Prospective Evaluation of Teleophthalmology in Screening and Recurrence Monitoring of Neovascular Age-Related Macular Degeneration
A Randomized Clinical Trial

Bo Li, MD; Anne-Marie Powell, RN; Philip L. Hooper, MD; Thomas G. Sheidow, MD

IMPORTANCE Teleophthalmology has the potential to reduce costs and inconveniences associated with frequent patient visits. Evaluating teleophthalmology in the management of age-related macular degeneration (AMD) will allow for future implementation of this technology.

OBJECTIVE To evaluate teleophthalmology as a tool for the screening and monitoring of neovascular AMD.

DESIGN, SETTING, AND PARTICIPANTS Prospective, randomized clinical trial that included 106 referral eyes for suspected neovascular AMD and 63 eyes with stable neovascular AMD. New referrals for patients with suspected neovascular AMD and patients with stable neovascular AMD were randomized into either routine or teleophthalmologic groups. In the routine group, patients received clinical assessment and diagnostic imaging at a tertiary hospital-based retina clinic. In the teleophthalmologic group, patients received basic examination and diagnostic imaging at a stand-alone teleophthalmologic site, where patient information and imaging studies were acquired and electronically sent over to tertiary hospital-based retina specialists. Patients in the teleophthalmologic group were called back to the tertiary treatment center if the teleophthalmologic data set suggested pathology or was inconclusive for diagnosis.

MAIN OUTCOMES AND MEASURES Patient wait times for diagnosis and/or treatment, referral accuracy, and visual outcome.

RESULTS For neovascular AMD screening, the average referral-to-diagnostic imaging time was 22.5 days for the teleophthalmologic group and 18.0 days for the routine group, for a difference of 4.5 days (95% CI, 11.8 to −2.8 days; P = .23). The average diagnostic imaging to treatment time was 16.4 days for the teleophthalmologic group and 11.6 days for the routine group, for a difference of 4.8 days (95% CI, 10.7 to −11 days; P = .11). For neovascular AMD monitoring, the average recurrence to treatment time was shorter for the routine group (0.04 days) compared with 13.6 days for the teleophthalmologic group, for a difference of −13.5 days (95% CI, −18.2 to −9.0 days; P < .01). There was no difference identified between end-of-study visual acuities in the 2 groups (P = .99).

CONCLUSIONS AND RELEVANCE A delay of referral to treatment time could not be identified when comparing teleophthalmologic screening for suspected neovascular AMD with retinal specialist-based screening. Teleophthalmologic monitoring for neovascular AMD recurrence resulted in longer wait times for treatment reinitiation, but no adverse visual outcomes were identified.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01581606

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Age-related macular degeneration (AMD) is the most common cause of severe visual impairment in adults older than 65 years in the developed world.1–6 With advancing age, the prevalence of AMD also increases.3,7,8 Therefore, the demand for AMD screening, intervention, and postintervention monitoring will continue to grow exponentially, resulting in a greater demand on eye care professionals. Several studies have documented visual decline and recurrence is common after therapy is discontinued.9–16 The high risk of disease recurrence after termination of treatment necessitates the development of a proactive and vigilant maintenance monitoring phase for patients with stable and nonactive disease. Such a maintenance program will be cost-effective for the health care system by ensuring that unnecessary treatments are not given, patient and family travel and time requirement are reduced, and the money spent by our health care system to regain visual acuity is not lost through recurrent and irrecoverable disease activity.

Teleophthalmology has the ability to provide localized community-based evaluations, limiting patient travel and inconvenience. It has been shown to be cost-effective and highly reliable in patients with diabetic retinopathy.17–20 Teleophthalmologic screening programs are currently in place for diabetic retinopathy in several Canadian provinces including Alberta and British Columbia. Teleophthalmology relies on the store-forward approach where a series of digital images are obtained by a technician locally and electronically forwarded to a retinal specialist for grading and evaluation. Along with the digital images (eg, colored fundus photographs or optical coherence tomography [OCT]), a standard ophthalmic examination, including a short patient history, visual acuity, and intraocular pressure measurement, can also be sent electronically to the retinal specialist. After reviewing the teleophthalmologic data set, any patient believed to require clinical assessment and treatment is then transferred to the nearest retinal specialist. This approach effectively eliminates unnecessary patient travel, reduces clinical visits and workloads for physicians, and increases patient access to retinal service for patients in remote and underserved communities.

