PRACTICAL USES OF TELEOPHTHALMOLOGY

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Abstract

Introduction: Telecommunications are becoming a part of every aspect of life – business, entertainment, medicine. As part of medicine ophthalmology is particularly amenable to the utilization of such applications. Teleophthalmology is gaining importance as an effective eye care delivery modality worldwide. While currently most efforts are concentrated on screening and referral to experts, it could be used as a research and clinical tool.

Aim and tasks: To assess the spread and use of telemedicine in ophthalmology.

Materials and methods: A structured literature search was done in search engines such as PubMed, Medline, and Google Scholar using the following keywords – teleophthalmology OR telemedicine OR teleophthalmology OR telediabetic screening OR teleglaucoma OR tele ROP OR telescreening AND Diabetic retinopathy OR retinopathy of prematurity OR macular diseases. One hundred and seventy five articles were reviewed.

Results: Most current research is focused on screening for retinopathy of prematurity (ROP), diabetic retinopathy (DR), glaucoma, age-related macular degeneration (ARMD), and other sight-threatening conditions. Studies report only 2% of screened eyes requiring in-person examination due to ungradable images. Tele-screening required less time than its bedside counterpart, and while further research is needed most studies suggest high specificity and sensitivity.

Conclusion: Teleophthalmology also allow for greater coverage of health care, providing access to an ophthalmologist even in distant and rural areas. At the same time it reduces time and travel costs, while providing high acceptance and satisfaction levels.

Keywords: *Screening, ophthalmology, telemedicine*

Introduction:

Telecommunications are becoming an integral part of every aspect of life – business, entertainment, medicine. As a branch of medicine ophthalmology is particularly amenable to the utilization of such applications. Teleophthalmology is gaining importance as an effective eye care delivery modality worldwide. While currently most efforts are concentrated on screening and referral to experts, it could be used as a research and clinical tool.

Teleophthalmology is becoming and integral part of modern medicine, giving us an effective way to deliver eye care worldwide. In developing countries, teleophthalmology is being utilized to provide quality eye care to the underserved urban population and the unserved remote rural population. The main focus on teleophthalmology are screening for retinopathy of prematurity (ROP), diabetic retinopathy (DR), glaucoma, age-related macular degeneration (ARMD), and other sight-threatening conditions. **[30]**

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To assess the spread and use of telemedicine in ophthalmology.

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Results:

Studies suggest teleophthalmology produces the desired clinical outcome with high specificity and sensitivity comparable to the traditional system. By creating remote portals for specialisied care accessibility and health care outcomes are improved for rural and distant areas. Sreelatha et al report a high satisfaction level and acceptance in majority of the studies because of increased accessibility and reduced traveling cost and time. **[30]**

Using teleophthalmology for the delivery of routine eye care for patients with diabetes mellitus is becoming an increasingly common practice. Paramount in the consideration of any new diagnostic test is an analysis of its diagnostic accuracy and reliability and how that compares with conventional care.

Over the past decade, there have been rapid strides in progress in the fields of telecommunication and medical imaging. There is growing evidence regarding use of teleophthalmology for screening of diabetic retinopathy. Surendran et al found telescreening for diabetic retinopathy to be a cost-effective, accurate, and reliable method for screening for diabetic retinopathy. **[31]**

Gomez-Ulla et al conducted a study on 70 diabetic patients (126 eyes), taking four digital retinal images of each eye. All eyes with DR were correctly identified ($\kappa = 1$) by inspecting the digital images. In 118 eyes, 57 with no DR and 61 with DR, there was an agreement between the gradation made after the direct examination and the gradation made after the inspection of the images (ICC = 0.92). In eight eyes with DR, there was disagreement in the grading made with both techniques. **[13]**

