Role of Telemedicine in Diabetic Retinopathy

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With the increasing prevalence of diabetic retinopathy (DR), screening is of the utmost importance to prevent vision loss for patients and reduce financial costs for the healthcare system. Telemedicine offers the opportunity to expand access to screening while reducing the economic and temporal burden associated with current in-person protocols.

diabetic retinopathy | telemedicine | artificial intelligence | teleophthalmology

1. Introduction

Diabetic retinopathy (DR) is a microvascular, ocular complication of diabetes mellitus that is prevalent across the globe. Approximately 463 million people were estimated to be affected by the condition in 2019, a figure projected to expand to 700 million by 2045. In particular, DR is expected to disproportionately affect populations in the Middle East, North Africa, and the Western Pacific [1]. Contending with the long-term effects of this disease constitutes a substantial monetary investment. A relatively recent economic model of patients with DR in Indonesia, a nation with a considerable burden of disease, identified that the summative healthcare costs to the government for DR comprised approximately 2% of the state budget in 2017. Much of this expense was attributable to treatments for patients with more advanced DR such as vitrectomy and intravitreal injection [2].

Preempting these costs requires the implementation of strategies to screen patients with diabetes mellitus in order to detect disease early. Traditional detection and management of DR depend upon in-person retinal examination, with professional ophthalmic care providers performing ophthalmoscopy or imaging the retina to capture damage to underlying vasculature. The sustainability of in-person universal screening, however, is questionable [3]. As the number of individuals with diabetes increases, an exponentially rising number of hours will be required from ophthalmologists to examine each patient once annually [4][5]. Financially, expenditures may surmount hundreds of millions of dollars, particularly when accounting for the hidden costs of healthcare including absences from work and transportation [6][7]. Other factors compounding these concerns include psychological and social considerations e.g., age, poor health literacy, and limited health insurance [8][9][10]. As such, despite concerted efforts to increase access to screening from various agencies and organizations, a substantial proportion of patients with diabetes mellitus do not receive annual eye examinations [11][12]. Accordingly, novel protocols integrating teleophthalmology are necessary to effectively address the unmet need of evaluating patients with DR.

Telemedicine is the distribution of remote healthcare services to physically separate clinical providers and patients. One of the first documented uses of telemedicine was in the 1950s, when psychiatric consultations were delivered via closed-circuit television at the Nebraska Psychiatric Institute and Norfolk State Hospital [13]. Since then, technical advancements have facilitated rapid changes in this space, thereby improving the efficiency of this healthcare delivery modality [14][15]. Internationally, healthcare systems have increasingly adopted telemedicine to deliver more accessible, cost-effective care, especially among remote or underserved communities [16]. These considerations are particularly pronounced in the context of the recent COVID-19 pandemic that mandated restriction of person-to-person contact between healthcare providers and patients. The resulting decreased access to medical services across all societal strata necessitated rapid innovation in order to enable clinicians to provide continuing effective healthcare for their patients. In this setting, for a smaller specialty such as ophthalmology, where a relatively limited number of practitioners are delivering ocular healthcare to a remarkably larger number of patients [17], telemedicine became progressively more essential for the successful provision of medical coverage [18][19][20]. Evidence of this phenomenon is found in an investigation by Portney and colleagues, who reported that a peak of 17% of all ophthalmic encounters in the U.S. state of Michigan were comprised of telehealth visits in early April 2020 [21].

2. Accuracy and Reliability of Teleophthalmology

To decrease rates of preventable vision loss, ophthalmologic telemedicine should both reliably diagnose early disease and appropriately refer high-risk patients for more-intensive follow-up. For tele-retinal imaging (TRI) to be considered a viable screening tool, it must accurately determine the likelihood for a patient to have DR [22]. A recent meta-analysis of multiple large-scale studies reported that TRI screening programs detect threshold-level DR with high sensitivity (91% (95% confidence interval, CI 0.82–0.96)) and specificity (88% (95% CI 0.74–0.95)), figures comparable to the traditional clinical examination [23]. A more granular meta-analysis of 33 articles involving more than 10,000 patients identified that teleophthalmology had a cumulative sensitivity for high-risk PDR of 76% (standard deviation (SD) ± 31%) and specificity of 94% (SD ± 9%) relative to gold-standard ophthalmoscopy [24]. For low-risk PDR, the mean sensitivity was 75% and the mean specificity was 98% (SD ± 2%). For severe NPDR, the mean sensitivity was 42% (SD ± 27%) and the mean specificity was 94% (SD ± 1%). Sensitivity and specificity were 87% and 91%, respectively, for detecting the absence of retinopathy.

