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The Impact of Physician Face Mask Use on Endophthalmitis After Intravitreal Anti–Vascular Endothelial Growth Factor Injections

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• PURPOSE: To evaluate the effect of physician face mask use on rates and outcomes of postinjection endophthalmitis.

• DESIGN: Retrospective, comparative cohort study.

• METHODS: Setting: Single-center. Study Population: Eyes receiving intravitreal anti–vascular endothelial growth factor injections from July 1, 2013, to September 1, 2019. Intervention: Cases were divided into "Face Mask" group if face masks were worn by the physician during intravitreal injections or "No Talking" group if no face mask was worn but a no-talking policy was observed during intravitreal injections. Main Outcome Measures: Rate of endophthalmitis, visual acuity, and microbial spectrum.

• RESULTS: Of 483,622 intravitreal injections administered, 168 out of 453,460 (0.0371%) cases of endophthalmitis occurred in the No Talking group, and 9 out of 30,162 (0.0298%) cases occurred in the Face Mask group (odds ratio, 0.81; 95% confidence interval, 0.41-1.57; $P = .527$). Sixteen cases of oral flora–associated endophthalmitis were found in the No Talking group (1 in 28,341 injections), compared to none in the Face Mask group ($P = .302$). Mean logMAR visual acuity at presentation in cases that developed culture-positive endophthalmitis was significantly worse in the No Talking group compared to the Face Mask group (17.1 lines lost from baseline acuity vs 13.4 lines lost; $P = .031$), though no difference was observed at 6 months after treatment ($P = .479$).

• CONCLUSION: Physician face mask use did not influence the risk of postinjection endophthalmitis compared to a no-talking policy. However, no cases of oral flora–associated endophthalmitis occurred in the Face Mask group. Future studies are warranted to assess the role of face mask use to reduce endophthalmitis risk, particularly attributable to oral flora. (Am J Ophthalmol 2021;222: 194–201. © 2020 Elsevier Inc. All rights reserved.)

THE USE OF INTRAVITREAL ANTI–VASCULAR ENDOthelial growth factor (anti-VEGF) injections has become the standard of care for the treatment of common retinal diseases including neovascular age-related macular degeneration, retinal vein occlusion, and diabetic macular edema. Since the introduction of intravitreal anti-VEGF therapy, intravitreal injections have become one of the most commonly performed procedures in all of medicine.[1]

Although these medications have excellent safety profiles, acute bacterial endophthalmitis remains an uncommon but potentially devastating complication.[2] Multiple prior studies have evaluated patient-related and procedure-related risk factors associated with postinjection endophthalmitis.[3–7] In particular, 1 study found that oral flora–associated endophthalmitis was reduced after instituting a "no talking" policy where speaking was minimized during the procedure.[7] Understanding potential risk factors for oral flora–associated endophthalmitis is of particular importance given its poor visual prognosis.[7–10]

Surgical face masks reduce transfer of nasopharyngeal flora from respiratory emissions. Previous studies demonstrated that surgical masks reduced forward bacterial dispersion into the surgical field.[11,12] Two laboratory investigations involving simulated intravitreal injections suggest that face mask use may reduce bacterial dispersion associated with speech.[13,14] Partly because of these data, some have suggested including face mask use as part of the standard of care for intravitreal injections.[7,15] However, it is unclear whether decreased bacterial dispersion in these simulations correlates with an impact on clinical practice. Both studies also found that maintaining silence during the simulated injection was equally as effective as wearing a face mask.[13,14] However, other studies have suggested that face mask use may increase bacterial dispersion and infection risk.[16–19]

There are no known clinical studies, to our knowledge, investigating the potential impact of physician face mask use during intravitreal injection administration in a clinic-based setting on the rates of endophthalmitis. This

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lack of data is particularly relevant, given that the use of personal protective equipment like face masks has become a standard of care for routine medical care by ophthalmic providers since the COVID-19 pandemic.[20] Prior to the COVID-19 precautions, within our practice, a subset of physicians have consistently worn face masks while performing intravitreal injections, while other physicians have used a no-talking technique without face mask use during the procedure. The purpose of this study is to evaluate the rate and outcomes of postinjection endophthalmitis with physician face mask use compared to a no-talking policy without face masks.

