PROSPECTIVE EVALUATION OF VISUAL ACUITY ASSESSMENT: A COMPARISON OF SNELLEN VERSUS ETDRS CHARTS IN CLINICAL PRACTICE (AN AOS THESIS)

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ABSTRACT

Purpose: The purpose of this study was twofold: first, to prospectively compare visual acuity (VA) scores obtained with Snellen charts versus Early Treatment Diabetic Retinopathy Study (ETDRS) charts in a "real world" retinal practice, and second, to see if there was a difference in visual acuity measurements obtained with ETDRS charts starting at 4 or 2 meters.

Methods: Prospective, consecutive evaluation of patients who underwent best-corrected visual acuity testing of their right eye performed at a single seating by the same experienced, certified vision examiner in the same room with standardized low light conditions using a projected Snellen chart at 20 feet, and two different back-illuminated ETDRS charts placed 4 and 2 meters from the patient.

Results: One hundred sixty-three eyes were included in the study. The mean Snellen VA was 0.67 logMAR (20/94), ETDRS VA at 4 meters was 0.54 logMAR (~20/69), and ETDRS VA at 2 meters was 0.51 logMAR (~20/65). The mean difference was 6.5 letters better on the ETDRS chart (P=.000000001). As the VA worsened, there was increased variability between the charts and the mean discrepancy between charts also increased. Subgroup analysis revealed the greatest difference between charts was in the poor vision subgroup (<20/200) with a difference of 0.2 logMAR (10 letters; P=.0000002). Patients with exudative age-related macular degeneration (AMD) had the greatest disparity on vision testing, but patients with dry AMD and diabetic retinopathy also exhibited significant differences.

Conclusions: Visual acuity scores were significantly better on ETDRS charts compared to Snellen charts. The difference was greatest with poor visual acuity (<20/200) and in patients with exudative AMD. Thus, caution should be exercised when comparing data using the different charts.

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INTRODUCTION

The most common measurement of visual function is visual acuity because the test is easily administered with simple equipment. Visual acuity is defined as the "spatial resolving capacity" of the eye or, put another way, the size of an object that can be resolved with an eye. It can be measured by identifying the angle subtended at the eye by the smallest recognizable optotype. Theoretically, this represents macular function, but really it represents the state of the entire ocular system, including the visual pathways. In practice, measurement of visual acuity is performed using specialized eye charts. These charts usually consist of uppercase letters arranged in rows with the largest letters at the top of the chart and progressively smaller letters down the chart.

Visual acuity testing is the "gold standard" for primary outcomes of clinical trials. In fact, the US Food and Drug Administration (FDA) will only accept vision or a surrogate that correlates with vision for a registration trial. Thus, standardization of visual acuity testing in clinical trials is paramount. Ideally, visual acuity testing should give a precise, reproducible result without influence from external factors, thereby identifying only changes related to disease or treatment. Unfortunately, visual acuity testing is influenced by numerous factors, including lighting in the testing room and the design of the test chart. There are numerous charts used for visual acuity testing, but the most common charts in the United States are the Snellen and ETDRS charts.

First introduced by Dutch ophthalmologist Dr Hermann Snellen in 1862, the Snellen chart is the current standard for measurement of visual acuity in clinical practice because it is readily available as well as quick and easy to perform. The chart has letters of different sizes arranged from largest at the top to smallest at the bottom, which are read, one eye at a time, at a distance of 6 meters (20 feet). Each letter on the chart subtends an angle of 5 minutes (min) of arc at the appropriate testing distance, and each letter part subtends an angle of 1 min of arc. Thus, it is designed to measure acuity in angular terms. In a healthy adult, the resolution limit is between 30 seconds and 1 min of arc. The scoring method used is the line assignment method, where a patient gets credit for lines, not letters, read. Accepted convention does not specify Snellen acuity in angular terms; instead, Snellen acuities are usually expressed as a fraction with the numerator equal to the distance from the chart and the denominator being the size of the smallest line that can be read. The reciprocal of the fraction equals the angle, in min of arc, that the stroke of the letter subtends on the patient's eye and is called the minimum angle of resolution (MAR). In some countries, visual acuity is expressed using a different notation. In the United Kingdom, a visual acuity of 20/20 (eg, the letter subtends an angle of 5 min of arc when viewed at 20 feet) is recorded as 6/6, as the reference distance is 6 meters, instead of 20 feet. In Japan and many European counties, visual acuity is expressed as a decimal that is equal to the numeric value of the Snellen fraction or the reciprocal of the visual angle in minutes, so 20/20 would become 1.0 and 20/40 would be 0.5 (Table 1).