Age-related macular degeneration is a condition ideally suited for the use of teleophthalmology because it is a disease of the macula. The macula can be easily imaged with high-resolution colored fundus photographs and OCT and the produced digital images can be stored and transferred electronically.26

The purpose of this study was to evaluate the use of teleophthalmology both in the initial screening and recurrence monitoring of neovascular AMD. The quality, timeliness, and patient satisfaction with teleophthalmology in AMD were established by this study.

Methods

This prospective randomized study evaluated the use of teleophthalmology in the initial screening of suspected neovascular AMD and recurrence monitoring of neovascular AMD. This trial was registered in the US National Institutes of Health trial registry and was approved by the Western University Research Ethics Board. Written informed consent was obtained from participants of this study. The CONSORT flow diagram of the study design is detailed in Figure 1.

Initial Screening of Neovascular AMD

New referrals to the retina service at the Ivey Eye Institute (IEI), in London, Ontario, Canada, between November 1, 2011, and

Figure 1. CONSORT Flow Diagram

<table>
<thead>
<tr>
<th>A</th>
<th>106 Patients randomized</th>
</tr>
</thead>
<tbody>
<tr>
<td>54 Patients received routine screening at the Ivey Eye Institute</td>
<td></td>
</tr>
<tr>
<td>2 Patients lost to follow-up owing to other medical conditions</td>
<td></td>
</tr>
<tr>
<td>52 Patients included in data analysis</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>B</th>
<th>63 Patients randomized</th>
</tr>
</thead>
<tbody>
<tr>
<td>36 Patients received teleophthalmologic screening at the Ocular Health Center</td>
<td></td>
</tr>
<tr>
<td>2 Patients lost to follow-up</td>
<td></td>
</tr>
<tr>
<td>52 Patients included in data analysis</td>
<td></td>
</tr>
<tr>
<td>34 Patients included in analysis for recurrence rate</td>
<td></td>
</tr>
<tr>
<td>30 Patients included in analysis for end-of-study visual acuity because 4 patients failed to follow up at the end of the study owing to other medical conditions</td>
<td></td>
</tr>
<tr>
<td>22 Patients included in analysis for end-of-study visual acuity because 3 patients failed to follow up at the end of the study owing to other medical conditions</td>
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</tbody>
</table>

Initial screening (A) and recurrence monitoring (B) of neovascular age-related macular degeneration.
Recurrence Monitoring of Neovascular AMD

Patients who were previously treated for neovascular AMD at the IEI in London, Ontario, and did not have evidence of disease activity at the time of enrollment (January 1, 2012–November 1, 2012) were enrolled in this part of the study. Patients were randomized in routine monitoring (2R) at the IEI or teleophthalmologic monitoring (2T) at the OHC and were monitored for recurrence of neovascular AMD during a 1-year period. The OHC in London, Ontario, stopped accepting patients in October 2012 owing to unanticipated closure. As a result, patients who were initially randomized in the 2T group after October 2012 were regrouped into the 2R group and were followed up at the IEI.

The 2R group received regular appointments with diagnostic imaging studies including OCT of the macula and an in-person evaluation by a retinal specialist at the IEI in London, Ontario, every 2 months for a 1-year period. Best-corrected visual acuity, intraocular pressure, biomicroscopy, and dilated indirect ophthalmoscopy were performed at the initial and follow-up assessments. If recurrence of neovascular AMD was detected, patients were treated as needed with the guidance of retinal specialists at the IEI.

The 2T group patients were assessed and followed up at the OHC in London, Ontario, every 2 months during a 1-year period. The diagnostic imaging studies (fundus photograph and OCT) and patient data obtained at each visit were stored in the OHC teleophthalmologic database and electronically sent to retinal specialists at the IEI for formal evaluation of neovascular AMD recurrence. Patients in the 2T group were followed up at the OHC on a bimonthly basis if there was no evidence of disease recurrence of neovascular AMD. Patients with evidence of neovascular AMD recurrence based on teleophthalmologic data sets were recalled to the IEI for treatment and continued to be followed up as needed.

Results

Initial Screening of Neovascular AMD

Patient Characteristics

A total of 106 patients (106 eyes) were enrolled in the initial screening of the neovascular AMD study. Of this total, 54 were randomized into the 1R group and 52 were randomized into the 1T group. Within the 1R group, 2 patients failed to show up for their scheduled diagnostic testing and clinic appointment and were lost to the study. Basic patient characteristics are listed in Table 1. There were no differences identified for age ($P = .82$), home to diagnostic center distance ($P = .77$), BCVA ($P = .14$), or duration of visual symptoms before referral to a retinal specialist ($P = .67$). For patients with prior diagnosis and treatment of neovascular AMD in 1 eye, the average duration of visual symptoms before referral was 8.6 weeks compared with 13.8 weeks for patients without prior diagnosis and treatment of neovascular AMD in the other eye for a difference of −5.2 weeks (95% CI, −17.6 to 7.3 weeks; $P = .41$).

