (16.7%) with proliferative membrane, 9 (18.8%) with VH and proliferative membrane, 9 (18.8%) with proliferative membrane and TRD, and 4 (8.3%) with TRD. All the eyes were phakic and none underwent phacoemulsification during PPV. The mean age of the patients was 52.4±8.4 years (range, 37-69 years) in the 27-G group and 54.0±7.6 years (range, 39-67 years) in the 25-G group. Among the patients, 13 were male in each group. The mean follow-up period was 9.8±3.3 months (range, 6-15 months) in the 27-G group and 9.1±2.7 months (range, 6-15 months) in the 25-G group. The clinical findings of the patients in both groups are summarised in Tables II and III.

Table II. Clinical findings of patients in the 27-gauge pars plana vitrectomy group.

Sex	Eye	Primary indication[a]	Preoperative PRP	Best-corrected visual acuity, logMAR		Intraocular pressure, mmHg		Operating time, min	Tamponade	Suturing site	Endodiathermy use	Retinal break	Follow-up, months	Postoperative vitreous hemorrhage
				Baseline	Final	Baseline	Final							
M	L	1	Y	1.398	1.000	15.4	14.8	38	BSS	N	N	N	6	N
M	R	1	Y	1.222	0.699	19.5	20.6	37	BSS	N	N	N	9	N
F	L	1+2+3	Y	2.600	0.523	11.6	12.5	45	Air	N	N	Y	6	N
F	L	2+3	N	1.699	0.398	12.9	11.2	44	Air	N	N	N	12	N
M	L	1+2	N	2.300	0.699	14.5	15.2	46	BSS	N	N	N	9	N
F	R	2	Y	1.000	0.301	15.3	16.8	44	BSS	N	Y	N	6	N
M	L	1	N	1.000	0.222	16.7	14.5	38	BSS	IT	N	N	15	N
M	L	1	Y	1.097	0.699	17.5	18.7	39	BSS	N	N	N	12	N
F	R	2	N	0.699	0.523	12.8	10.7	37	BSS	N	N	N	6	N
F	R	2+3	Y	2.300	1.097	13.6	12.5	44	Air	N	N	N	9	N
M	R	1+2	Y	1.222	0.699	17.4	14.9	43	BSS	N	N	N	12	N
M	R	1+2	N	2.300	1.000	18.9	15.6	42	BSS	N	N	N	15	N
F	L	1	N	0.699	0.398	19.6	18.7	36	BSS	IT	N	N	9	N
F	R	1+2	N	0.523	0.222	15.4	17.5	37	BSS	N	N	N	6	N
M	L	1	Y	1.097	0.699	12.7	11.8	38	BSS	N	N	N	9	N
M	L	2+3	Y	1.000	0.398	13.3	12.7	43	Air	N	Y	Y	15	N
F	R	1	N	0.699	0.301	14.2	14.8	38	BSS	N	N	N	12	Y
F	L	1	Y	1.000	0.523	17.5	16.9	39	BSS	ST	N	N	9	N
M	L	2	N	1.000	0.222	16.9	15.5	38	BSS	N	N	N	9	N
F	R	1	N	0.699	0.301	18.8	17.2	39	BSS	N	N	N	6	N
M	L	2	N	1.097	0.523	20.2	18.4	40	BSS	N	N	N	6	N
M	R	1	Y	1.000	0.301	15.5	14.4	39	BSS	N	N	N	12	N
M	R	2+3	N	2.300	0.699	13.7	12.9	41	Air	N	N	N	15	N

[a]Primary indication: 1, vitreous hemorrhage; 2, proliferative membrane; 3, traction retinal detachment. BSS, balanced salt solution; F, female; IT, inferior and temporal sites; L, left; logMAR, logarithm of the minimum angle of resolution; M, male; N, no; PRP, panretinal photocoagulation; R, right; ST, superior and temporal sites; Y, yes.

Table III. Clinical findings of patients in the 25-gauge pars plana vitrectomy group.