There are numerous disadvantages of Snellen charts.[1] First, each line has a variable letter size and there are variable letters per line. For instance, the poor vision lines (20/200 and 20/400) usually contain only 1 or 2 letters, while the good acuity lines contain up to 8 letters. It is unclear why this design feature was chosen, outside the fact that it allowed the designer to have rows of letters of similar length. Second, when testing Snellen acuity, the tester uses a line assignment method. Thus, missing 1 letter on the good acuity lines has less effect than missing 1 letter on the poor vision lines. Put another way, using the line assignment method with variable letters per line, a change in acuity of 1 letter can result in change of vision of an entire line, and this occurs more frequently with the poorer vision lines. The line assignment method also prevents measurement of visual acuity on a fine scale. Because of this lack of

From The Cleveland Clinic Cole Eye Institute, Cleveland, Ohio.

standardized progression between lines, Snellen visual acuity is difficult to assess statistically. Parametric analysis cannot be performed with this decimal progression sequence, even if converted to another form. Third, there is an irregular and arbitrary progression of letter sizes between lines. This introduces considerable error when changing the viewing distance of the chart and leads to overestimation of vision at the lower end of acuities. Moreover, a loss or gain in a line of vision does not have the same meaning in different parts of the chart. Fourth, the letters on a Snellen chart are not always the same legibility. Some letters (eg, C, D, E, G, O) are easier to read than others (eg, A, J, L).[1-3] Fifth, the distance between letters and rows is not standardized. Studies have shown that when letters are spaced too closely, there is an effect from the adjacent contours called a crowding phenomenon, that diminishes acuity.[4] Contour interactions vary throughout the Snellen chart. For example, the poor vision lines have minimal crowding, whereas the good acuity lines have greater crowding. Except for the size of the letters, the testing of any given line should present an essentially equivalent task to the patient; however, having different numbers of letters and different spacing prevents this from occurring. Thus, patients with poor central vision who can read single letters more easily than a row of letters may not be able to read a line because of this phenomenon, and not because of an inability to see the letters. Finally, the term "Snellen chart" has never been standardized, so the criteria to label a chart design as "Snellen" are not defined. Snellen charts from different manufacturers may use different fonts, different letters, and different spacing ratios, and they may be illuminated or projected differently.[5] When projected, mirrors can be used to simulate the 20-foot optical testing distance. This is useful in clinical lanes shorter than 20 feet.

TABLE 1. CONVERSION OF SNELLEN ACUITY INTO LOGMAR, DECIMAL, AND METRIC UNITS

logMAR	SNELLEN	DECIMAL	SNELLEN (METRIC)
1.5	20/640	0.03	6/192
1.4	20/500	0.04	6/152
1.3	20/400	0.05	6/120
1.2	20/320	0.063	6/96
1.1	20/250	0.08	6/76
1.0	20/200	0.10	6/60
0.9	20/160	0.125	6/48
0.8	20/125	0.16	6/38
0.7	20/100	0.20	6/30
0.6	20/80	0.25	6/24
0.5	20/63	0.32	6/20
0.4	20/50	0.40	6/15
0.3	20/40	0.50	6/12
0.2	20/32	0.63	6/10
0.1	20/25	0.80	6/7.5
0.0	20/20	1.00	6/6
-0.1	20/16	1.25	6/5
-0.2	20/12.5	1.60	6/3.75
-0.3	20/10	2.00	6/3

logMAR, logarithm of the minimum angle of resolution.