A research by Ng et al screened more than 5500 patients (9016 visits) assessed in Alberta, by teleophthalmology programs. Out of those consulted 930 patients have been referred for additional testing or treatment. Approximately 2% of teleophthalmology assessments have required referral for in-person examination due to ungradable image sets, most commonly due to cataract, corneal drying, or asteroid hyalosis. **[26]** Andonegui et al trained GPs to screen for DR obtaining the same results. From a total of 1223 patients, in 26 cases (2%) the retinography images were unreadable. **[1]** In a similar study Boucher et al found only 0.7% of the images could not be interpreted because of poor image quality and had to be referred for a traditional examination. Out of the screened diabetics 85.6% did not require a traditional ophthalmologic examination. On the other hand, ophthalmologists were required to provide urgent (within 30 days) services to 2% of the cohort, either because of threatening DR or because of incidental findings requiring rapid ophthalmologic attention. The study also suggested pupil dilation with tropicamide 1% was useful or necessary in 33.7% of their studys' cohort. **[3]** Chin et al. screened 872 patients (1,744 eyes) from rural sites and 517 subjects (1,034 eyes) from an urban sites. Images were of good quality for evaluation in 82.4% and 85.7% of subjects, respectively. Telescreening can be a useful tool in both rural and urban settings to screen for diabetic retinopathy in patients who are nonadherent to the recommended dilated annual eye exam. **[4]** Specificity of GPs for detecting diabetic retinopathy by non-mydriatic retinography was 83%, sensitivity - 90.9%; the sensitivity for detecting treatable lesions was 99.2%. Andonegui et al concluded that adequately trained GPs can screen for treatable lesions of diabetic retinopathy with a very high level of reliability using non-mydriatic retinography. **[1]**

Tennant et al assessed 100 patients for diabetic retinopathy transferred images to a tertiary eye center for review by a retinal specialist. All eyes identified by stereoscopic digital imaging with treatable disease were confirmed by clinical examination with contact lens biomicroscopy. The team concludes that stereoscopic digital imaging of the retina enables the identification of diabetic retinopathy, although further research is needed to delineate the sensitivity and specificity of method. **[33]** This was done by a team lead by Tennant a year later. The correlation between the two techniques for severe nonproliferative diabetic retinopathy (NPDR) was 0.86 and for high-risk proliferative diabetic retinopathy 1.00 ($p < 0.001$). **[32]**

Whited summarizes existing data on the diagnostic accuracy and reliability of teleophthalmology. The sensitivity of teleophthalmology for detecting diabetic retinopathy has been shown to be comparable, if not better, than clinic-based examinations, it's values ranged from 50% to 93%. The specificity of teleophthalmology, like clinic-based examinations, has been consistently high. High levels of diagnostic reliability, analyzed by both simple agreement and kappa values, have been found between ophthalmoscopy and teleophthalmology for detecting and classifying diabetic retinopathy Teleophthalmology, compared with both gold standards, has, overall, been a highly sensitive and specific test. Based on existing data, teleophthalmology appears to be an accurate and reliable test for detecting diabetic retinopathy and macular edema. **[31]**

Whited et al also compared cost-effectiveness of a nonmydriatic digital teleophthalmology system (Joslin Vision Network) versus traditional clinic-based ophthalmoscopy examinations. In the base-case analyses the Joslin Vision Network was both less costly and more effective. Based on our economic model, the Joslin Vision Network has the potential to be more effective than clinicbased ophthalmoscopy for detecting proliferative diabetic retinopathy and averting cases of severe vision loss, and may do so at lower cost. **[42]**

Nathoo et al assessed 394 patients (788 eyes) over the 3-year period. Teleophthalmology saved approximately 450 round trips over the 2-year period, equating to approximately 1900 hours and 180 000 km of driving. Teleophthalmology can effectively identify DR while reducing travel time and distance for patients with diabetes living in a rural community. However, many patients did not follow up or attend referral appointments in a timely fashion, underscoring the need for ongoing quality assessment. **[25]**