These findings have been replicated across various populations and settings using a myriad of protocols and screening devices. A focused investigation employing mobile screening devices noted that telemedicine with handheld nonmydriatic images could adequately examine and accurately diagnose fundus pathology [25]. A total of 200 patients were evaluated on-site by an ophthalmologist. Additionally, fundoscopic images were captured using both handheld nonmydriatic and conventional fundus cameras. All photographs were randomized and presented digitally to two remote ophthalmologists. Although the nonmydriatic camera provided lower image quality and a smaller field of view (FOV), nearly 80% of the images were classified as excellent (22.7%) or good (55.7%), indicating that less than 50% of the fundus field was blurred and an appropriate diagnosis could be made. The diagnosis agreement rate with the on-site exam was comparable between the handheld nonmydriatic and conventional fundus images at 90.7% and 95.2%, respectively.

Yeh and colleagues reported similar findings in their investigation of the viability of handheld devices for teleophthalmology screening [26]. Eighty-eight patients underwent comprehensive eye examinations, including an indirect ophthalmoscope exam with a retinal specialist. A total of 176 fundus images were captured. Deidentified photos were remotely reviewed by two retinal specialists and independently graded according to the same criteria as the on-site indirect exam. Referral recommendations for each participant were based on the American Academy of Ophthalmology (AAO) Practice Pattern Guideline [27]. Over 95% of the images were of acceptable or ideal quality for assessing details and emergent findings of the fundus based on the modified FOTO-ED scale [28]. Relative to the gold-standard indirect fundus exam, there was considerable agreement between the two reviewers' assessments and the on-site diagnosis (88.6–89.8% with a Cohen's k coefficient of 0.78–0.80). Sensitivity and specificity were 78% and 99%, respectively. Likewise, the two reviewers averaged 94.8% (k = 0.81) agreement with the on-site referrals. Overall, telemedical screening using handheld retinal imaging created sufficient quality fundus photographs that can be utilized for referral-driven diagnosis comparable to standard slit lamp ophthalmoscopy.

Date et al. conducted a broader population-level assessment of the accuracy of teleophthalmology screening for referable DR grading with 24,138 Harris Health System (HHS) patients [29]. Where appropriate, low-income diabetic patients were referred by their primary care provider (PCP) to 1 of 12 outpatient sites to obtain single-field 45-degree nonmydriatic color fundus imaging. Images were uploaded to a HIPAA-compliant server and assessed by a trained ophthalmologist following the International Clinical Diabetic Retinopathy Disease Severity Scale with follow-up recommendations for patients with severe non-proliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR), or significant diabetic macular edema (DME). On the basis of these TRI readings, 1767 patients were included for dilated fundus examination (DFE) in the clinic. Those with lower levels of DR were asked to return in six months to one year. The positive predictive value for detecting referable-level DR (severe NPDR or PDR) was 71.3%. When comparing the DR severity grading on TRI with that of in-clinic DFE, there was moderate agreement, with a weighted k coefficient of 0.45. Nonetheless, a significant portion of TRI grades for severe NPDR (90%) were within one DR severity level of the clinical examination grade. As for PDR, 78% of TRI grading was an exact match, and 7% was within 1 severity level. Among those with >2-step discrepancy in DR grading, 69.3% were over-estimated by TRI. Overall, these accuracy levels reassuringly highlighted that TRI could assign correct DR severity and ensure appropriate follow-up recommendations, even when screening at a population level.

It should be noted, however, that the results of teleophthalmology programs are dependent on the eye care providers serving as the readers, with individual experience levels varying substantially. Using a set of masked images, Liu et al. assessed the variability between an optometrist, a general ophthalmologist, and a fellowship-trained retina specialist for tele-retinal evaluation of DR [30]. Among those cases deemed gradable (*n* = 65), there was substantial agreement on the absence of any retinopathy (88% (SD ± 4.6%)), presence of moderate non-proliferative or worse retinopathy (87% (SD ± 3.9%)), and macular edema (99% (SD ± 0.9%)). All cases (*n* = 7) of clinically significant DR identified by the retinal specialist were similarly identified by the other two readers. There was comparable agreement with referral recommendations for urgent (one month), nonurgent (two to six months), and routine (one year) follow-ups. Conversely, agreement was limited regarding the presence of referable nondiabetic eye pathology (61% (SD ± 11%)). Furthermore, the intrareader agreements among providers were variable for diagnoses and dispositions, with the general ophthalmologist and optometrist having a lower degree of intrareader agreement (60%) than the retina specialist (90%) [30].

3. Access to and Cost-Effectiveness of Teleophthalmology

Teleophthalmology is becoming more widespread due to its ability to provide timely and appropriate treatment to patients who may not be able to attend appointments as frequently, particularly those residing in rural areas. Because DR is asymptomatic in its early stages, patients with diabetes mellitus must be screened regularly if they are found to have retinopathy [31]. Utilization of teleophthalmology may improve multiple aspects of DR management, including access to treatment, rates of follow-up, early treatment, and cost of care.

