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BRIEF COMMUNICATION

Clinical impact of COVID-19 on patients with choroidal neovascularization on intravitreal anti-VEGF therapy

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The response to the evolving coronavirus disease 2019 (COVID-19) pandemic required rapid restructuring of clinical practice in order to allow for increased critical care capacity and resource repurposing, while limiting transmission risk within the clinical environment. Ensuring uninterrupted healthcare provision in the context of high-risk diseases requiring frequent treatment, such as neovascular age-related macular degeneration (nAMD), necessitated reorganization of monitoring and treatment protocols. Accordingly, following lockdown imposition by the UK government, the Royal College of Ophthalmologists published initial guidance recommending maintenance on 8-weekly treatment for all patients with nAMD already receiving anti-vascular endothelial growth factor (anti-VEGF) injections [1]. No clinical assessment was deemed necessary, unless there was subjective impression of reduced visual function [1]. This guidance was revised at the end of the first pandemic wave [2] to permit return to pre-pandemic normality, however this plan was hampered by the subsequent resurgence of COVID-19. It is therefore essential to investigate the effect of implementing such changes on clinical outcomes in order to evaluate any visual loss suffered as an indirect result of COVID-19. We believe this information may guide further service reconfiguration in case future pandemic waves necessitate the reinstatement of similar contingency plans.

An audit on visual outcomes of 513 eyes of 419 patients treated with intravitreal anti-VEGF for choroidal neovascularization (CNV) at Royal Liverpool University Hospital during the first lockdown period was conducted. Patients with booked clinic appointments during the first 5 weeks after lockdown enforcement on March 23rd, 2020 (https://www.instituteforgovernment.org.uk/sites/default/files/timeline-lockdown-web.pdf), were selected and outcomes were followed up until their first visit after termination of the UK government-proposed shielding period on July 4th, 2020. During this period, clinicians triaged clinics in advance and telephoned patients to encourage or defer attendance.

Table 1 summarizes the baseline characteristics of the patients, number of clinic visits during lockdown, and follow-up interval at each visit. Eyes with CNV secondary to various causes were included in this study, and nAMD was the most prevalent indication for treatment (440/513 eyes, 85.8%). Nine eyes of 8 patients were diagnosed with CNV during the study period. Most patients (251/419, 59.9%) attended twice during lockdown. Thirty-two patients (7.6%) did not attend booked appointments during the study period; 6 of these 32 patients additionally did not attend

Table 1. Baseline patient characteristics, number of clinic visits, and intended follow-up intervals during lockdown.

Total number of patients	419
Median age (range)	80 years (32–100)
Sex	
Male (%)	157 (37.5%)
Female (%)	262 (62.5%)
Patients with bilateral disease (%)	94 (22.4%)
Total number of eyes	513
Right/left eye	259/254
Mean initial CVA (± SD) ($n = 511$ eyes)	62.9 (±15.4) letters
Lesion subtype	Number of eyes (%)
AMD, classic CNV	82 (16.0%)
AMD, occult CNV	247 (48.1%)
AMD, predominantly classic CNV	10 (1.9%)
AMD, minimally classic CNV	30 (5.8%)
AMD, RAP	71 (13.8%)
PCV	37 (7.2%)
Myopic CNV	14 (2.7%)
CSCR with secondary CNV	5 (1.0%)
CNV associated with angioid streaks	4 (0.8%)
CNV secondary to posterior uveitis	3 (0.6%)
CNV associated with macular telangiectasia	2 (0.4%)
Unspecified	8 (1.6%)
Number of visits during lockdown	Number of patients (%)
0	32 (7.6%)
1	75 (17.9%)
2	251 (59.9%)
3	58 (13.8%)
4	3 (0.7%)
Patients with follow-up interval ≥8 weeks	Number of patients (% attending)
At pre-lockdown visit	193/419 (46.1%)
At visit 1 during lockdown	290/387 (74.9%)
At visit 2 during lockdown	264/312 (84.6%)
At visit 3 during lockdown	33/61 (54.1%)
At visit 4 during lockdown	0/3 (0%)
At first post-lockdown visit	331/394 (84.0%)

CVA corrected visual acuity (measured in early treatment diabetic retinopathy study letters), *SD* standard deviation, *AMD* age-related macular degeneration, *CNV* choroidal neovascularization, *RAP* retinal angiomatous proliferation, *PCV* polypoidal choroidal vasculopathy, *CSCR* central serous chorioretinopathy.