Kumar et al tried to evaluate the diagnostic capability of a smartphone handset compared with a standard office computer workstation for teleophthalmology fundus photo assessments of diabetic retinopathy. The κ coefficient between the gold standard workstation display and iPhone images to detect retinopathy-related changes for both readers was more than 0.9. The image quality of the iPhone was scored high by the ophthalmologists. **[20]**

There will be an estimated 552 million persons with diabetes globally by the year 2030. Over half of these individuals will develop diabetic retinopathy, representing a nearly insurmountable burden for providing diabetes eye care. Telemedicine can offer a solution to that problem. In most programmes, however there is a heavy reliance on specially trained retinal image graders, a resource in short supply worldwide. These factors necessitate an image grading automation process to increase the speed of retinal image evaluation while maintaining accuracy and cost effectiveness. Several automatic retinal image analysis systems designed for use in telemedicine have recently become commercially available. Such systems have the potential to substantially improve the manner by which diabetes eye care is delivered by providing automated real-time evaluation to expedite diagnosis and referral if required. Furthermore, integration with electronic medical records may allow a more accurate prognostication for individual patients and may provide predictive modelling of medical risk factors based on broad population data. **[29]**

Decencière et al created a prototype for the automatic detection of normal examinations on a teleophthalmology network for diabetic retinopathy screening in their study. Such a system should reduce the burden on readers on teleophthalmology networks. **[9]**

Hansen et al photographed *with* and *without* pharmacological pupil dilation using a digital non mydriatic camera, 83 patients (165 eyes). At patient level, the automated red lesion detection and image quality control combined demonstrated a sensitivity of 89.9% and specificity of 85.7% in detecting DR when used on images captured *without* pupil dilation, and a sensitivity of 97.0% and specificity of 75.0% when used on images captured *with* pupil dilation. **[14]**

Maker et al evaluated 106 patients (211 eyes) with varying levels of DR. Partially ungradable images were present in 3.4% of ETDRS photos versus 31.8% of ARIS images. Exact agreement and agreement within one level between ETDRS photos and ARIS images using only completely gradable image sets occurred in 69% and 90% of cases, respectively. Results suggest that semiautomated ARIS images compare favorably with ETDRS photos when full image sets can be obtained; however, partially ungradable image sets occurred almost 10 times more frequently with ARIS images than with ETDRS photos. Outside of them, ARIS can obtain retinal images comparable to ETDRS photos while requiring less highly trained personnel than generally needed for standard ETDRS photos. **[23]**

Walton et al studied a total of 15 015 consecutive patients with diabetes. The reported sensitivity was 66.4%, with a false-negative rate of 2%. The specificity was 72.8%, positive predictive value was 10.8% and the negative predictive value was 97.8%. In this large urban setting, the IRIS computer algorithm-based screening program had a high sensitivity and a low false–negative rate, suggesting that it may be an effective alternative to conventional reading center image interpretation. **[38]**

Teleglaucoma is a novel area that was first explored a more than a decade ago. The early studies highlighted the technical challenges of teleglaucoma screening, which todays' advanced technologies have since mostly overcome. These technologies can improve the efficiency of healthcare systems, with additional benefits of e-learning and e-research. **[16]**