Patient Wait Times

The average referral to diagnostic imaging time was 22.5 days for the 1T group compared with 18.0 days for the 1R group, for a difference of 4.5 days (95% CI, 1.8 to −2.8 days; $P = .23$). Within the 1T group, 19 patients were diagnosed as having neovascular AMD and the average diagnostic imaging to treat-

Patient satisfaction questionnaires were completed by both 1R and 1T patients near the end of their initial screening visit either at the IEI or OHC. The ease of access or travel, parking, registration process, appointment changes, and staff friendliness were assessed based on the patient questionnaires.
A total of 63 patients (63 eyes) were enrolled in the monitor-
ing of neovascular AMD. Of the 63 patients, 36 patients were randomized into the 2R group and 27 patients were randomized into the 2T group. Four patients who were initially randomized into the 2T group were placed in the 2R group owing to the unanticipated closure of the OHC. During the course of the study, 2 patients were lost to follow-up owing to medical illness and 2 patients died before neovascular AMD recurrence was detected. Six patients were lost to follow-up after AMD recurrence was detected; as a result, end-of-study visual acuity was not measured for those patients. One patient without signs of AMD recurrence was lost to follow-up near the end of the study and no end-of-study visual acuity was measured. Basic patient characteristics are listed in Table 3. There was no difference identified between the 2 groups in age (P = .83), home-to diagnostic center distance (P = .31), and BCVA (P = .45).

Neovascular AMD Recurrence
The overall neovascular AMD recurrence rate among both 2R and 2T groups was 71.2%; no statistical difference was identified between the 2R (67.7%) and 2T (76%) groups (P = .60) (Table 4). The average time to recurrence for the 2T group was 103.9 days compared with the 2R group at 108.1 days, for a difference of ~4.2 days (95% CI, −49.2 to 41.2 days; P = .85). The overall mean BCVA at the time of disease recurrence was 20/154.8 and there was no statistical difference identified between the 2R (20/155.2) and 2T (20/154.2) groups (P = .99). The overall detection of disease recurrence to treatment time was 6.2 days. The 2R group had an average detection of disease recurrence to treatment time of 0.04 days compared with the 2T
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group at an average of 13.6 days, for a difference of −13.5 days (95% CI, −18.2 to −9.0 days; \( P < .001 \)). At the end of the 12-month study, the overall average BCVA was 20/180.4; no statistical difference was identified between the 2R group at 20/180.7 and the 2T group at 20/184.8 (\( P = .99 \)).

### Discussion

Age-related macular degeneration is a vision-disabling disease with increasing prevalence with advancing age. In the aging population, the cost of screening, treatment, and monitoring of AMD are expected to increase significantly and pose increased financial burdens to the health care system and patients and their families. Effective screening and monitoring tools for AMD have the potential to bring significant cost savings and reduce inconvenience associated with unnecessary patient visits, travel, and physician workloads. To our knowledge, this is the first study that evaluated the use of teleophthalmology in the screening and monitoring of neovascular AMD.

In this study, we could not identify a delay in measures of wait times with the use of teleophthalmology performed in the initial screening of neovascular AMD when compared with traditional retina clinic-based screening. This study suggests that the use of teleophthalmology may be a timely screening tool for neovascular AMD. In the study, the 1R group had a shorter average diagnostic imaging to treatment onsite.

In our study, the referral accuracy for neovascular AMD was 42.3%. A large percentage of referrals were diagnosed as having conditions that did not require treatment by a retinal specialist. Forty-one percent of referrals for suspected neovascular AMD were diagnosed as having either dry AMD or untreatable disciform scarring; those patients could potentially be followed up by the referring optometrists or ophthalmologists without having to see a retinal specialist. Eleven percent of referrals were diagnosed as having non–AMD-related pathology that required follow-up and/or treatment by a retinal specialist on a nonurgent basis. Overall, 44% of total referrals for suspected neovascular AMD did not require consultation, follow-up, or treatment by a retinal specialist. The high false-positive rate of referrals indicated that teleophthalmologic screening for AMD may have been able to reduce the number of unnecessary clinic visits to retinal specialists, therefore, reducing work loads and wait times within retinal clinics. The reduced patient load at the retinal clinic should re-