Theoretically, if visual acuity is tested multiple times on a particular chart, the expected difference should be zero. However, in reality, even in the absence of any clinical change, there is a distribution of scores that reflects the underlying variability in the chart measurement. This is called test-retest variability (TRV). The ability to detect true change in vision decreases as the TRV increases. Owing to the deficiencies of the Snellen chart, its TRV between visits is very large, varying from ±5 to 16.5 letters in normal subjects, and up to 3.3 lines in cataractous, pseudophakic, or early stage glaucoma patients.[6,7] Thus, a person can have up to a 3.5-line change in vision and this may not even represent true change, but chance. Others have shown that up to 13% of patients can display a 2-line discrepancy in vision on repeated testing with a Snellen chart.[8,9] In clinical practice, this may be acceptable; however, in clinical research it is not. The visual outcomes after an intervention should ideally be independent of the chart used. With a Snellen chart this may not be the case.

To overcome the deficiencies of the Snellen chart, several suggestions have been made to improve chart design and measure visual acuity more accurately. The most popular redesign was first proposed by Drs Ian Bailey and Jan Lovie in 1976.[1] The Bailey-Lovie chart had the following design features: (1) The letters had almost equal legibility. While not the ideal legibility as the "Landolt C" or

"illiterate E" letters, the letters on the Bailey-Lovie chart did have a height equal to 5 stroke widths and were without serif. This ensured that letter size was the sole determinant of difficulty on a given line. (2) Each row had 5 "Sloan" letters, and there were 14 rows of letters (70 letters). The Sloan letters were proposed by Dr Sloan in 1952 and are composed of 10 non-serifed, uppercase letters formed within a square outline, with a stroke width of one-fifth the letter height (C, D, H, K, N, O, R, S, V, Z), and with equal legibility.[10] (3) There was consistent spacing between letters and rows, proportional to letter size. The between-letter spacing was 1 letter-width and the between-row spacing was equal to the height of the letters in the smaller row. This controlled the crowding phenomenon seen with the Snellen chart. (4) There were equal (0.1) logarithmic intervals (a ratio of 1.26×) in the progression of letter sizes between lines. Thus, the letters double in size every 3 lines, and a 3-line worsening of vision is the same regardless of initial vision. (5) There was a geometric progression of the chart difficulty based on the distance from the patient. The chart was designed to be read at a standard 6 meters with visual acuities that could be measured at this distance equal to 6/60 to 6/3 (Snellen equivalent of 20/200 to 20/10). If the chart was moved closer to the patient by a 0.1 log step (6 to 4.8 meters or 4.8 to 3.8 meters), then there was a 25% increase in angular size of the letters and the patient should be able to read 1 additional row on the chart. Thus, one could precisely vary the size of the letters based on testing distance allowing the testing distance to be varied as desired. The Bailey-Lovie chart was also easily scored in logMAR (logarithm of the minimal angle of resolution) units. By scoring in this method, one knew the exact size of the letters on the chart. This also made adjusting visual acuity scores based on non-standardized viewing distances easier. Finally, these design features offered another advantage for clinical trials in that it could be scored by letter, not line. By using single-letter, forced-choice testing, this chart showed consistent TRV with different days, examiners, and clinical sites.[5,11,12]

The Bailey-Lovie chart was further modified in 1982 based on the recommendations of the Committee on Vision of the National Academy of Sciences, National Research Council, and Working Group 39, and by Dr Rick Ferris for use in the Early Treatment Diabetic Retinopathy Study (ETDRS).[13-15] This "ETDRS chart" and the protocol to test vision with this chart have become the "gold standard" for most current clinical trials. ETDRS charts were theoretically superior to Snellen charts because interpatient differences were more accurately measured and longitudinal follow-up measurements had more consistent precision, regardless of whether the patients had high or low levels of visual acuity.[16] The TRV of the ETDRS charts were considerably better than Snellen charts, varying from ±3.5 to 10 letters, depending on whether the patients had normal acuity or ocular pathology such as age-related macular degeneration (AMD).[17-21]