Sex	Eye	Primary indication[a]	Preoperative PRP	Best-corrected visual acuity, logMAR		Intraocular pressure, mmHg		Operating time, min	Tamponade	Suturing site	Endodiathermy use	Retinal break	Follow-up, months	Postoperative vitreous hemorrhage
				Baseline	Final	Baseline	Final							
M	R	1	N	1.000	0.523	16.8	14.7	36	BSS	N	Y	N	9	N
F	R	1+2+3	Y	2.600	0.398	21.7	18.9	44	Air	N	N	Y	6	N
M	L	1	Y	1.097	0.699	14.5	13.5	38	BSS	IT	N	N	12	N
F	R	2	N	0.699	0.301	15.3	16.8	37	BSS	N	N	N	9	N
M	L	1	Y	1.097	1.000	16.7	14	40	BSS	N	N	N	6	N
M	L	1	Y	1.000	0.523	17.5	18.4	41	BSS	ST	N	N	12	N
F	R	2+3	N	2.300	0.699	12.8	11.7	42	Air	N	N	Y	15	N
M	L	1	Y	0.699	0.398	13.6	12.5	37	BSS	IT	Y	N	12	N
F	L	2	N	1.000	0.523	17.8	16.4	38	BSS	N	N	N	6	N
M	L	1+2	N	1.097	0.523	18.9	15.4	39	BSS	SN	N	N	6	Y
M	L	1+2	Y	0.699	0.398	19.6	20.7	37	BSS	ST	N	N	9	N
F	R	1+2+3	N	1.699	1.000	15.4	14.3	39	BSS	N	N	N	12	N
F	L	1	Y	0.523	0.398	12.7	11.5	36	BSS	ST	N	N	9	N
M	L	2+3	N	1.699	0.699	13.3	12.8	40	Air	N	N	N	6	N
F	R	2+3	Y	1.222	0.523	14.2	12.5	39	Air	N	N	N	12	N
M	R	2	Y	1.000	0.398	15.4	16.2	37	BSS	N	Y	N	12	N
M	L	1	N	1.097	0.699	12.7	11.5	38	BSS	SN	N	N	9	N
F	L	2+3	Y	2.300	0.523	13.3	14.7	43	Air	N	N	Y	9	Y
M	R	1+2	Y	2.300	1.000	14.2	13.3	41	Air	N	N	Y	6	N
F	L	1+2	Y	1.000	0.398	17.5	15.6	39	BSS	N	N	N	6	N
M	R	2	N	0.699	0.523	16.9	14.2	38	BSS	IT	N	N	9	N
F	R	1+2	N	1.097	0.699	18.8	17.6	39	BSS	IT	N	N	9	N
F	R	1	N	1.000	0.398	11.5	9.5	37	BSS	ST	N	N	12	N
M	L	1+2+3	Y	1.699	0.699	15.5	16	43	Air	N	N	Y	9	N
F	L	2+3	N	1.398	1.000	17.1	18.4	41	Air	N	N	N	6	N

[a]Primary indication: 1, vitreous hemorrhage; 2, proliferative membrane; 3, traction retinal detachment. BSS, balanced salt solution; F, female; IT, inferior and temporal sites; L, left; logMAR, logarithm of the minimum angle of resolution; M, male; N, no; PRP, panretinal photocoagulation; R, right; SN, superior and nasal sites; ST, superior and temporal sites; Y, yes.

BCVA and CFT. As shown in Fig. 1, in the 27-G group, the mean BCVA improved from 1.30±0.62 preoperatively to 0.64±0.25 at 1 month after surgery (P<0.001) and 0.54±0.26 at the final postoperative visit (P<0.001). In the 25-G group, the mean BCVA improved from 1.28±0.58 preoperatively to 0.65±0.18 at 1 month after surgery (P<0.001) and 0.60±0.22 at the final postoperative visit (P<0.001). The differences in the mean BCVA changes were not significant between groups at preoperation (P>0.99), 1 month after surgery (P>0.99) and at the final postoperative visit (P>0.99). There was no significant difference in the mean CFT between the 27-G group (258.17±46.44 μm) and the 25-G group (266.88±45.13 μm) at the final postoperative visit (P=0.51).