Tuulonen et al found satisfaction was comparable between traditional screening and telescreening for glaucoma. Nearly all patients in the telemedicine group (96%) wanted to have their next visit in their own healthcare center instead of the university clinic. As benefits of telemedicine were presented reduction in traveling (97%), costs (92%), and time (92%). The costs of the telemedicine and conventional visits were equal, but decreased traveling saved $55 per visit. However, the quality of the images obtained in the remote center was poorer than that of the images obtained at the university clinic. **[35]** Bai et al conducted a similar study on a smaller group of 14 subjects (22 eyes) using a hand-held fundus camera. The images received were considered to be of excellent quality and readily interpreted by ophthalmologists in terms of the likely presence of glaucoma. **[2]** In a study lead by De Mul out of 1729 evaluated patients the quality of the images was at least satisfactory in most cases (89%), and the agreement between the optometrists and the hospital about normal or suspect test results was high (81%). Only 27% of the patients were called for additional testing at the hospital department and 11% consulted an ophthalmologist. **[8]** Similary Li et al found some digital images as too dark for assessing fine glaucomatous disc changes. However, agreement among digital images and 35-mm slides of the eyes was: 65% and 100%. Evaluations of cup-to-disc ratio (C/D) using both methods were in general agreement. Stereo digital images taken with a nonmydriatic camera by nonophthalmic photographers is a promising alternative for glaucoma screening in primary care settings. **[21]** A team led by Kiage examined 309 diabetic, out of them 74 (24%) were deemed unreadable due to media opacities, patient cooperation, and unsatisfactory photographic technique. The ability to diagnose glaucoma based on the overall assessment showed moderate agreement. The use of FDT to detect glaucoma in the presence of disc damage (VCDR > 0.7) showed substantial agreement. The process showed 77.5% positive predictive value and 82.2% negative predicative value. Poor quality photographs can severely limit the ability of TG assessment to diagnose optic nerve damage and glaucoma. The TG approach provides a novel, and promising method to diagnose glaucoma, a major cause of ocular morbidity throughout the world. **[18]**

Thomas et al concluded that, teleglaucoma is more specific and less sensitive than in-person examination. The pooled estimates of sensitivity was 0.832 and specificity was 0.790.

The relative odds of a positive screen test in glaucoma cases are 18.7 times more likely than a negative screen test in a non-glaucoma cases. Teleglaucoma can accurately discriminate between screen test results with greater odds for positive cases. It detects more cases of glaucoma than in-person examination. Both patients and the healthcare systems benefit from early detection, reduction in wait and travel times, increased specialist referral rates, and cost savings. Teleglaucoma is an effective screening tool for glaucoma specifically for remote and under-services communities. **[34]** Yogesan et al found similar results - agreement between gold standard and estimated vertical cup: disk ratios (VCDR) from photographs were 0.87, 0.45, and 0.84 respectively (specificity between 79% and 97%, sensitivity between 70% and 95%). Kappa values obtained between gold standard and estimated VCDR from digital images were 0.52, 0.49, and 0.49, respectively (specificity between 68% and 79%, sensitivity between 67% and 87%). Moderate to good agreement indicates that the digital images from the portable fundus camera may be suitable for optic disk assessment in the current configuration. **[44]** Clarke et al identified adverse disagreement between face-to-face and virtual review in 7 out of 204 patients, where virtual review failed to predict a need to accelerated follow-up identified in face-to-face review. Misclassification events were rare, occurring in 1.9% of assessments. The low rate of adverse misclassification, combined with the slowly progressive nature of most glaucoma, and the fact that patients will all be regularly reassessed, suggests that virtual clinics offer a safe, logistically viable option for selected patients with glaucoma. **[5]** Kumar et al examined the the use of telemedicine-friendly devices in glaucoma screening. The team found that a combination of age and family history of glaucoma alone has a sensitivity of 35.6% (specificity 94.2%) and an addition of telemedicine friendly or conventional visual field tests optimized the sensitivity to 91.1% (specificity 93.6%). Analysis indicates good agreement between VCDR by ophthalmoscopy and digital image reading. The study indicates that evaluations of cup-to-disc ratio and visual field, using telemedicine-friendly devices, are most useful tools in screening for glaucoma. When used together these devices may be an alternative for conventional glaucoma screenings. **[19]**

Age-related macular degeneration (ARMD) occurs with aging. Oxidative stresses and inflammatory processes during the lifetime are accused of being the underlying etiologies. It is estimated that in 2010, 2.85 millions of people were blind because of ARMD. Early detection and regular follow-up of the disease have significant roles in preventing blindness. Screening of populations at risk for ARMD with positive family history or other risk factors through telemedicine would be great helpful.