Using a pretest–posttest model, Daskivich and colleagues examined the implementation of teleophthalmology to improve services rendered to patients of the Los Angeles County Department of Health Services. At baseline, the average wait time for ophthalmology screening for DR in the Los Angeles County safety net was more than 8 months for underinsured patients [32]. Following the institution of a primary-care-based teleretinal DR screening program, during which 21,222 patients were evaluated over 2 years, screening rates improved by 16%, and median wait times were reduced from 158 days to 17 days. Their findings suggested that the U.S. safety net for underinsured and uninsured populations would reap substantial benefits by investing in telehealth programs that could broaden access to care.

Teleophthalmology is similarly more cost-effective in a myriad of circumstances. A DR screening initiative in the Bronx, the most diverse and lowest-income borough of New York City, illustrated both the cost-effectiveness and potential profitability of such programs [33]. Treatment of DR-associated pathology identified on screening resulted in a gain of 9 quality-associated life years (QALY) in addition to USD 49,052 of savings. Furthermore, on the basis of the reimbursement rates from the Centers for Medicare and Medicaid Service (CMS), treatment of DR-related pathology generated USD 208,535 in revenue [33]. In Southeastern Brazil, a similarly diverse setting, an assessment of the economic viability of DR teleophthalmology screening revealed an average cost reduction of USD 28.76 per patient. The authors calculated that achievement of the break-even point (where revenue and cost are identical) would require a mere 112 exams per month or 1344 exams per year [34]. Rachapelle et al. evaluated the cost-effectiveness of implementing various DR teleophthalmology screening intervals in India, which possesses a relatively large rural population. Utilizing the World Health Organization definition of cost-effectiveness, they determined that teleophthalmology for DR screening was more cost-effective relative to no screening if the frequency interval of examination was greater than one year [16].

Greater multidisciplinary cooperation may further expand upon the cost-effectiveness of teleophthalmology screening for DR. Although some PCPs and optometrists may recognize evidence of the disease, there are circumstances where it is misdiagnosed or underdiagnosed, thereby conferring a greater lifetime cost to the healthcare system and the patient. A relatively recent economic analysis evaluated the cost-effectiveness of a pilot DR teleophthalmology screening program by employing a decision tree model [35]. Images were captured by PCP, uploaded to a standardized system, and then graded by a retina specialist. The costs of screening 566 patients via the teleophthalmology pilot program were compared against in-person screening. Findings indicated that the screening program accurately diagnosed more patients (496 vs. 247) and was cost-saving (USD 82.4 vs. USD 237.8). In effect, teleophthalmology can differentiate patients with DR who can be screened remotely (minimal to mild DR) versus those who need comprehensive evaluations (moderate to severe DR), enabling more efficient use of specialists' time and increased access to those requiring specialty visits [36][37].

4. Patient Perceptions of Teleophthalmology

Patient recognition and acceptance of teleophthalmology as an effective tool for early screening of DR is a key factor in its success. Overall, patients generally possess a favorable perception of telemedicine, in part due to its convenience as a method for obtaining DR screening. An investigation evaluating the factors that may impact patients' attitudes toward telemedicine found that most patients viewed the service as convenient [38]. Other factors likewise influenced patient perceptions of teleophthalmology. Patients with a larger number of ocular comorbidities and those with limited access to in-person care were more likely to view teleophthalmology as a convenient alternative to traditional screening methods. Alternatively, patients who valued their patient–physician relationships or had long-standing diabetes mellitus were less receptive to the technology.

The appeal of telemedicine screening is additionally influenced by patient satisfaction with the experience. A study conducted on a remote island with indigenous populations noted that approximately 97.5% of patients (n = 90) were satisfied with the utilization of the telemedicine screening program and were receptive to future participation in telemedicine encounters [26]. While this high degree of satisfaction among these specific participants may be surprising considering their background, the findings corroborate the concept that patients lacking eye care resources and residing in a locale with a high prevalence of ocular diseases have better perceptions of the value of telemedicine screening for DR (and correspondingly, higher satisfaction).

Lastly, DR telemedicine screening has been demonstrated to be a valuable and effective tool for patient education and early detection of ocular diseases. According to a survey of patients who participated in the Toronto Teleretinal Screening Program, 71.7% of individuals who had never been screened previously revealed a lack of awareness of DR. Nonetheless, 91.6% attested to the usefulness of the screening services, further demonstrating the efficacy of telemedicine screening for detecting DR [39]. A study by Ramchandran et al. showed that 35% of participants cited the ability to detect diseases early and stay informed about their eye health as reasons for undergoing teleophthalmology exams during primary care visits [40]. The addition of these screening methods provides a sense of reassurance to patients that there are no potentially vision-threatening conditions present, as well as the opportunity for early detection of DR so that treatment can be pursued to prevent vision loss. Telemedicine screening further offers the opportunity for patients to receive personalized education from their healthcare providers about their eye health through accessible retinal images. Conversely, concerns remain, particularly among older patients, regarding the level of expertise and thoroughness of teleophthalmology exams provided by primary care providers.

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