For statistical analysis, acuity scores from both charts can be converted into logMAR notation that is the logarithm to the base 10 of the angular subtense of the stroke widths at 6 meters. Some investigators have mistakenly called the Bailey-Lovie principles and ETDRS charts "logMAR charts." It is important to note that logMAR is not a type of chart, but a term that refers to a geometric notation used to express visual acuity. MAR is the width of one bar on a Snellen E. In logMAR notation, lower scores correspond to better vision, and as acuity becomes worse, the value of the logMAR increases. For every line of logMAR change there is 0.1 Δ, and for each letter there is 0.02 Δ. In Snellen notation, 20/20 vision corresponds to logMAR = 0 and the MAR is equal to 1.0 arc minute. The MAR, in arc minutes, is equal to the inverse of the Snellen fraction. As acuity improves better than 20/20, the logMAR score will have an increasing negative sign value. However, although the Snellen and ETDRS charts can be "compared" with logMAR mathematical conversions, this is misleading because the two charts measure different things.

Despite ETDRS charts being shown to be more accurate, currently most reports published in major ophthalmology journals use Snellen charts to measure visual acuity.[22] The main reason for this is that clinical testing with ETDRS charts is felt to take longer, require specialized lanes, and be more difficult to administer than testing with Snellen charts, so widespread adoption of ETDRS charts has not occurred.[23] In contrast, FDA registration trials require ETDRS charts for visual outcomes. This makes it difficult to correlate "real world" vision and these smaller clinical trials with findings from phase III clinical trials. For example, the Verteporfin in Photodynamic Therapy (VIP) Study recommended treatment with ocular photodynamic therapy in patients with "occult with no classic" choroidal neovascularization with lesion sizes greater than 4 disc areas only when ETDRS protocol vision was worse than "20/50."[24] Since some investigators have suggested that patients can have better visual acuity scores on ETDRS charts compared to Snellen charts, what visual acuity should we use as a cutoff to perform photodynamic therapy in these patients when we use Snellen charts in our clinical practice?[23] Similarly, treatment for branch vein occlusions based on the Branch Vein Occlusion Study (BVOS) should proceed only when the ETDRS protocol vision is worse than "20/50."[25] Again, what Snellen visual acuity should we use as a cutoff to decide when laser should be applied? Conversely, it is a frequent occurrence nowadays when screening patients for a clinical trial for their visual acuity to "improve" from their Snellen acuity when tested on the ETDRS chart to the point where the patient is not eligible for the clinical trial. As clinicians, we simply need to understand how visual acuity scores correlate when measured on Snellen vs ETDRS charts.

Another aspect of visual acuity testing that concerns clinical researchers in the United States is that the FDA now requires all visual acuity testing with ETDRS charts to begin at 4 meters, instead of 2 meters. For patients in a study where most have good visual acuity, this is a reasonable starting distance, as patients can readily see the chart at 4 meters; however, in studies where most patients have poor visual acuity (eg, a phase I AMD study), this requirement adds considerable time to the visual acuity testing, as the chart has to be tested first at 4 meters, then moved forward to 2 meters if none of the letters can be read. It is unclear if there is a difference in visual acuity scores between ETDRS charts starting at 4 vs 2 meters to justify the difference in time and money for patients and study sponsors in a clinical trial. Thus, the purpose of this study was twofold. First, we wanted to prospectively compare visual acuity scores obtained with Snellen charts vs ETDRS charts in a "real world" retinal practice. Second, we wanted to see if there was a difference in visual acuity measurements obtained with ETDRS charts starting at 4 or 2 meters.

PATIENTS AND METHODS

After Institutional Review Board approval was obtained, a prospective, consecutive, case series was performed between October 2003 and February 2004 of patients who met the following inclusion criteria: ability to give informed consent, visual acuity better than counting fingers in their study eye, ability to read English letters, ability to understand and comply with the vision testing protocols, not enrolled in any current clinical trial, and willing to give written informed consent. Patients with visual acuity in their right eye of counting fingers or worse, or who could not complete the visual testing, were excluded from the study. Because the study was performed before registration of clinical trials was routinely required, it was not registered on www.clinicaltrials.gov. Patients were not screened for ocular pathology before entry into the study. The vision of the right eye of each patient was assessed.