Ulrich et al. defined early AMD as any type of non-exudative changes with a visual acuity >20/200 and advanced AMD as any exudative changes or advanced atrophic disease with a visual acuity (≤ 20/200). **[36]** Mohammadpour et al showed that evaluation of digital retinal images in the diagnosis of neovascular AMD in comparison with specialists' diagnosis showed high sensitivity (95%) and specificity (90%). Smartphones are available everywhere and are great tools for monitoring patients with AMD. Patients can do self-testing by using Shape-discrimination hyperacuity (SDH) and MultiBit Test (MBT). **[24]** A team lead by Pirbhai found exact agreement between photographic evaluation and gold standard ranged from 89.2% to 82.5%. As a screening tool for high-risk dry changes and active exudative changes, overall sensitivity specificity, positive predictive value, and negative predictive value were 82.1%, 79.1%, 70.4%, and 88.0%, respectively. Digital, non-stereo color fundus photographs are highly sensitive and have high negative predictive value as a screening tool. Very few treatable lesions are missed using telemedicine in age-related macular degeneration. **[27]** A similar study was done by Zimmer et al, where they found a good agreement for low-risk lesions and excellent agreement for high-risk lesions. Thirty-five of 36 eyes with intermediate or advanced disease were correctly identified with DigiScope images. Choroidal neovascularization was identified in all cases with the DigiScope due to the presence of subretinal hemorrhage or subretinal fibrosis. The DigiScope was found less capable of detecting subretinal fluid than standard stereo fundus photographs. This pilot study suggests that the DigiScope may be a useful screening tool for AMD. **[45]**

De Bats et al reported the ability of detecting ARMD remotely using nonmydriatic digital fundus camera. Approximately 16% of the gradable digital images were identified having ARMD. Age, positive family history of ARMD, and postcataract surgery are the risk factors for ARMD. **[7]**

Kelly et al managed 50 patients with suspected macular conditions via telemedicine consultation over 1 year. Seventeen cases (34%) were managed in the community and are a potential cost improvement. Innovation and quality improvement were demonstrated in both optometry to ophthalmology referrals and in primary optometric care by use of telemedicine with spectral domain optical coherence tomography images. E-referral of spectral domain optical coherence tomography images assists triage of macular patients and swifter care of urgent cases. **[17]**

Kanagasingam et al explored the possibilities of telescreening of age-related macular degeneration (ARMD) using automated and semiautomated grading systems and retinal image analysis techniques for early detection and follow-up of the disease. The study foun OCT imaging modality to be appropriate for telemedicine-based screening and management. **[15]**

Retinopathy of prematurity (ROP) remains a significant threat to vision for extremely premature infants despite the availability of therapeutic options. It has been shown in many controlled trials that application of therapies at the appropriate time is essential to successful outcomes in premature infants affected by ROP. Bedside binocular indirect ophthalmoscopy has been the standard technique for diagnosis and monitoring of ROP in these patients. Modern technology, including the development of wide-angle ocular digital fundus photography, coupled with the ability to send digital images electronically to remote locations, has led to the development of telemedicine-based remote digital fundus imaging (RDFI-TM) evaluation techniques. These techniques have the potential to allow the diagnosis and monitoring of ROP to occur in lieu of the necessity for some repeated on-site examinations in NICUs. **[11]**

Weaver et al performed a total of 582 telemedicine examinations on 137 infants. Good outcomes were noted in all cases, with none progressing to stage 4 or 5 ROP. Telemedicine ROP screening detected patients at a remote site in need of laser treatment, allowing prompt transfer with no poor outcomes over a 4.5-year period. **[40]**