### Table 2. Patient Satisfaction at the Ivey Eye Institute and the Ocular Health Center

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Average Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ease of Access</td>
</tr>
<tr>
<td></td>
<td>(1 = No Difficulties; 4 = Extreme Difficulties)</td>
</tr>
<tr>
<td>Screening group</td>
<td></td>
</tr>
<tr>
<td>Routine (n = 54)</td>
<td>1.24</td>
</tr>
<tr>
<td>Teleophthalmologic (n = 52)</td>
<td>1.10</td>
</tr>
<tr>
<td>( P ) value</td>
<td>.15</td>
</tr>
</tbody>
</table>

### Table 3. Baseline Patient Demographics of 63 Teleophthalmologic Monitoring Study Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean Age, y</th>
<th>Men to Women Ratio</th>
<th>Home to Imaging Center Distance, km</th>
<th>Baseline Visual Acuity at Time of Randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Routine (n = 36)</td>
<td>81.7</td>
<td>8:28 (22% Men)</td>
<td>36.1</td>
<td>20/106.0</td>
</tr>
<tr>
<td>Teleophthalmologic (n = 27)</td>
<td>82.1</td>
<td>9:18 (33% Men)</td>
<td>25.2</td>
<td>20/78.0</td>
</tr>
<tr>
<td>Overall</td>
<td>81.8</td>
<td>17:46 (27% Men)</td>
<td>31.4</td>
<td>20/93.8</td>
</tr>
</tbody>
</table>

### Table 4. Neovascular AMD Recurrence Rates and Treatment Wait Times

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Neovascular AMD Recurrence Rate, %</th>
<th>Time to Recurrence, d</th>
<th>Visual Acuity at Time of Recurrence</th>
<th>Recurrence to Treatment Time, d</th>
<th>End-of-Study Visual Acuity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring group</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Routine (n = 36)</td>
<td>67.7</td>
<td>108.1</td>
<td>20/155.2</td>
<td>0.04</td>
<td>20/180.7</td>
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<tr>
<td>Teleophthalmologic (n = 27)</td>
<td>76.0</td>
<td>103.9</td>
<td>20/154.2</td>
<td>13.6</td>
<td>20/184.8</td>
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<tr>
<td>( P ) value</td>
<td>.60</td>
<td>.85</td>
<td>.99</td>
<td>.001</td>
<td>.99</td>
</tr>
</tbody>
</table>

Abbreviation: AMD, age-related macular degeneration.
result in improved access, faster follow-up, and reduced wait times for patients who have conditions that require management by retinal specialists.

There were no differences identified in this study in terms of patient satisfaction between the teleophthalmologic and routine groups among all measures of satisfaction, except for the higher level of satisfaction with parking at the teleophthalmologic site. With implementation of teleophthalmologic sites in communities that require less patient travel, it is likely that patients will be more satisfied with community-based teleophthalmologic sites.

This study demonstrated a high recurrence rate (71.2%) and short recurrence time (106.2 days) for patients with stable neovascular AMD. The frequent recurrence of neovascular AMD necessitates a program with robust and frequent monitoring. Monitoring of disease recurrence with the use of teleophthalmology for patients offers an alternative to the traditional retina clinic–based follow-up model. In our study, the wait time from recurrence to treatment was shorter in the 2R group; this is because the traditional retina-based follow-up model allowed for same-day treatment. In contrast, teleophthalmology required patients with recurrence to be booked in the retina clinic at a later date than when treatment could be offered. The average wait time for treatment for the 2T group was about 2 weeks. However, the 2 weeks’ wait time for treatment reinitiation did not result in worse final visual outcomes.

In this study, the use of teleophthalmology in screening and recurrence monitoring for neovascular AMD was robust, timely, and with high patient satisfaction. However, there were a number of limitations. This study used a stand-alone screening site located in the same city as the treatment center. Therefore, we were not able to evaluate the benefit of teleophthalmology in terms of reduced patient travel. The other limitation was the short follow-up period. The end-of-study BCVA was taken at the study end date, which varied for both groups and within groups, with no longer-term follow-up available in either group to assess potential adverse visual outcomes associated with the longer wait times for treatment reinitiation in patients with neovascular AMD recurrence.

Conclusions

Teleophthalmologic screening as performed in this study did not identify a relevant average delay of all measures of wait times. This study suggested that a teleophthalmologic monitoring program for neovascular AMD recurrence resulted in an average longer wait time for treatment reinitiation but that an average worse visual outcome was not identified with such delay. This work further supports the need for a network of teleophthalmologic imaging sites in remote areas. It allows general ophthalmologists and optometrists to offer expanded basic retinal services under the teleophthalmic guidance of retinal specialists. With the aging population and ever-increasing incidence of AMD, teleophthalmology will hopefully bring convenience and cost-saving opportunities both to the health care system and patients and caregivers.

REFERENCES


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