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Editorial

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Discussion of the Royal College of Ophthalmologists ManagementPlans during the COVID-19 pandemic: *Practical Implications of National Guidelines in Times of Crisis*

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Abstract

The global COVID-19 pandemic has represented a true test to healthcare services in every country, posing a significant burden on over-stretched facilities and staff. In parallel, concerns about its potential spread among patients, careers and healthcare workers as well as efforts to conserve clinical service capacity has meant that triaging efforts have been stepped up forall non-COVID patients, beit for new presentations or follow-up cases. Ophthalmology departments have had to rationalise their efforts and have looked to national professional bodies for guidance on how to do that in a way that avoids neglecting non-COVID cases that warrant clinical attention.

Pro active institutions representing centres of expertise within the profession have come out with advice on how t manage patient presentations and follow-up during the pandemic. These represent a distillation of collective and respected thought, yet practitioners may find that individual needs, practical concerns and empirical evidence necessitate at times a different approach. We discuss the management plans produced by The Royal College of Ophthalmologists in the area of medical retinal conditions in new patients.

Certain interventions, either to thought of as non- acute, may in practical terms still be warranted during the pandemic, as they aim to preserve vision and prevent complications and irreversible loss of structure and function. It is understandable that most elective treatments will be postponed till hospitals and clinics are ready to receive patients, yet clinical needs, a prolonged disruption to regular service and the logistical effects of social isolation will dictate that especially vulnerable patients are stratified according to risk and managed promptly in order to reduce their overall morbidity and maintain their quality of life and independence. In practice this will also help to prevent departments and frontline staff from being overwhelmed by a post COVID-19 overflow.

Keywords and Abbreviations: *COVID-19: Corona Virus Disease 2019; RCOphth: The Royal College of Ophthalmologists, London; PRP: Pan Retinal Photo-Coagulation, using Argon laser; Anti-VEGF: anti vascular endothelial growth factor; NVD: New Vessels at the Optic Disc; NVE: New Vessels Elsewhere; NVI: New Vessels on the Iris; NVA: New Vessels in the Irido-Corneal Angle;*

Commentary: Introduction

It is early May 2020 and the global COVID19 pandemic is the acutetrans-national emergency that global efforts are directed to fighting and who's effects every news bulletin is reporting on. The pandemic, with its first recorded cases in the city of Wuhan in China in December 2019, has now claimed the lives of more than 302 thousand people, and hospitalized hundreds of thousands more, across 210 countries and territories [1]. Efforts to limit the spread of the disease have led to massive closures, strict social distancing measures, cancellations of major events around the world and has affected nearly every aspect of our lives.

All sectors have been affected and, not least of all, the healthcare sector. From frontline workers in primary care, emergency departments, respiratory wards and intensive care units dealing directly with COVID 19 patients to every

group of medical personnel and specialty, it has affected how we manage our work and resources in a way that positively contributes to crisis management. This has meant that, where possible, we prioritize care for patients who require it in a time-sensitive manner and postpone encounters and interventions for those patients whocan safely wait.

Within ophthalmology, we have to balance the need to manage our new and existing patients safely and effectively while adhering to social distancing measures, with standing pressure on health care resources and contributing to fighting the spread of the pandemic. That has meant that, in varying degrees, except for the most essential, most patient encounters have been cancelled or postponed.

The Royal College of Ophthalmologists in London, a highly respected professional body for the profession, has been working hard to help ophthalmology departments navigate these difficult and unfamiliar waters. It has produced Management Plans during COVID 19, which follow a pragmatic approach and were last updated on 30 March [2].

These serve as guidelines that aid departments in triaging both new and follow-up cases, to limit unnecessary clinical encounters and ensure that patient managementis conducted under a safe framework given the exceptional circumstances. Ophthalmology teams, working on the front line, have been busy consolidating this guidance with practical considerations on the grounds as well as the possibility that the current crisis will carry on beyond earlier estimated time horizons.

Indeed it is clearly acknowledged by the Royal College that the guidance is subject to amendment as circumstances progress and that local conditions will ultimately mean that individual clinics and departments will have their own way of addressing clinical issues. Unfortunately we must be conscious of the fact that while the effects of the COVID-19 pandemic will likely extend in to most of the present year, there is a real specter of seasonal surges of Corona virus or further outbreaks of other infectious diseases and therefore we must have refined strategies for dealing with arepeatof the current circumstances. This portends the need to have sustainable plans for managing patients and cases in a safe and efficient manner.

Objective

Our aim is to consolidate RCOphth management plans with practical considerations as well as requirements for evidence-based practice.

The Royal College's crisis-related guidance comprises three parts, addressing general ophthalmology department issues as well as management plans related to Glaucoma patients and to Medical Retina cases. We will focus on medical retina cases, and in particular those guidance notes related to new patients presenting to ophthalmology clinics and departments.

A) Wet AMD: exudative or neo-vascular age-related macular degeneration

The College's guidance advises that:

a. Diagnosis should be confirmed with OCT and OCTA, if available.
b. For new wet AMD cases: a loading phase of 3 anti-VEGF injections is advised and then continued on 8 weekly maintenance injection. Consent is taken on the day of first injection.
c. Clinic review is to be avoided if possible.