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Table 2. Treatments administered during lockdown and visual outcomes.

Total number of eyes		513
Previous treatment (%)		
Anti-VEGF		465 (90.6%)
Anti-VEGF + PDT		37 (7.2%)
None		11 (2.1%)
	Treatment (*n* eyes receiving treatment/total eyes at visit, %)	
Visit	Anti-VEGF	None
1	446/476 (93.7%)	30/476 (6.3%)
2	366/383 (95.6%)[a]	17/383 (4.4%)
3	65/72 (90.3%)	7/72 (9.7%)
4	3/4 (75.0%)	1/4 (25.0%)
Post-lockdown	430/485 (88.7%)	55/485 (11.3%)
Mean initial CVA (±SD) for all eyes ($n = 511$)		62.9 (±15.4) letters
Mean initial CVA (±SD) for eyes with complete data ($n = 371$)[b]		63.9 (±14.8) letters
Mean final CVA (±SD) ($n = 371$ eyes)[b]		61.8 (±15.2) letters
Mean change in CVA (±SD) ($n = 371$ eyes)[b]		−2.3 (±8.3) letters
n eyes (%) with stable or improved CVA		151/371 (40.7%)
n eyes (%) with visual loss of less than 5 letters		89/371 (24.0%)
n eyes (%) with visual loss of at least 5 letters		131/371 (35.3%)
n eyes (%) with visual loss of at least 15 letters		23/371 (6.2%)
Subjective impression of visual function at first post-lockdown visit ($n = 100$ eyes)[b]		Number of eyes (%)
Better		4/100 (4.0%)
Worse		2/100 (2.0%)
Stable		94/100 (94.0%)

PDT photodynamic therapy, *n* number, *CVA* corrected visual acuity, *SD* standard deviation.
[a]One eye underwent additional PDT.
[b]Formal CVA assessment was performed in $n = 371$ eyes, while for $n = 100$ eyes only subjective impression of visual change was documented. No CVA or subjective visual impression was noted for $n = 14$ eyes.

their first post-lockdown visit, and 9/32 were considered suitable for safe discharge. The percentage of patients with intended follow-up interval of 8 weeks or longer increased significantly from 46.1% at baseline to 84% at the end of the lockdown period.

Treatments and visual outcomes are summarized in Table 2. During a total of 935 clinical episodes registered during the lockdown period, treatment was delivered on 880 occasions (94.1%). Eyes with available visual acuity (VA) data at last visit (after July 4th, 2020) ($n = 371$) experienced an average loss of 2.3 letters; 131/371 eyes (35.3%) lost at least 5 letters, and 23/371 eyes (6.2%) lost at least 15 letters. Patient-reported subjective impression of visual function only was documented at final follow-up in 100 eyes of 83 patients, with stable or improved vision noted for 98 eyes (98%).

Our study is limited by the non-availability of clinical and imaging information that would allow correlation of visual outcomes with changes in macular structure, nevertheless visual outcomes are inherently associated with the altered clinical protocol employed during lockdown. Despite this limitation, our descriptive analysis suggests that visual outcomes in eyes that underwent formal visual assessment at final follow-up, were comparable to previously reported real-life treatment outcomes in nAMD [3–5]; additionally, no significant subjective visual decline was reported by 83 patients with no available VA data. While it is sensible to conclude that no significant visual loss occurred as an indirect result of the response to COVID-19, it is important to consider a pragmatic approach for management of nAMD in the future. Implementing flexible clinical pathways which minimize resource usage (e.g. retinal imaging) and need for direct clinical encounters (e.g. frequent slit lamp examinations), will increase throughput and confer greater adaptability if social distancing and increased acute care capacity are intermittently needed in the future.

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AUTHOR CONTRIBUTIONS

EIA designed the study, collected and analysed the data, and wrote the manuscript. DM, NH, DMcD, and LS contributed to data collection and manuscript revision. SM and NAVB contributed to study design and manuscript revision. All authors reviewed and approved the final version of the manuscript.

COMPETING INTERESTS

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ADDITIONAL INFORMATION

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