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CLINICAL ADVISORY

MANAGING NEOVASCULAR AMD DURING COVID-19 PANDEMIC

The Coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly spread worldwide and resulted in a pandemic as declared by the World Health Organisation (WHO).

“Circuit Breaker” Period (7th April to 1st June, 2020)

- On the 7 April 2020, Singapore implemented an elevated set of safe distancing measures as a circuit breaker (CB) for 1 month (ending 4 May) to pre-empt the trend of increasing local transmission of COVID-19. The initial CB was subsequently extended until 1 June.
- During this period, only essential healthcare services are allowed to operate. The Ministry of Health’s stance on essential healthcare service provision include:
 - Deferring all clinical services considered as non-essential.
 - Essential services include procedures or surgeries required to prevent deterioration of the patient’s condition.

The College of Ophthalmologists has released a Summary of Key Actions document which covered broad and practical aspects of clinical care in ophthalmology addressing key issues for best practice regarding staff protection, screening of patients, infection control, outpatient care, surgery and communication. Recommendations included actively reducing patient attendances and patient time in clinics in accordance to “safe-distancing” principles.

This document serves to provide guidance on the provision of VEGF inhibitor therapy for neovascular age related macular degeneration (nAMD) during this challenging period and beyond. Due to the frequent and large numbers of treatments, some modifications may be necessary in our practice patterns to mitigate the risk of contracting COVID-19.

Specific concerns for patients with nAMD

- Current evidence shows that frequent follow up and treatment are necessary to prevent blindness in nAMD.
- Delayed treatment can lead to irreversible visual loss.
- A proactive treatment regimen is more likely to maintain vision than a reactive regimen.
- Patients with nAMD are also patients that are most susceptible to mortality if exposed and infected with COVID-19 due to their age and comorbidities.

Balancing risk of COVID-19 infection against visual loss

- Stratify patients’ risk categories by reviewing case records.
- ‘Stable patients’ - Patients whose condition has remained quiescent for an extended period without the need for retreatment may have their appointments postponed if review can be delayed safely. Resupply of medications, e.g. AREDS supplement, glaucoma eye drops for patients with co-existing glaucoma should be offered when appointments are rescheduled.
 - some examples of stable patients include: patients that have not received treatment in the preceding 3-6 months despite monthly monitoring because of disease inactivity and have good vision in the fellow eye; patients on quarterly follow up with disease quiescent for the last 2 years.
- ‘Active patients’ - Patients who are currently receiving anti-VEGF therapy should continue their treatment. However, efforts should be made to reduce the duration of their clinic visit and minimize investigations. Attention should be paid to those in their first 2 years of treatment as the risk of recurrent activity is high during this period.

- Set up appropriate avenue to address patients' enquiry, and emergency service for those with acute deterioration.

Fluorescein and Indocyanine green Angiography

- Treatment-naive patients: Fluorescein angiography is the gold standard for diagnosing nAMD. However, if the diagnosis is clear based on other multimodal imaging (such as OCT, OCTA), invasive angiography may be omitted at the discretion of the treating physician.
- Treated patients: If initial response to treatment is suboptimal, or if initial diagnosis is in question, FA+/- ICGA should be performed.

Intravitreal anti-VEGF therapy

- Treat-and-extend regimen is recommended to minimize need for separate monitoring and treating visits.
- Loading phase: During the first 3 months, injections at monthly intervals is still standard of care. During loading phase, visual acuity and OCT scan at the time of loading dose 2 and 3 may be omitted at the physician's discretion. We suggest having an OCT scan at the time of the 3rd loading dose, in order to decide if the 4th dose can be extended by 2 to 4 weeks.
- Titration phase: Following the initial monthly loading phase, retreatment intervals should be titrated based on T&E. During initial titration phase, patients should have their visual acuity assessed and disease activity assessed with an OCT scan. Intravitreal injection should be performed at every visit. If disease activity is absent, 4-weekly extension may be considered instead of 2-weekly extension. Maximum retreatment interval up to 16 weeks may be considered.
- Maintenance phase: For patients who have reached an established/stable retreatment interval beyond the titration phase, anti-VEGF injection may be performed without OCT scans unless there is significant deterioration reported or on vision testing.
- For patients with bilateral active disease, both eyes can be injected on the same day after explaining the risk of bilateral infection as well as assessing risk of systemic complications. The injection is to be done as two separate procedures with strict aseptic precautions to avoid contamination between the two procedures. For Bevacizumab, it is preferable to use two medication from different batches.

- For patients with contralateral ocular issues, follow up appointments for the other eye should factor in the scheduling process.

| Stable Patients | VA | OCT +/- OCTA | Angiography (FA +/- ICGA) | Treatments | Interval |
|--|----|--------------|---------------------------|---|----------------------------|
| Quiescent condition, No active treatment | - | - | - | Continue supply of AREDs, other concurrent eye medication | Consider deferring past CB |

| Active Patients | VA | OCT +/- OCTA | Angiography (FA +/- ICGA) | Treatments | Interval |
|-------------------------------|----|--|--|---|---|
| New disease and loading phase | √ | √ Only for first visit OCT suggested at third loading dose | √ Only if diagnosis is in doubt or response is suboptimal | 3 loading injections as treatment only visits | Monthly (treatment only visits) |
| Titration phase | √ | √ | X* | Treat at every visit | Maximise extension interval (consider 4 weekly) |
| Maintenance phase | √ | X* | X* | Treatment only visits | Follow same interval |

*consider investigations if vision drops objectively or subjectively or clinically indicated by physician's best judgement.

Infection Control during intravitreal injection (IVT) procedure

- Establish a screening process at triage to identify patients and visitors at greater risk of COVID-19 infection
- PPE for IVT procedure:
 - **Mandatory:** surgical mask, sterile gloves (changed between procedure), good hand hygiene between procedure.
 - **Recommended:** N95 mask, face/ eye protection, especially for healthcare workers not wearing spectacles.
 - **Optional:** Gowns/aprons and caps.

- Patient should wear a mask during IVT. Taping the mask over the bridge of the nose may be considered to achieve a good fit. A disposable mask is preferred as there may be iodine staining during preparation of the eye.
- Wherever possible, injections may be done on the same day as the consultation without the need to revisit the clinic.
- Clinicians should also take into consideration the guidelines prescribed by their respective clinics/hospitals/institutions.

Communicating with patients and carers

- Rationale for strategies to mitigate risk of exposure to COVID-19 while preventing avoidable visual outcomes should be clearly communicated to patients and carers. These modifications may differ from patients' prior treatment plan and need to be clearly explained.
- Reassurance should be given that care is accessible and that all measures to protect patients against COVID-19 infection are in place if a visit is necessary.

Planning forward for post Circuit breaker period

- Consider continuing above measures beyond the immediate CB period as the principles of reducing outpatient load and safe distancing remain important to combat COVID-19.
- Consider setting up a taskforce to coordinate auditing of clinical outcomes, updating clinical guidelines and manpower planning.
- Explore incorporating novel technologies such as home monitoring or video consultation, although currently there remains no mature platform to support the specific needs (e.g. privacy, remote access of investigation results) for medical retina consultation.

These recommendations have been designed to consider the long-term clinical care for patients with nAMD outside of the CB or COVID period. With minimal modifications, these recommendations can be implemented in routine clinical practice. They aim to balance optimal care based on current evidence while considering aspects like safe distancing and minimising clinic visits. However, the clinician should consider the unique ocular and systemic issues of individual patients while adopting the above principles.

References

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➤ <https://www.rcophth.ac.uk/2020/04/covid-19-update-and-resources-for-ophthalmologists/>

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