VISUAL ACUITY TESTING

The visual acuity testing was performed at a single seating by the same experienced, certified vision examiner in the same room with standardized low light conditions (approximately 10 cd/m^2). Since daily clinical testing in a retina practice does not usually include standardized visual acuity testing, to reduce variability of these measurements only one experienced, certified visual examiner was used throughout the study. The vision examiner was certified in the ETDRS protocol for multiple, phase III clinical trials, including the Treatment of Age-Related Macular Degeneration With Photodynamic Therapy (TAP) Study, Submacular Surgery Trials (SST), and the VIP Study, and has taught vision examination courses to other vision examiners for their individual study certification requirements. Breaks during the testing were allowed as needed. Patients were seated comfortably with the charts placed at eye level and were told not to lean forward. Testing proceeded slowly at the pace set by the patient.

Before visual acuity testing, the certified vision examiner performed a manifest refraction of the right eye (study eye for all patients), with the left eye covered, using the ETDRS Chart R (catalog No. 2123; Precision Vision, La Salle, Illinois); a description of chart lighting follows. Once the best-corrected manifest refraction was completed, visual acuity testing on the study eye was carried out, one test immediately after the other, with the chart and testing method used first, alternating between patients (eg, one patient started with Snellen testing, the next started with ETDRS chart testing). Visual acuity was tested with the patients' pupils in their natural state.

Snellen Chart Testing

Using the best correction in a trial frame, the Snellen chart was presented with a projector (Nikon Chart Projector NP-3S; Nikon Inc, Melville, New York) with a new halogen bulb (6 volt, 20 watt, 480 lumens; Osram-Sylvania Inc, Danvers, Massachusetts) inserted before the study was initiated. A distance of 20 feet was used for testing, and the size of the projected letters was compared to the Nikon test scale sheet before initiating the study to ensure correct focus and magnification of the projector. The vision testing started with the top of the chart and continued until a line was reached where more than half the letters (eg, 2 of 4, 3 of 5) were read incorrectly or the patient read all letters on the chart. The actual projections consisted of 5 charts: (1) 20/400 line; (2) 20/200 line; (3) 20/100, 20/80, and 20/70 lines; (4) 20/60, 20/50, and 20/40 lines; (5) 20/30, 20/25, and 20/20 lines (Figure 1).

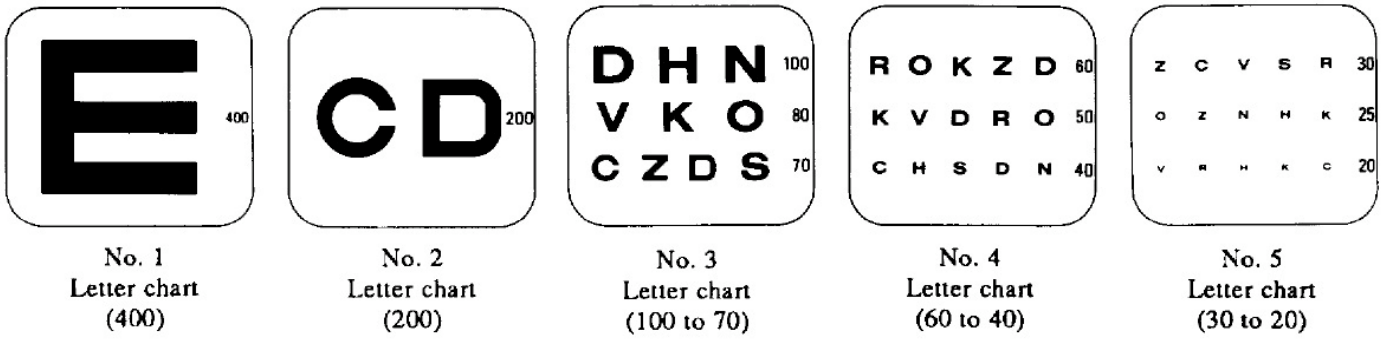

FIGURE 1

Snellen projection charts used by the Nikon Chart Projector NP-3S.