IOP. As shown in Fig. 2, the mean preoperative IOP was 15.8±2.5 mmHg, while the IOP was 11.1±2.0 mmHg at 1 day after surgery (P<0.001), 14.2±2.2 mmHg at 1 month after surgery (P<0.01), 14.6±2.3 mmHg at 3 months after surgery (P<0.05) and 15.2±2.7 mmHg at the final follow up (P=0.36) for the 27-G group. For the 25-G group, the mean preoperative IOP was 15.8±2.5 mmHg, and the IOP changed to 12.6±2.1 mmHg at 1 day after surgery (P<0.001), 14.2±1.5 mmHg at 1 month after surgery (P<0.05), 14.7±2.0 mmHg at 3 months after surgery (P<0.05) and 14.8±2.7 mmHg at the final follow-up (P=0.05). No case of ocular hypertension (IOP >25 mmHg) or hypotension (IOP <6 mmHg) was detected in either group after surgery (data not shown). In both groups, the IOP decreased in the early postoperative period and recovered at the final follow-up. There was no significant difference in the IOP between the two groups at preoperation (P>0.99), and 1 day (P=0.15), 1 month (P>0.99), 3 months (P>0.99) and the final follow up (P>0.99) after surgery.

Operating time and suturing rate. As shown in Table I, the difference in suturing rate was significant among three eyes (13%) in 27-G group and 10 eyes (40%) in 25-G group (P=0.04). There were no statistically significant differences in operating time between 27-G group (40.2±3.0 min) and 25-G group (39.2±2.3 min) (P=0.18). During the surgery, no case required intravitreal forceps or scissors to remove the fibrovascular membrane in the 27-G group, and no case required conversion to larger gauge instrumentation due to severe fibrovascular tissues that were difficult to remove in both groups.

Surgical complications. As shown in Table I, intraoperative iatrogenic retinal breaks occurred in two eyes (9%) in the 27-G group and five eyes (20%) in the 25-G group (P=0.42). The retinal breaks occurred during membrane removal and were treated during surgery using endolaser photocoagulation. There was no significant difference in the rate of endodiathermy use between the 27-G group (two eyes; 9%) and the 25-G group (three eyes; 12%) (P>0.99). Postoperative VH (POVH) occurred in one eye (4%) in the 27-G group and two eyes (8%) in the 25-G group (P>0.99). No other complications such as postoperative endophthalmitis, sclerotomy-related retinal tears or choroidal detachments were observed. Typical cases of both groups were shown in Figs. 3 and 4, which demonstrate 2 patient with PDR who underwent 27-G and 25-G vitrectomy, respectively, and who experienced good rehabilitation in terms of vitreoretinal anatomy after surgery.

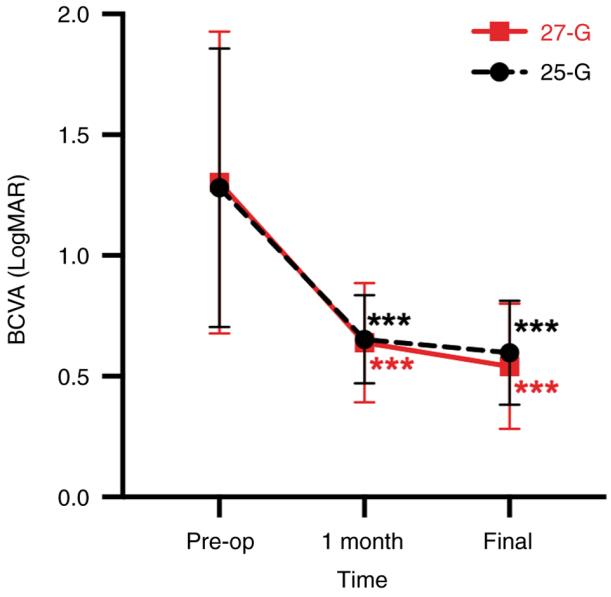

Figure 1. BCVA changes during the follow-up period in the 27-G and 25-G groups. Preoperative intra-group comparison of BCVA showed it improved significantly after surgery in each group. There was no significant difference in the BCVA between the two groups at preoperation (P>0.99), 1 month after surgery (P>0.99) and at the final postoperative visit (P>0.99). ***P<0.001 vs. pre-op. 25-G, 25-gauge; 27-G, 27-gauge; BCVA, best-corrected visual acuity; LogMAR, logarithm of the minimum angle of resolution; Pre-op, preoperative.