Prompt diagnosis and initiation of treatment is implied in the brief guidance, but it remains important to clarify an advisory timeframe based on evidence. As clinically significant visual loss has been identified as a real effect of delay in treatment following diagnosis of exudative AMD or while managing active disease, this is a time- sensitive condition [3]. The common recommended service target in the UK is 2 weeks [4], where as a retrospective study of patients observed inperiod 2013 –2015, and where there was no added pressure of a global pandemic, found that the mean time from initial ophthalmic assessment to first intravitreal injection was more than double that at 31.5 days [5].

In ophthalmology, we should focus on creating and enabling patient pathways that take into account the need for social distancing and vigilance while allowing patients who require prompt assessment and treatment to have access to it. In fact, the postponing of elective clinical procedures may mean that service capacity is available to time-sensitive cases where delay will likely lead to irreversible deterioration in vision.

The guidance allows individual departments to exercise clinical judgement in their choice of first and second-line anti-VEGF agents; this will depend on local formularies, availability and established practice. In terms of maintenance therapy following the loading phase, the 1-year results from a large randomised clinical trial suggest that a treat-and-

extend regimen is a viable and effective alternative the fixed monthly therapy option in treatment- naive neo-vascular AMD patients [6].

As the guidance recommends avoiding on-site clinic review as far as is possible, this is as good as any an opportunity to leverage available technology to exploring and implementing virtual AMD assessment and follow-up clinics. Virtual medical retina clinics can be realized using available resources; they can serve as rapid access clinics that carry out symptom recording, visual acuity and function testing (e.g. color vision, visual field screening, Amsler grid) as well as essential investigations such as OCT [7]. This offers a promising solution to enable patients to be seen and treated promptly, allowing important clinical information to be exchanged and decisions to be made while adhering to social distancing and virus transmission control measures.

B) DMO: Diabetic Macular Oedema

In new cases of DMO, the College management plan recommends that:

a. Patients with diabetic retinopathy graded as 'R3', i.e. pre-proliferative, are to be treated with PRP.\
b. Those with less advanced retinopathy should have their treatment deferred for 6 months.

DMO in the presence of non-proliferative disease: Deferring the treatment of patients who have good visual acuity >6/9 and central involving CSME could be safe option considering virtual observation and addressing systemic risk factors (optimal control of HbA1c, Blood pressure, and Lipids levels). Clear treatment benefit was achieved when pre-treatment visual acuity was <6/9 and was most beneficial when vision was between 6/12 and 6/24 [8]. Focal Laser treatment should be considered on individual basis for patients with non-centre involving CSME as the rate of moderate visual loss (15 or more letter loss on ETDRS charts) was reduced from 24% to12% at 3 years [9].

DMO in the presence of proliferative disease: New patient referrals could be referred with both PDR and clinically significant oedema (CSMO). Normally, it is advisable to treat the maculopathy either at the same time or prior to peripheral scatter retinal photo coagulation (PRP) as Laser PRP could worsen Macular oedema. In young patients with active new vessels it is generally recommended to treat the new vessels first with PRP (or concurrently with macular laser) since new vessels in these patients may run an aggressive course. It is recognized that VEGF overproduction in peripheral ischaemic retina drives macular changes in some cases, based on wide field angiography studies. With the advent of the pattern scanning laser systems this technique may no longer be necessary as some data has shown that single session laser treatment does not cause an increase in macular oedema [8]. In patients with lower risk PDR, it is reasonable to treat the macula first or concurrently with PRP [9].

Reducing the number of visits to the clinics or hospital setting is necessary During COVID-19 crisis and treating CSME which requires usually monthly intravitreal injections may add pressure to hospital setup complying with safety restrictions. Therefore, if COVID -19 crises continue on a longer time scale. Safety and efficacy of macular grid laser or sub threshold macular laser have been studied and could be considered to delay further intervention and case by case assessment is necessary.

C)BRVO: Branch Retinal Vein Occlusion

It is recommended in the College guidance that clinic review of new BRVO cases is deferred for 4 months. In practical terms, if a new patient is referred with suspected BRVO or a known patient with BRVO is due for review, we may need to know the current best corrected visual acuity (BCVA) and to arrange an OCT test, either to institute treatment if required in the new patient or in order to inform any further management for the follow-up patient.

We may also want to arrange for the patient to have are view and mitigation of their underlying modifiable risk factors such as hypertension, either by their GP or medical physician, and it would be beneficial to mention this. A meta-analysis demonstrated that BRVO can be a warning sign for the presence of underlying risk factors, with 10 % of patients developing retinal vein occlusion in the fellow eye [10]. BRVO can be classified into macular and major BRVO, as well as ischaemic and non-ischaemic, with those having non-macular BRVO more likely to develop neo-vascularisation [11].The major cause of impaired vision in BRVO is cystoids macular oedema (CMO), which occurs in 30 % of cases. Direct treatment of CMO mainly relies on the use of intra-vitreal anti VEGF and steroid, with the aim of resolving it before photoreceptor layer in the foveal area is damaged [12].