Ells et al showed in their study digital photography had a sensitivity of 100% and a specificity of 96% in detecting referral-warranted (RW)-ROP. The positive predictive value of digital photography was 92%, and the negative predictive value was 100%. In 87% of eyes, referral-warranted ROP was diagnosed by digital photography before or at the same time as indirect ophthalmoscopy. Longitudinal remote reading of digital photographs using the RetCam-120 system has excellent specificity and sensitivity in detecting referral-warranted ROP. **(10)** Lorenz et al screened 1,222 prematures at risk and found sensitivity for detecting ROP was 100%, and the positive predictive value for ROP 82.4%. All ROP was detected in time, showing the potential of telemedical screening programs. **[22]** The KIDROP program (http://www.kidrop.org) in rural India has employed trained nonphysicians to perform retinal imaging. From 51 322 imaging sessions in 81 centers, Vinekar et al found sensitivity, specificity, positive predictive value, and negative predictive value for treatment-requiring disease of 95.7%, 93.2%, 81.5%, and 98.6%, respectively. The e-ROP Study found a higher sensitivity and specificity in their nonphysicians compared with their expert ophthalmologists. Technicians in our method missed 0.9% of infants needing treatment. **[37]** A study by Wang et al from 2015 screened 1216 total eyes. Twenty-two (3.6%) of the infants screened met criteria for treatment warranted (TW)-ROP. Reported sensitivity was 100%, specificity of 99.8%, positive predicative value of 95.5%, and negative predicative value of 100% for the detection of TW-ROP. **[39]** Fijalkowski et al in their SUNDROP telemedicine initiative have shown similar results and have not missed any TW-ROP in its four-year evaluation period. A total of 410 infants (820 eyes) were imaged. Telemedicine had a calculated sensitivity of 100%, specificity of 99.8%, positive predicative value of 92.9% and negative predictive value of 100% for the detection of TW-ROP. The results for the SUNDROP telemedicine initiative were highly favourable with respect to diagnostic accuracy. Telemedicine appears to be a safe, reliable, and cost-effective complement to the efforts of ROP specialists, capable of increasing patient access to screening and focusing the resources of the current ophthalmiccommunity on infants with potentially vision-threatening disease. **[12]**

Daniel et al took a total of 5520 image sets. Their data suggest that the e-ROP system for training and certifying nonphysicians to grade ROP images under the supervision of a reading center director reliably detects potentially serious ROP with good intragrader and intergrader consistency and minimal temporal drift. **[6]**

A study lead by Ying found thath among 979 infants without RW-ROP, 149 (15.2%) developed RW-ROP. According to tehm significant predictors for RW-ROP were male sex, nonblack race, low birth weight (BW), younger gestational age, number of quadrants with preplus disease, stage 2 ROP, the presence of retinal hemorrhage, the need for respiratory support, and slow weight gain. These characteristics predicted the development of RW-ROP significantly better than BW and gestational age. These predictors may help identify infants in need of timely eye examinations. **[43]**

Richter et al found in their study that telemedicine was significantly faster than ophthalmoscopy (P < .0001). The ophthalmologist time requirement for telemedical ROP diagnosis is significantly less than that for ophthalmoscopic diagnosis. Additional time requirements associated with bedside ROP diagnosis increased this disparity. Telemedicine has potential to alleviate the time commitment for ophthalmologists who manage ROP. **[28]**

Conclusion:

In rural and distant areas, many patients with eye diseases do not receive an annual dilated eye examination. Teleophthalmology is beneficial because it decreases the time to treatment, allows treated patients to be followed remotely, and prevents unnecessary referrals. Health care costs may be reduced by the introduction of comprehensive teleophthalmology examinations by enabling testing and treatment to be planned prior to the patient's first visit. **[26]**

Teleophthalmology, compared to gold standards, has show high sensitivity, specificity, positive and negative predictive value. Based on existing data, teleophthalmology appears to be an accurate and reliable test for detecting diabetic retinopathy, glaucoma ROP and ARMD. **[31]** Further studies of patient safety, cost-effectiveness, and widespread applications of this type of algorithm should be pursued to better understand the role of teleretinal imaging and automated analysis in the global health care system. **[38]**

Ophthalmic images transmitted through both smartphone and Internet techniques match well with each other. Despite current limitations, smartphones could represent as a tool for fundus photo assessments of eye diseases. Further studies are needed to investigate the economic and clinical feasibility of smartphones in ophthalmology. **[20]**

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