Only the Snellen chart projections were used, and the additional features of the projector, including "illiterate E" charts (charts 10, 11, and 12), vertical masking, horizontal line masking, and single letter isolation, were not used. The luminance of the projected chart was measured by a digital light meter (Sper Scientific, Scottsdale, Arizona) and found to be 71 cd/m^2. Patients were encouraged to guess if they were not sure of the letter. If patients could not see the top letter of the chart (20/400), they were presented with a single printed letter "E" (20/200) on a card held precisely 10 feet from their head, which was progressively moved forward at 1-foot intervals until the patient could correctly identify the direction of the letter. Patients were allowed only a single reading of the chart. The visual acuity was scored using line assignment scoring, with the value of the lowest line, where at least half the letters (eg, 2 of 4, 3 of 5) were correctly identified scored as the patient's visual acuity plus/minus any additional letters seen/not seen on next/previous line (eg, if all letters on the 20/30 line and 2 letters were seen on the 20/25 line, the vision was scored as 20/30^{+2}).

ETDRS Chart Testing

Using the best correction in a trial frame, ETDRS chart 1 (catalog No. 2121; Precision Vision, La Salle, Illinois) was placed 4 meters from the patient (Figure 2) in a back-illuminated stand. The ETDRS chart was printed with high-contrast lettering on a translucent white polystyrene panel lit from behind and displayed in a standard light box. The light box was illuminated by two fluorescent lamps with a reusable fenestrated sleeve (diffuser) that produced a chart luminance, measured by a digital light meter of 168 cd/m^2, which is in compliance with recommendations of the ETDRS protocol (80 to 320 cd/m^2).[1] The chart had 5 letters per line arranged in 0.1 logMAR steps as specified in the ETDRS protocol. If a patient could not read the largest letters at 4 meters, then the chart was moved 50% closer to the patient (4 meters to 2 meters, or 2 meters to 1 meter). By precisely varying the distances the charts moved, the relative difficulty of the task was increased exponentially. The vision testing started with the first letter on the top row of the chart. The testing continued using a forced-choice paradigm from the top of the chart to the bottom until the patient made a complete line of errors, read all letters on the chart, or could not read any letters of the chart when placed 1 meter away from the patient. Patients were allowed only a single reading of the chart. The patients' responses were tabulated on a scoring sheet with correctly identified letters circled on the sheet. Failure to read any letters was assigned 1.7 logMAR (Snellen equivalent 20/1000). Patients were required to identify each letter and were encouraged to guess if not sure, as per the ETDRS protocol. The examiner pointed to each new line. The ETDRS chart was scored using a single letter scoring method with credit given for any letter correctly identified. Visual acuity testing was repeated with ETDRS Chart 2 (catalog No. 2122; Precision Vision, La Salle, Illinois) placed 2 meters from patient using the same termination rules and scoring procedures as the ETDRS chart starting at 4 meters (Figure 2).