METHODS

• **OVERVIEW:** This retrospective, single-center, comparative cohort study received prospective approval from the institutional review board at Wills Eye Hospital. Data were collected in accordance with Health Insurance Portability and Accountability Act of 1996 guidelines, and the study conformed to the tenets of the Declaration of Helsinki. Billing records and endophthalmitis logs were used to identify patients who developed endophthalmitis following anti-VEGF injections. Billing data were used to determine the total number of intravitreal injections, patients, type of anti-VEGF injection (bevacizumab, ranibizumab, and aflibercept) used, sex, age, and indication for treatment. Charts of all patients who were treated for endophthalmitis were reviewed, and the diagnosis was confirmed. Recorded data included date of causative injection; date of tap and injection and/or vitrectomy; best available visual acuity (VA) based on the better of habitual correction or pinhole testing before causative injection, at time of tap and inject and/or vitrectomy, at 6 months post procedure, and at last follow-up; and microbial culture results. Physician face mask use was determined by a survey of physician practice patterns.

• **INCLUSION AND EXCLUSION CRITERIA:** All patients diagnosed with presumed infectious endophthalmitis following an intravitreal injection of bevacizumab, ranibizumab, or aflibercept were included in this study. Dates of inclusion were July 1, 2013, to September 1, 2019. Endophthalmitis was defined as patients who presented with a clinical suspicion that was high enough to warrant either intravitreal antibiotic injection with vitreous/aqueous tap or pars plana vitrectomy with injection of antibiotics. In general, these patients presented with decreased VA and pain, and had signs of intraocular inflammation on examination (generally ≥2+ anterior segment cellular reaction and/or posterior segment vitritis). Culture-positive endophthalmitis was defined as any patient with bacterial growth on culture or a positive gram stain from a vitreous or anterior chamber tap. A culture was considered to be oral flora associated when *Enterococcus* or *Streptococcus* species was grown on culture. Endophthalmitis was considered culture negative when both the gram stain and culture plates were negative. Patients with presumed inflammatory endophthalmitis treated with topical steroids without additional interventions were excluded.

• **INJECTION TECHNIQUE:** All intravitreal anti-VEGF injections were performed in office-based settings, either in a designated procedure room or in a clinical room where the examination was conducted. All eyes were routinely prepared with topical anesthetic. No physicians routinely used lidocaine gel, topical pledgets, or subconjunctival lidocaine for anesthesia. After ocular anesthesia, all eyes received topical 5% povidone-iodine at least 60 seconds prior to injection, and povidone-iodine administration was repeated just prior to injection at physician discretion. Injections were performed with a 30 gauge needle for ranibizumab and aflibercept injections, or a 31 gauge needle for bevacizumab injections, and inserted 3.5-4 mm from the limbus. Lid retraction was achieved through manual lid retraction with no routine use of lid speculum by any of the providers. Surgical gloves, surgical caps, and sterile drapes were not used by physician providers for intravitreal injection administration during the study period. Injection techniques were not altered during the study period and were otherwise similar between the 2 groups (Supplemental Table, available at AJO.com).

For the "No Talking" group, all injections were administered under a strict policy of silence in which the physician, patient, and others in the room, including technicians and family members, did not speak during the injection procedure. During the informed consent portion of the procedure, patients are informed of the importance of minimizing speech during the procedure prior to entering the injection room. Families are asked to not come into the injection room unless required for certain reasons, such as help with mobility, as their presence may encourage conversation. Technicians are trained not to talk during preparation of the injection or during the procedure. Physicians do not talk during the procedure except to cue the patient to look in a certain direction prior to uncapping the injection needle. When speaking close to the patient, physicians directed their faces away from the eye to be injected.