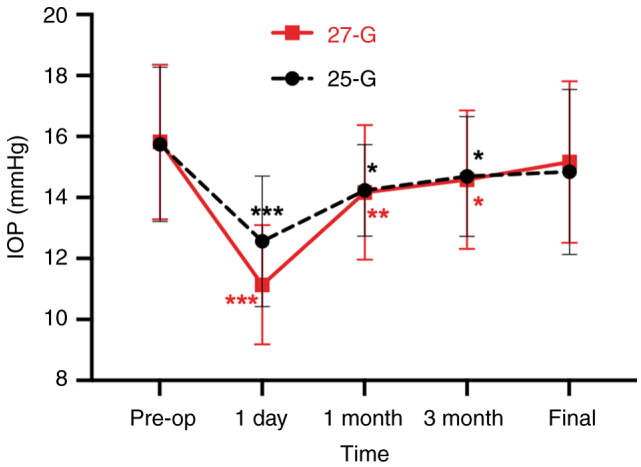

Figure 2. IOP changes during the follow-up period in the 27-G and 25-G groups. Preoperative intra-group comparison of IOP in 27-G and 25-G groups, retrospectively, showed the postoperative IOP was significantly decreased at 1 day, 1 and 3 months, and recovered at the final follow-up. There was no significant difference in the IOP between the two groups at preoperation (P>0.99), and 1 day (P=0.15), 1 month (P>0.99), 3 months (P>0.99) and the final follow up (P>0.99) after surgery. *P<0.05, **P<0.01, ***P<0.001 vs. pre-op. 25-G, 25-gauge; 27-G, 27-gauge; IOP, intraocular pressure; Pre-op, preoperative.

Discussion

Since the introduction of MIVS in 2002 (23), vitrectomy instruments have been progressing towards smaller sizes with less trauma caused. Compared with conventional 20-gauge vitrectomy, smaller gauge PPV has gained wider adoption with the use of more innovative instruments that offer less

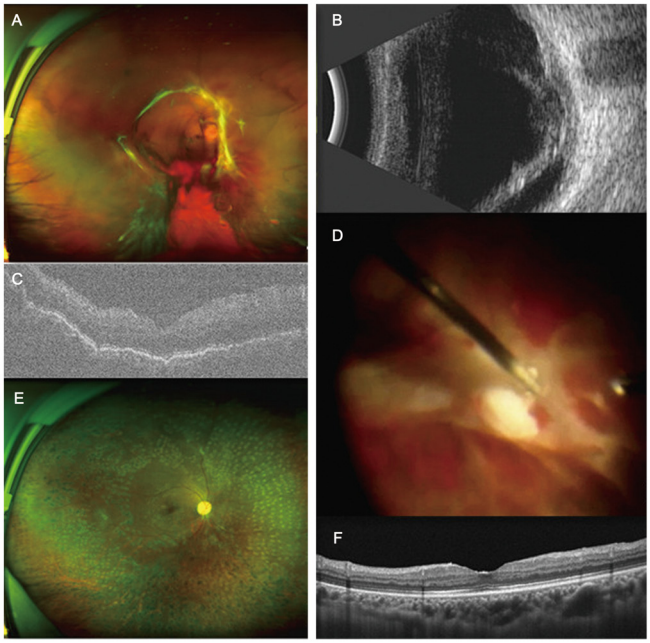

Figure 3. A patient with proliferative diabetic retinopathy in the right eye underwent 27-G vitrectomy. (A) Preoperative SLO showing VH with severe fibrovascular membranes and TRD at the posterior pole. (B) Preoperative B-ultrasound scan showing vitreous turbidity, fibrovascular membranes and TRD. (C) Preoperative OCT was not definitive concerning the presence of VH. (D) Intraoperative image obtained during 27-G microincision vitrectomy surgery. The fibrotic membrane could be segmented and dissected using 27-G vitrectomy with only slight intraoperative bleeding. (E) SLO and (F) OCT obtained 3 months after surgery showing that the retina had reattached successfully. 27-G, 27-gauge; VH, vitreous haemorrhage; TRD, tractional retinal detachment; OCT, optical coherence tomography; SLO, scanning laser ophthalmoscopy.