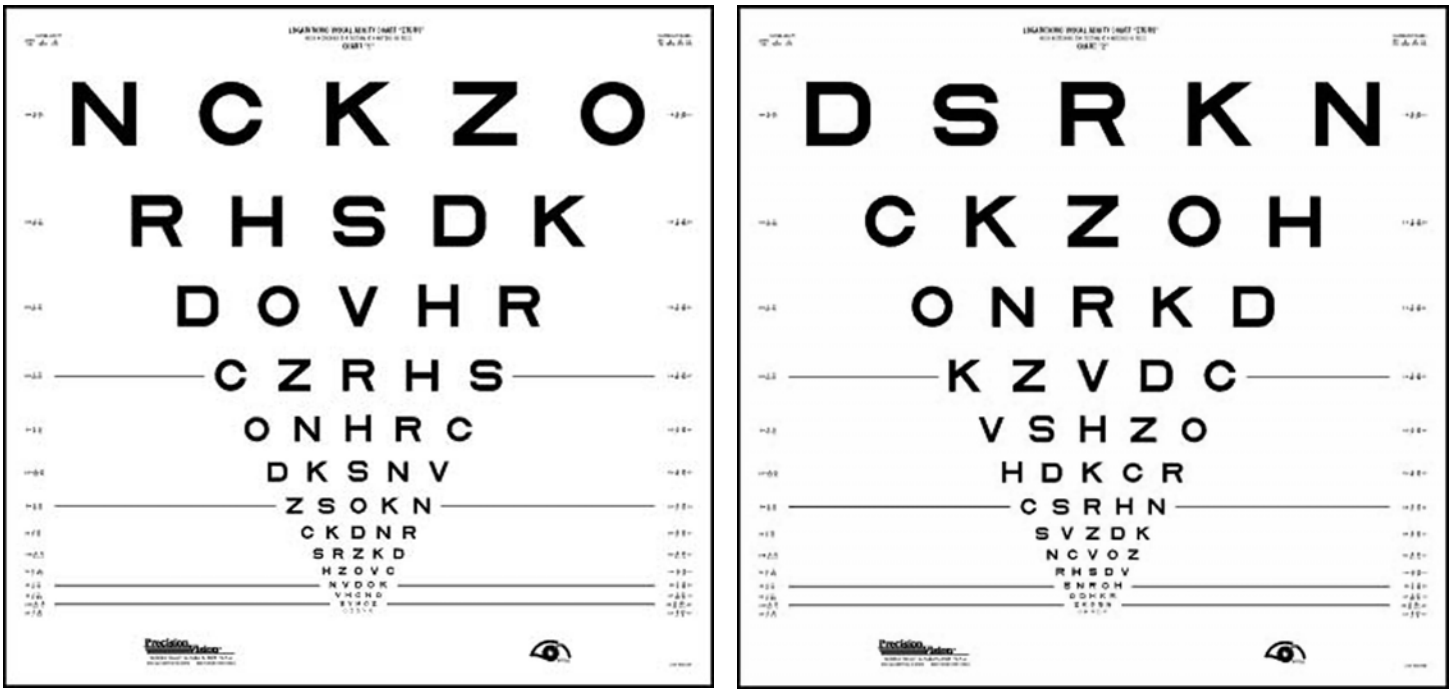

FIGURE 2

Early Treatment Diabetic Retinopathy Study (ETDRS) chart 1 (left) and chart 2 (right) from Precision Vision.

STATISTICAL ANALYSIS

The Snellen fraction was converted to logMAR for statistical analysis without taking into account the differences in number of letters per line. This was done by taking the log to the base 10 of the reciprocal of the Snellen fraction. The score was further modified by adding/subtracting 0.02 logMAR to converted values for letters correctly/incorrectly identified on previous/next line (eg, 20/30 = +0.18 logMAR and 20/30^{-2} = +0.22 logMAR). The ETDRS chart visions were scored using the interpolated method described by Ferris and colleagues[14] such that 0.02 logMAR units were given for each letter correctly identified on the entire chart. Refractions were converted to spherical equivalents. Data summaries were based on mean, median, standard deviation, and range for continuous measurements, and the frequency and percent for categorical variables. Statistical comparisons for univariate analysis were based on paired *t* tests. Other univariate analysis used the Pearson linear correlation method. Wilcoxon rank sum test was used when nonparametric values were analyzed and the normality assumption not met. Bland-Altman analyses were performed to contrast the variability between the two charts.[5] Analysis of covariance (ANCOVA) was used to identify the magnitude and significance of covariates (eg, age, sex, refraction, diagnosis) on the differences between the two charts. Except for situations involving multiple comparisons, statistical significance was assumed at the $P < .05$ level. Bonferroni adjustments were used when multiple comparisons were made. Statistical analysis was performed using Stata SE (Version 10.0; StataCorp, College Station, Texas).

RESULTS

One hundred sixty-three eyes of 163 patients were included in the study and completed visual acuity testing with both charts. There were 43 men and 120 women ranging in age from 18 to 93 years with a mean age of 65.6 ± 18.9 years. The age distribution for all patients is shown in Figure 3. The spherical components of refractive error ranged from +3.50 D to -6.50 D with astigmatism up to -2.00 D.