For the "Face Mask" group, a subset of physicians wore a surgical mask (Procedure Mask McKesson Pleated Earloops #91-2002; McKesson, Irving, Texas, USA) when administering an intravitreal injection. Additionally, technicians who assisted with drawing drug from the vial, placing the needle on a prefilled syringe, or assisting with lid retraction wore a face mask. During the timeframe of the study, patients did not wear face masks during the injection administration. Patients and others in the room were still asked not to speak during the procedure as per the no-talking policy above, but the physician could speak to give instructions and reassurance.

• **ENDOPHTHALMITIS TREATMENT PROTOCOL:** All eyes developing presumed infectious endophthalmitis immediately underwent a pars plana vitreous tap with aspiration or anterior chamber paracentesis with injection of intravitreal antibiotics or consideration for immediate pars plana vitrectomy with vitreous culture and intravitreal antibiotics. Patients typically received intravitreal vancomycin (1 mg/0.1 mL) and ceftazidime (2 mg/0.1 mL). Intravitreal amikacin (400 μg/0.1 mL) was substituted for ceftazidime for patients with penicillin allergy at the discretion of the treating physician. A subset of patients did not have microbiologic specimens sent for processing if they were being treated at a satellite office without immediate access to a microbiology facility. Patients were variably prescribed cycloplegic agents, topical antibiotics, and topical steroid drops based on physician discretion.

• **STATISTICAL ANALYSIS:** All data were analyzed using statistical software (IBM SPSS 25 Statistics; IBM Corp, Armonk, New York, USA). The primary outcome was the rate of endophthalmitis following intravitreal injection in the Face Mask group compared to the No Talking group. The secondary outcomes were VA and microbial spectrum of culture-positive cases. VA at 6 months was used for the analysis, based on prior studies.[21] Snellen VA was converted to logMAR equivalent for the purpose of statistical analysis. As established by prior studies,[22,23] vision levels of count fingers, hand motion, light perception, and no light perception were assigned VA values of 1.0/200, 0.5/200, 0.25/200, and 0.125/200 (logMAR equivalent 2.3, 2.6, 2.9, 3.2, respectively). For categorical variables, significant differences between groups were analyzed using a Pearson χ^2 test or Fisher exact test. For continuous variables, significant differences between groups were analyzed using 2-sample *t* test, Mann-Whitney *U* test, or analysis of variance with a Tukey honest significant difference post hoc test. Statistical significance was considered to be a 2-sided *P* value $< .05$.

RESULTS

DURING THE STUDY PERIOD, 20 PHYSICIANS CONTRIBUTED cases with a mean (standard deviation [SD]) 21,279 (12,438) (range, 704-41,672) injections per physician. A total of 483,622 intravitreal anti-VEGF injections (67,578 bevacizumab, 267,002 ranibizumab, and 149,042 aflibercept) were performed, with 453,460 injections in the No Talking group and 30,162 injections in the Face Mask group. Overall, a total of 177 cases of suspected endophthalmitis after intravitreal injection were identified (0.036%; 1 in 2,732 injections). Over the 6-year study period, the annualized rate of postinjection endophthalmitis ranged from 0.0295% (1 in 3,386 injections) to 0.0431% (1 in 2,319 injections) with no significant difference among the annualized rates ($P = .933$). Cultures were performed in 128 of these cases, and mean follow-up for all suspected endophthalmitis cases was 32.5 months (range, 14 days to 80.5 months). Mean (SD) duration of follow-up was 27.7 (15.8) months (range, 0.5-80.5 months) for the Face Mask group and 32.7 (21) months (range, 9-53 months) for the No Talking group ($P = .380$).