postoperative inflammation, quicker recovery and improved manoeuvrability (24). These advantages are crucial for patients with PDR, who are characterised by a hard-to-remove fibrovascular membrane, new vessels prone to bleeding during surgery and a higher risk of nonspecific inflammatory reaction after surgery (25). The use of 27-G instrumentation for routine macular surgery is well established (26,27). However, few studies have evaluated its efficacy in PDR (28,29), and they have not assessed the effect of preoperative intravitreal anti-VEGF injection. The present study explored the use of 27-G or 25-G PPV combined with preoperative intravitreal injection of conbercept for the treatment of patients with PDR. At 1 month and the final follow-up visit, BCVA was significantly improved after surgery, but no statistical difference in the BCVA and CFT changes were observed between the two groups. This suggested that the 27-G technique could be used to obtain equal functional and anatomical improvements to those achieved with the 25-G system in PDR treatment.

In the 27-G system, the internal diameter of the cutter is decreased to 0.275 mm (compared with 0.347 mm in 25-G) (24), which might raise a concern on the possible reduction of flow rates during surgery according to the Hagen-Poiseuille law: The velocity of the steady flow of a fluid through a narrow tube (such as a blood vessel or a catheter) varies directly with the pressure and the fourth power of the radius of the tube, and inversely with the length of the tube and the coefficient of viscosity (30). Previous studies have reported longer operating times using the 27-G vitrectomy system for epiretinal membranes and RRD (31,32). However, the mean operating time in the 27-G group was similar compared with that of the 25-G group in the present study. This may be explained by a reduction in flow rate, which was compensated by the faster cutting rate in the 27-G system. The dual-pneumatic-driven ultrahigh-speed 27-G vitrectomy system can reach a cutting rate as high as 7,500 cpm, while only 5,000 cpm is observed for the 25-G system (24). Additionally, we consider that the operating time may be compensated by the improved manoeuvrability during fibrovascular membrane dissection and lower suturing rate using the 27-G vitrectomy system. Thus, the present study demonstrated that, with an appropriate parameter setting, high efficiency could be achieved even in complex cases such as PDR using the 27-G vitrectomy system.

In addition to the smaller external diameter of the cutter in the 27-G system, the opening of the vitrectomy probe is wider and the distance between the cutting port and the tip is shortened to 0.221 mm (compared with 0.330 mm in the 25-G vitrectomy probe) (7). The improvement in design further enhances the manoeuvrability in handling the proliferative membrane during PDR surgery. In the present study, in the region with loose adhesion, the small-gauge cutter could be more easily inserted into the small space between the fibrovascular membrane and retina to complete the membrane dissection and removal. After this step, the whole piece of membrane was split into smaller pieces. Therefore, the shorter distance between the cutting port and tip showed a great advantage in the management of the proliferative membrane, which means the 27-G cutter may be superior to the 25-G cutter. In addition, the probe could move horizontally on the surface of the retina to shave the fibrovascular tissue into the cutter port. As mentioned in the literature (28,33), when using a larger gauge PPV, such as a 23-G or 25-G PPV, the complex manipulation typically requires multiple instruments, including a membrane forceps to grasp the proliferative membrane, scissors to separate the membrane from the retinal surface and a vitrectomy cutter to remove the membrane. However, in the present study, there was no need for membrane forceps or scissors in the 27-G group. The findings of the present study indicated that 27-G vitrectomy could act as a multifunctional tool for successful membrane segmentation, dissection and removal, which reduced the need for instrument change and shortened the overall operating time.

Intraoperative complications commonly occur during PPV in patients with PDR. Among these complications, the high incidence of iatrogenic retinal breaks (3-50%) (34) and intraocular bleeding (>50%) (35) are two major concerns. In the present study, the 27-G system had a low incidence of iatrogenic retinal breaks, endodiathermy use and POVH compared with the 25-G system. However, the differences between the two systems were not significant for all complications.