Two of the variables identified as positive prognostic factors for CMO resolution and improvement in vision were the duration of CMO and a patient's favourable response to early treatment [13]. Additionally, it was found that the duration between CMO-related symptom onset and initial intravitreal anti-VEGF (in this case Bevacizumab) can

affect the recurrence rate of CMO [14].

BRVO does have a better visual prognosis overall compared to CRVO, with 50 – 60 % of eyes recovering visual acuity to 6/12 or better without any ophthalmic treatment; yet there remain many others that do not improve [12]. Therefore it is justified to stratify patients early on into those who have macular oedema vs. those patients who do not in order to then promptly treat and follow-up appropriately.

D) CRVO: Central Retinal Vein Occlusion

a. The college guidance on CRVO advises stratifying patient groups based on visual potential:
It is advised that patients with CRVO and macular oedema causing loss of vision with favourable visual prognosis are given loading with 6 mandated doses of intra- vitreal injections and then reviewed in clinic.
b. For patients with poor visual prognosis, it is advised to carry out extensive PRP laser to reduce the risk of rubeotic glaucoma, though this will be associated with reduced visual outcome.

Macular oedema (MO) is the leading cause of decreased visual acuity associated with retinal vein occlusion (RVO). The addition of Anti-VEGFs has proven to be valuable in restoring better visual outcomes and it is important to highlight that these are the preferred group of agents, while different centres may make choice of compound based on preferences and availability. It is crucial to distinguish ischaemic as opposed to non- ischaemic CRVO as well as taking note of the duration of macular oedema in planning prompt treatment intervention; evidence shows that better visual gains are achieved with Anti-VEGF therapy in those with a shorter duration of macular oedema [15]. Therefore, it is recommended that the college's guidance of 6 injections is considered at the time of presentation without delay.

Patients with ischaemic CRVO will likely be considered as having negative visual potential. Yet those with ischaemic retinal signs including non-perfusion area of >10 disc diameters determined by FFA and no signs of neo-vascularisations (NVE, NVD, NVI, NVA) should be monitored monthly in order to recognize complications in a timely fashion. If monthly regular check-ups are not logistically practical during COVID-19 restrictions, then evidence agrees with considering prophylactic treatment with PRP though review with in two months is recommended to ensure adequacy [16].

E) CSCR: Central serous chorio-retinopathy

For central serous chorio-retinopathy, the College recommends delaying any appointments for 6 months or longer, at which time the patient can be seen in clinic. Indeed, for patients with a new episode and no prior history, there appears to be a consensus that any active intervention can be postponed for 4-6 months, given the strong chance of spontaneous resolution [17]. In fact, prompt treatment with photocoagulation has been noted to carry a risk of CNV and has not been shown to improve final visual outcome or prevent recurrence [18]. Topicalnon-steroidalanti-inflammatorydrug (NSAID) therapy is variably used in clinical practice. A retrospective review of new-onset symptomatic CSCR compared eyes that had been treated with either Bromfenacor Nepafenac with a follow up period of 4-5 weeks. The results demonstrated a statistically significant reduction in central sub-retinal fluid volume in the treatment group, at 64.3 % vs 11.1% and a p-value < 0.02, but the related improvement in visual acuity using the ETDRS scale was not statistically significant [19].

It is important to distinguish between new cases and those that have recurred or are chronic, defined as symptoms lasting beyond 3-6 months, for which a consideration of active management, for example with photodynamic therapy (PDT), may be undergone. For all cases, it is useful to confirm diagnosis with OCT and to record baseline BCVA, any current visual symptoms and their duration. While observation may be the mainstay of management for new cases, it is of benefit to counsel patients about local or systemic steroid cessation, identification and management of stress and mitigation of underlying modifiable risk factors such as sleep apnea and hypertension [20]. It has been demonstrated that these measures can help resolve the fluid and recover normal vision.

The College guidance also addressed issues related to the care of patients with uveitis, inherited retinal diseases and those who are involved in clinical trials. These can each comprise diverse groups of patients and therefore merit further exploration.

Final Note

What is clear is that ophthalmology care cannot be simply postponed until the Covid-19 related crisis and its ramifications subside. We must ensure that patients, today and every day, receive care that is practical, effective and appropriate and that achieves maximal benefit and minimal harm.

How we manage patients will rely on balancing the following factors:

1. Healthcare providers' assessment of clinical urgency and a duty to prevent unnecessary harm.
2. Our knowledge of the natural history and response of various ophthalmological presentations.
3. Trusted clinical guidelines based on validated evidence.
4. Practical considerations such as available staff, skills mix, space and resources.
5. Factors imposed by our response toCovid-19,such as social distancing, demandon resources due to the care of Covid patients and a need to prevent hospital over-crowding during the active phase of the pandemic and beyond it.
6. Learning from continuous data collection including patient spresentations, issues and outcomes

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