In the No Talking group, suspected endophthalmitis occurred in 168 cases of 453,460 injections (0.0371%; 1 in 2,699 injections), of which 47 cases were culture positive (Table 1). The most common causative organism was *Staphylococcus epidermidis* in 18 cases. There were 16 cases of oral flora–associated endophthalmitis (0.00353%; 1 in 28,340 injections), and causative organisms included 6 cases of *Streptococcus mitis*, 5 cases of *Streptococcus viridians*, 2 cases of *Streptococcus pneumoniae*, and 3 cases of undifferentiated *Streptococcus*.

In the Face Mask group, suspected endophthalmitis occurred in 9 cases of 30,162 injections (0.0298%; 1 in 3,351 injections), of which 5 cases were culture positive (Table 1). Causative organisms included 3 cases of gram-positive cocci (by stain), 1 case of *Staphylococcus epidermis*, and 1 case of *Staphylococcus aureus*. There were no cases of oral flora–associated endophthalmitis.

Overall, patients with presumed endophthalmitis presented an average of 5.54 days after intravitreal anti-VEGF injection (range, 1-29 days). The vast majority of cases presented within 7 days of intravitreal injection (81.4%). Patients in the Face Mask group presented an average of 6.3 days after injection, compared with an average of 5.5 days in the No Talking group ($P = .484$).

Of the cases sent for culture, in the Face Mask group, 5 of 7 (71%) cases were culture positive, compared to 47 of 119 (39%) endophthalmitis cases in the No Talking group ($P = .124$). Endophthalmitis cases in the Face Mask group were oral flora associated in 0 of 9 (0%) cases, compared to 16 of 119 (13%) cases for the No Talking group ($P = .306$).

Of the 30,162 injections in the Face Mask group, 4,100 (14%) were bevacizumab, 16,611 (55%) were aflibercept, and 9,451 (31%) were ranibizumab. Of the 453,460 injections in the No Talking group, 63,478 (14%) were bevacizumab, 132,431 (29%) were aflibercept, and 257,551 (57%) were ranibizumab. Compared to the No Talking group, the Face Mask group was more likely to use aflibercept ($P < .001$) and less likely to use ranibizumab ($P < 0.001$). Overall, there were 80 cases of endophthalmitis after ranibizumab injection (0.029%; 1 in 3,337 ranibizumab injections), 75 cases of endophthalmitis after aflibercept injection (0.05%; 1 in 1,987 aflibercept injections), and 22 cases of endophthalmitis after bevacizumab injection (0.03%; 1 in 3,071 bevacizumab injections). Endophthalmitis cases were associated with ranibizumab in 80 of 177 (45%) cases, aflibercept in 75 of 177 (42%) cases, and bevacizumab in 22 of 177 (12%) cases. Endophthalmitis cases in the No Talking group were associated with bevacizumab in 21 of 168 (13%) cases, aflibercept in 68 of 168 (41%) cases,

TABLE 1. Rates of Endophthalmitis After Intravitreal Anti–Vascular Endothelial Growth Factor Injection in the Face Mask Group vs No Talking Group

Medication Type		Face Mask Group (N = 30,162)	No Talking Group (N = 453,460)	Odds Ratio (95% CI)	*P* Value
All medications (n = 483,622)	Suspected endophthalmitis, n (%)	9 (0.0298%) 1 in 3,351 injections	168 (0.0371%) 1 in 2,699 injections	0.805 (0.41-1.57)	.527
	Culture-positive endophthalmitis, n (%)	5 (0.0166%) 1 in 6,032 injections	47 (0.0104%) 1 in 9,647 injections	1.60 (0.64-4.02)	.258
	Oral flora–associated endophthalmitis, n (%)	0 (0%) 0 in 30,162 injections	16 (0.00353%) 1 in 28,340 injections	–	.302
Aflibercept (n = 149,042)	Suspected endophthalmitis, n (%)	7 (0.0421%) 1 in 2,373 injections	69 (0.0521%) 1 in 1,919 injections	0.809 (0.37-1.76)	.593
Ranibizumab (n = 267,002)	Suspected endophthalmitis, n (%)	1 (0.0106%) 1 in 9,451 injections	79 (0.0307%) 1 in 3,260 injections	0.345 (0.04-2.48)	.290
Bevacizumab (n = 67,578)	Suspected endophthalmitis, n (%)	1 (0.0244%) 1 in 4,100 injections	21 (0.0331%) 1 in 3,022 injections	0.737 (0.09-5.48)	.298

CI = confidence interval.