The concept of a 'sphere of influence' was first proposed by Dugel *et al* (12) in 2012, and this was described as the affected sphere of the vitreous cutter on adjacent tissue structures. According to this principle, a smaller gauge vitrectomy cutter will offer a smaller sphere of influence compared with larger-gauge vitrectomy probes (11,12). In addition, with an optimal duty cycle, set at 50/50 in the present study, the ultrahigh speed vitreous cutter in the 27-G system makes it easy to

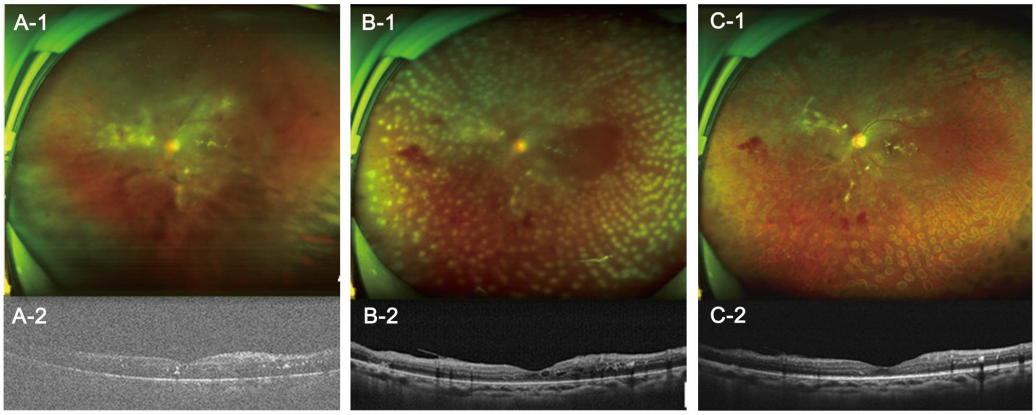

Figure 4. A patient with proliferative diabetic retinopathy in the left eye underwent 25-G vitrectomy. (A-1) Preoperative SLO showing VH with fibrovascular membranes. (A-2) Preoperative OCT revealed an attached retina, although there was a little vitreous hemorrhage. (B-1 and B-2) SLO and OCT obtained 1 day after 25-G microincision vitrectomy surgery indicated that (B-1) the fibrotic membrane was peeled and the VH was cleared up; (B-2) there were small cyst cavities in the macular region. SLO and OCT 1 month after surgery indicated that (C-1) no postoperative VH or (C-2) macular oedema had developed. 25-G, 25-gauge; VH, vitreous haemorrhage; OCT, optical coherence tomography; SLO, scanning laser ophthalmoscopy.

cut the vitreous into small pieces (36), thereby reducing the vitreal viscosity (37) and incidence of cutter blockage (38). Consequently, we consider that 27-G vitrectomy is considered safer due to the reduction of the vitreoretinal traction from the probe tip. Furthermore, the shortened port-tip distance further makes it easy to remove fibrovascular tissue by vitreous cutter. These factors may account for the lower, although not significantly different, rates of endodiathermy use, iatrogenic retinal breaks and POVH in the 27-G PPV group compared with the 25-G PPV group in the present study.

Wound leakage may increase the risk of hypotony and endophthalmitis after vitrectomy (39), thus wound self-sealing is another concern. A previous reports has proposed that the 27-G (0.40-mm) needle is the optimal size for easy self-sealing of scleral wounds with a low incidence of complications (24). In the present study, the 27-G system was demonstrated to be advantageous in self-sealing by presenting a significantly decreased suturing rate compared with the 25-G system. By contrast, hypotony due to wound leakage is one of the major concerns of sutureless 27-G PPV (40). It has been reported that the incidence of transient postoperative hypotony is 5-9% (26) after PPV using the 27-G system. In the present study, no case of ocular hypotony was observed in either the 25-G group or the 27-G group. In addition, there were no other wound leakage-related complications, such as postoperative endophthalmitis, sclerotomy-related retinal tears and choroidal detachments. This may be attributed to the adoption of oblique incisions and conjunctiva displacement, which can reduce wound leakage (41).