TABLE 2. Visual Acuity Outcomes for Endophthalmitis After Intravitreal Anti–Vascular Endothelial Group Factor Injection in the Face Mask Group vs No Talking Group

	Face Mask Group (N = 9)	"No Talking" Group (N = 168)	*P* Value
Mean logMAR VA at causative injection	0.46	0.61	.453
Mean logMAR VA at endophthalmitis presentation	1.51	2.01	.08
Average lines of Snellen VA lost from baseline	10.4 lines	14.0 lines	.114
Mean logMAR VA at 6 months	0.84	1.06	.500
Average lines of Snellen VA lost from baseline at 6 months	3.8 lines	4.5 lines	.783
Three lines or more of Snellen VA lost from baseline at 6 months, n (%)	3 (33%)	63 (40%)	.685
VA of CF or worse at 6 months, n (%)	0 (0%)	24 (15%)	.205
Mean logMAR VA at last follow-up	1.08	1.17	.793
Average lines of Snellen VA lost from baseline at last follow-up	6.2 lines	5.6 lines	.838
Three lines or more of Snellen VA lost from baseline at last follow-up, n (%)	6 (67%)	80 (48%)	.273
VA of CF or worse at last follow-up, n (%)	1 (11%)	36 (22%)	.454

CF = count fingers; VA = visual acuity.

and ranibizumab in 79 of 168 (47%) cases. Endophthalmitis cases in the Face Mask group were associated with bevacizumab in 1 of 9 (11%) cases, aflibercept in 7 of 9 (78%) cases, and ranibizumab in 1 of 9 (11%) cases. There was no significant difference in the risk of endophthalmitis between the Face Mask group and the No Talking group based on drug type (Table 1).

• **VISUAL OUTCOMES:** Overall average baseline VA at the causative injection prior to endophthalmitis was logMAR 0.60 (approximately 20/80), with no significant difference between the Face Mask group (logMAR 0.46; approximately 20/60) and the No Talking group (logMAR 0.61; approximately 20/80) ($P = .453$) (Table 2). At 6 months follow-up, average VA was logMAR 0.842 (approximately 20/140) for the Face Mask group vs logMAR 1.06 (approximately 20/230) for the No Talking group ($P = .500$). For the Face Mask group, 0 of 9 (0%) cases had a VA of count fingers or worse at 6 months follow-up, compared to 24 of 168 (15%) for the No Talking group ($P = .205$). At

TABLE 3. Visual Acuity Outcomes for Culture-Positive Endophthalmitis After Intravitreal Anti–Vascular Endothelial Group Factor Injection in the Face Mask Group vs No Talking Group

	Face Mask Culture-Positive Group (N = 5)	"No Talking" Culture-Positive Group (N = 47)	*P* Value
Mean logMAR VA at causative injection	0.24	0.58	.093
Mean logMAR VA at endophthalmitis presentation	1.58	2.29	.036*
Average lines of Snellen VA lost from baseline at endophthalmitis presentation	13.4 lines	17.1 lines	.031*
Mean logMAR VA at 6 months	0.87	1.53	.157
Average lines of Snellen VA lost from baseline at 6 months	6.3 lines	9.5 lines	.479
Three lines or more of Snellen VA lost from baseline at 6 months, N (%)	2 (40%)	27 (66%)	.258
VA of CF or worse at 6 months, N (%)	0 (0%)	11 (27%)	.184
Mean logMAR VA at last follow-up	1.22	1.65	.383
Average lines of Snellen VA lost from baseline at last follow-up	9.8 lines	10.8 lines	.834
Three lines or more of Snellen VA lost from baseline at last follow-up, n (%)	4 (80%)	30 (65%)	.505
VA of CF or worse at last follow-up, n (%)	1 (20%)	17 (37%)	.451

CF = count fingers; VA = visual acuity.
*$P < 0.05$.

6 months follow up, 3 of 9 (33%) cases in the Face Mask group lost 3 or more lines of VA from baseline, compared to 63 of 168 (40%) cases in the No Talking group ($P = .685$). At last follow-up, average VA was logMAR 1.08 (approximately 20/240) for the Face Mask group vs logMAR 1.17 (approximately 20/300) for the No Talking group ($P = .793$). For the Face Mask group, 1 of 9 (11%) cases had a VA of count fingers or worse at last follow-up, compared to 36 of 168 (22%) for the No Talking group ($P = .454$).

Average VA at presentation for culture-positive endophthalmitis cases was logMAR 1.58 (approximately 20/760) in the Face Mask group compared to logMAR 2.29 (approximately 20/4000) in the No Talking group ($P = .036$) (Table 3). At 6 months follow-up, average VA for the culture-positive endophthalmitis cases was logMAR 0.868 (approximately 20/150) in the Face Mask group vs logMAR 1.53 (approximately 20/700) in the No Talking group ($P = .157$). For the culture-positive endophthalmitis cases in the Face Mask group, 0 of 5 (0%) cases had a VA of count fingers or worse at 6 months follow-up, compared to 11 of 47 (27%) for the No Talking group ($P = .184$) Furthermore, at 6 months follow up, 2 of 5 (40%) cases in the culture-positive Face Mask group lost 3 or more lines of VA from baseline, compared to 27 of 47 (66%) cases in the culture-positive No Talking group ($P = .258$).

At last follow-up, average VA for culture-positive endophthalmitis cases was logMAR 1.65 (approximately 20/900) in the No Talking group vs logMAR 1.22 (approximately 20/330) in the Face Mask group ($P = .383$). For the culture-positive endophthalmitis cases in the Face Mask group, 1 of 5 (20%) cases had a VA of count fingers or worse at last follow-up, compared to 17 of 47 (37%) for the No Talking group ($P = .451$).

Overall, visual outcomes were significantly worse for culture-positive and oral flora–associated endophthalmitis cases. Comparing vision loss from baseline, at 6 months follow-up, oral flora–associated cases lost an average of 17 lines of VA, non–oral flora–associated culture-positive cases lost 9.1 lines of VA, and culture-negative cases lost 2.9 lines of VA ($P < .001$).

DISCUSSION

THIS STUDY EXAMINED THE IMPACT OF PHYSICIAN FACE mask use on the rates and outcomes of endophthalmitis after intravitreal anti-VEGF injections. In this single-center study of 483,622 intravitreal injections, we found that physician face mask use did not affect the overall rate of postinjection endophthalmitis. Injection techniques for both the Face Mask and No Talking groups were similar. However, the injecting physicians in the Face Mask group likely did not uniformly adhere to a strict policy of silence for all people in the room during the procedure, compared to the physicians in the No Talking group. Despite this, no cases of oral flora–associated endophthalmitis were observed in the Face Mask group.

Although all forms of endophthalmitis are visually threatening, oral flora–associated endophthalmitis is associated with a particularly poor visual prognosis.[8–10] Therefore, there is significant interest in understanding potential risk factors and prophylaxis measures for reducing the incidence of oral flora–associated endophthalmitis. A meta-analysis of the literature covering 105,536 intravitreal injections from 2005 to 2009 found that *Streptococcus* species were 3 times more likely to be the causative organism in postinjection endophthalmitis cases than in intraocular surgeries in which a surgical mask is typically worn.[24] Furthermore, prior studies have established that oral flora–associated endophthalmitis may be reduced with the implementation of a strict "no-talking" policy by the physician and patient during intravitreal injection administration.[7,10] Refraining from speaking during an intravitreal injection is thought to minimize the potential to contaminate the uncapped needle or conjunctival surface with oral flora immediately before or during the injection.