For patients with PDR, anti-VEGF therapy has been widely reported to be a promising modality for reducing the incidence of intraoperative bleeding and postoperative recurrent VH (42-44). In most countries, bevacizumab is the most commonly used anti-VEGF agent that is directed against VEGF-A (45,46). Compared with bevacizumab, conbercept, a novel recombinant, soluble fusion protein, has shown its superiority in the treatment of ocular neovascularisation due to its high affinity for PIGF, VEGF-B and all isoforms of VEGF-A (47). According to its molecular structure, conbercept is composed of the second immunoglobulin (Ig) domain of VEGF receptor 1 (VEGFR1), the third and the fourth Ig domain of VEGFR2, and the constant region of human IgG (48). Furthermore, conbercept also binds to VEGF-B and placental growth factor, another member of the VEGF superfamily (48,49). Previous studies have provided sufficient evidence of reducing the chances of intraoperative bleeding after preoperative intravitreal injection of conbercept in the management of PDR (20,50).

In the present study, an intravitreal injection of conbercept was administered 7-14 days before PPV. Due to the low incidence of intraoperative haemorrhage after intravitreal conbercept injection, the use of endodiathermy decreased in both groups compared with that in previous studies without anti-VEGF treatment (50-52). This was consistent with the results reported for patients with PDR administered adjunctive injection of bevacizumab before vitrectomy (35). The incidence of postvitrectomy VH in PDR without preoperative anti-VEGF agents has previously been reported to be 12-32% (35). Li *et al* (53) demonstrated that the adjunctive use of preoperative and postoperative intravitreal conbercept injection decreased early POVH recurrence. The present study demonstrated a relatively low incidence of postvitrectomy VH in both the 27-G (4%) and 25-G (8%) groups, which was lower than that reported by Someya *et al* (54) (23%). The low incidence of POVH can be attributed to pretreatment with the anti-VEGF agent, conbercept (35). Consequently, we hypothesised that preoperative intravitreal conbercept injection could achieve comparable effects to those of bevacizumab in reducing intraoperative and postoperative intraocular bleeding, subsequently helping to simplify the removal of the fibrovascular membrane and shortening the operating time.

The present study had several limitations, such as its mostly retrospective nature, the small sample size and the short follow-up period. Further randomised and prospective studies are required that include patients with PDR with a larger sample size and longer follow-up period. The main focus of the present study was to determine whether there were any differences between 27-G and 25-G PPV in PDR after intravitreal conbercept injection. Whether there are any differences between conbercept and other anti-VEGFs, such

as ranizumab and aflibercept, will be explored in the future. In addition, the present study focused on the clinical difference between 27-G and 25-G PPV in PDR after intravitreal conbercept injection, therefore, only data on surgical-related indicators were collected. In the future, specimens such as vitreous body and fibrovascular membrane will be collected and basic research will be conducted to detect the effect of inflammatory factors and VEGF in the process of fibrovascular membrane formation.

In conclusion, the present study reported the surgical outcomes of 27-G vitrectomy combined with preoperative intravitreal injection of conbercept for the management of PDR. The use of 27-G vitrectomy achieved equally favourable anatomical and functional results, lower suturing rates and good manoeuvrability without extending the operating time compared with the 25-G system. With reference to the literature, preoperative intravitreal conbercept injection is associated with a low incidence of intraoperative and postoperative complications, and it may be an effective and safe approach in the management of PDR.

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Availability of data and materials

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

Authors' contributions

DF performed the data analyses and wrote the manuscript. WX critically revised the manuscript. SZ, YW and WX contributed to the conception of the study and study design, and helped perform the analysis with constructive discussions. YW and DF confirm the authenticity of all the raw data. XJ, CX, SH, ZZ and WX contributed to data interpretation and clinical data collection. XJ and YW contributed to manuscript preparation. ZZ assisted in data analyses. SZ took part in the manuscript preparation and provided useful advice. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was performed with the approval of the Institutional Review Board of Zhongshan Ophthalmic Center at Sun Yat-sen University (approval no. 2018KYPJ144; Guangzhou, China). The requirement for informed consent was waived and all procedures were in accordance with the principles outlined in the Declaration of Helsinki.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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