Similarly, face mask use by the physician administering the injection may serve to further limit bacterial dispersion during speech. Within the neurology literature, multiple outbreaks of iatrogenic oral flora–associated meningitis have been reported. As a result, face mask use has become the standard of care for any clinician performing spinal injections.[25–27] In 1 case of iatrogenic meningitis, the causative bacteria was genotyped and shown to be identical to that of a throat swab taken from the neurologist who performed the lumbar puncture.[25] Within ophthalmology, an in vitro study involving 10 surgeons and 4 simulated intravitreal injection scenarios found that the rate of oral flora bacteria was significantly reduced when speaking with face masks compared to speaking without face masks.[14] Furthermore, another in vitro study of 15 volunteers who underwent simulated intravitreal injection administrations demonstrated that significantly more bacterial dispersion occurred when speaking without a face mask compared to speaking while wearing a face mask.[13] However, there was no significant difference in bacterial dispersion when speaking with a face mask compared to not speaking without a face mask (simulating a "no-talking" policy). These in vitro studies correlate with our study findings, as all intravitreal injections were administered with either a "no-talking" policy or face mask use by the physician.

Some studies have suggested that the presence of a beard[17] or the tendency to excessively move one's face beneath a surgical mask[16,17] may increase bacterial dispersion and shedding, presumably from the beard and facial skin. In addition, other studies have suggested that extended use of the same face mask may increase infectious risk, as the external surface can function as a fomite.[19] Furthermore, physicians speaking with a loose-fitting face mask may result in upward or downward bacterial dispersal.[18] Collectively, these concerns may explain why the majority of retina physicians surveyed in 2 recent studies did not wear face masks during intravitreal injections.[28,29] At a minimum, our study findings suggest that physician face mask use does not increase the risk of postinjection endophthalmitis and may be equivalent to a strict "no talking" policy. These findings are particularly relevant, as routine use of face masks by physicians has exponentially increased with the emergence of the COVID-19 pandemic, and it is unclear what the duration of these precautions will be.[20] Although this study focused on the impact of physician and technician assistant face mask use, current COVID-19 guidelines recommend universal face mask protocols for all individuals in the injection room, which includes the patient. With regard to patient face mask use, it is possible that bacterial dispersion around the edges of the face mask may be directed toward the eye, which could potentially increase the risk of endophthalmitis. Indeed, current guidelines from the Centers for Disease Control and Prevention recommend a cloth face covering, which may not adhere to the face as well.[30] Further studies are indicated to understand the effects of universal face mask use on rates of various types of endophthalmitis.

Overall, VA outcomes following endophthalmitis were similar in the Face Mask group compared to the No Talking group. VA at the causative injection, at endophthalmitis presentation, and at 6 months following treatment were similar between the 2 groups. Patients in the No Talking group were more likely to have a VA of count fingers or worse at 6 months compared to the Face Mask group (15% vs 0%), though these findings were not statistically significant. Regardless of face mask use, our findings were similar to prior studies that have established that visual outcomes are worse for culture-positive cases compared to culture-negative cases.[6,31] When assessing culture-positive endophthalmitis cases, visual outcomes at endophthalmitis presentation were worse for the No Talking group, with a mean loss of 17.1 lines of vision from baseline acuity compared to a loss of 13.4 lines for the Face Mask group. Furthermore, at 6 months follow-up, patients in the No Talking group were more likely to have a VA of count fingers or worse compared to the Face Mask group (27% vs 0%), though these findings were not statistically significant.

Strengths of the study include the large number of intravitreal injections from a single institution with a standardized injection protocol, including injection technique and preparation, among multiple retina specialists. Endophthalmitis following intravitreal injection is an uncommon event with reported incidence rates ranging from as high as 1 in approximately 500 injections to as low as 1 in 19,000 injections, with the majority of large recent studies reporting an incidence rate of 1 in 2,000 to 3,000 injections.[5,6,21,31–34] Therefore, any prophylaxis measure to potentially lower the risk of endophthalmitis requires an assessment of a large number of intravitreal injections to achieve adequate power to detect a difference. Although

we report one of the largest single center studies of postinjection endophthalmitis, our study findings may be limited by the study's imbalanced sample size, with 30,162 injections in the Face Mask group compared to 453,460 injections in the No Talking group. Assuming the risk of oral flora–associated endophthalmitis is 1 in 28,340 injections as reported in this study, and that face mask use may reduce the risk of oral flora–associated endophthalmitis to 1 in 100,000 injections, a study would need 993,182 injections to be sufficiently powered to detect a significant difference between the 2 groups with a confidence of 0.95 and power of 0.8. Ideally, a randomized controlled study could evaluate the risk of endophthalmitis with and without physician face mask use; however, the low incidence of endophthalmitis makes such a study prohibitive.

Furthermore, the granularity of physician-specific practice patterns, like face mask use, may not be captured in large-scale insurance claims databases or clinical registries. Another limitation is the imbalance in medication distribution, as the Face Mask group was more likely to use aflibercept and less likely to use ranibizumab compared to the No Talking group. These findings may be particularly relevant, as the prefilled syringe use for ranibizumab was introduced during the study period, and prior studies have reported that prefilled syringes may reduce the risk of endophthalmitis.[6,35] Furthermore, during the study period, there was a clustered spike in cases with intraocular inflammation after intravitreal aflibercept injections,[36] which may explain the increased proportion of endophthalmitis associated with aflibercept compared to ranibizumab or bevacizumab in this study. The authors' standard practice is to have a low threshold to administer intravitreal antibiotics whenever the examining physician believes there is a possibility the case could represent infectious endophthalmitis; however, when sterile inflammation is suspected, topical medications alone were typically prescribed. Regardless, there were no differences in endophthalmitis risk between the Face Mask group and No Talking group based on drug type. Another limitation is that microbiologic cultures were obtained in 128 of 177 (72%) cases. However, there were similar rates between the 2 groups, as cultures were performed in 121 of 168 (72%) cases for the No Talking group and 7 of 9 cases (77%) for the Face Mask group ($P > .99$). Recent studies have suggested that culture results have limited impact on clinical management.[31,37] Furthermore, another limitation is that a positive Gram stain was considered culture positive even if there was no bacterial growth on culture. However, prior studies have suggested that any bacteria detected on Gram stain of a sterile site specimen, such as vitreous or aqueous samples, should be considered significant.[38] In addition, a culture result was considered to be oral flora associated when *Enterococcus* or *Streptococcus* species was grown, which may not represent all potential oral flora. However, there were no cultures that grew other common oral flora, including *Lactobacilli*, *Corynebacteria*, or *Bacteroides*, in either group. Furthermore, *Streptococcus*-associated postinjection endophthalmitis is of particular concern given the poor visual prognosis relative to other forms of endophthalmitis.[7–10] Additional limitations of this study are inherent in its retrospective nature. It is possible that patients could have developed endophthalmitis and sought treatment at an outside institution, although it is unlikely, given the tertiary care nature of our institution.

In summary, our study indicates that physician face mask use did not influence the risk of endophthalmitis or visual outcomes compared to a strict no-talking policy during the injection procedure. No cases of oral flora–associated endophthalmitis occurred in the group in which the injecting physician wore a face mask, though this study was underpowered to detect a difference. These findings are particularly relevant, as routine use of face masks by retina specialists has increased with the emergence of the COVID-19 pandemic. However, it is important to note that patients in the Face Mask group did not wear a mask, which is unlike the current universal face mask protocols in place. Additional studies are warranted to assess the potential role of face mask use to reduce the risk of endophthalmitis, particularly that attributable to oral flora.

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