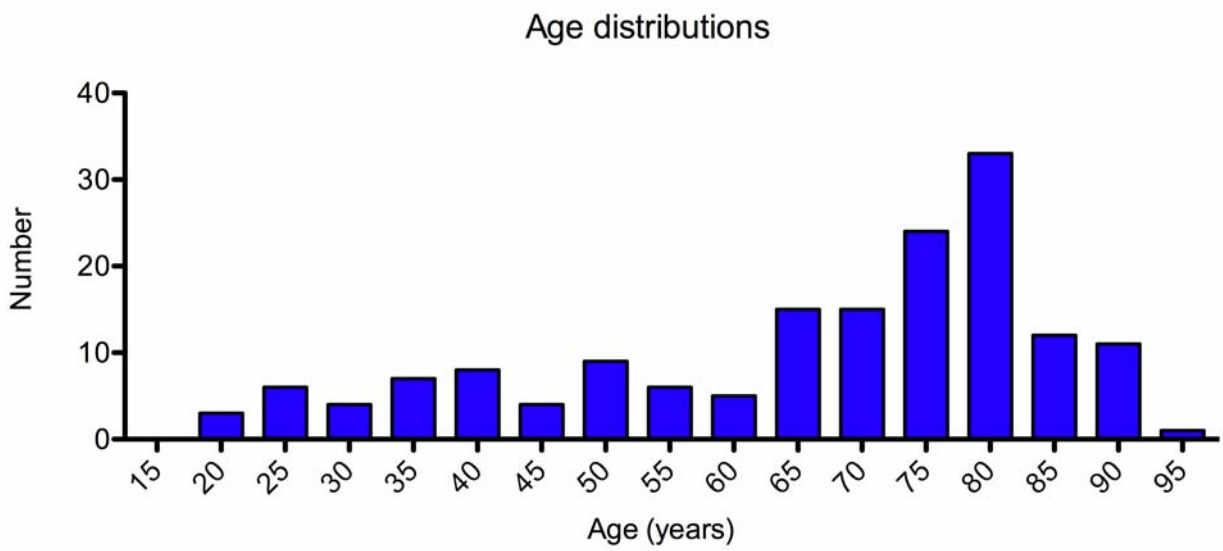

FIGURE 3

Frequency distribution of ages for all patients in the clinical study.

The visual acuity scores for all patients are listed in Table 2. The mean Snellen visual acuity was 0.67 ± 0.52 logMAR (range, 0 to 2.3; 20/94), ETDRS at 4 meters was 0.54 ± 0.48 logMAR (range, 0 to 1.7; Snellen equivalent of 20/69), and ETDRS at 2 meters was 0.51 ± 0.47 logMAR (range, 0 to 1.7; Snellen equivalent of 20/65). The distribution of visual acuity scores for all patients is shown in Figure 4. The average difference between Snellen and ETDRS charts for all tested eyes was 0.13 ± 0.18 logMAR or 6.5 letters better on the ETDRS chart at 4 meters (P = .000000001) and 0.16 ± 0.18 logMAR or 8 letters better on the ETDRS chart at 2 meters (P = .000000001). The relationship between measurements of visual acuity score on ETDRS charts starting at 4 meters vs 2 meters (Figure 5) was very strong (R^2 = 0.9909), and the regression slope was significantly different from 1.0 (P < .00001) due to the differences seen in eyes with poor acuity. However, since only the ETDRS vision starting at 4 meters is accepted by the FDA, all additional analysis was performed only on the ETDRS chart at the 4 meters testing distance.

TABLE 2. COMPARISON OF LOGMAR VISUAL ACUITY SCORES FOR SNELLEN AND ETDRS CHARTS

GROUP*	N	AGE (yr)	SNELLEN†	ETDRS†	DIFFERENCE‡	*P* VALUE
All eyes	163	65.6±18.9	0.67±0.52 (0 to 2.3)	0.54±0.48 (0 to 1.7)	0.13±0.18	.000000001
Good VA	69	64.8±19.9	0.20±0.13 (0 to 0.40)	0.12±0.11 (0 to 0.54)	0.08±0.10	.000000001
Intermediate VA	38	52.0±19.1	0.59±0.09 (0.46 to 0.74)	0.49±0.13 (0.14 to 0.7)	0.10±0.15	.00026
Poor VA	56	75.4±10.1	1.29±0.31 (0.96 to 2.3)	1.10±0.33 (0.42 to 1.7)	0.20±0.25	.0000002

ETDRS, Early Treatment Diabetic Retinopathy Study; logMAR, logarithm of the minimum angle of resolution; N, number of eyes; VA, visual acuity.
*Good VA is 20/20 to 20/50; intermediate VA is <20/50 to 20/200; poor VA is <20/200.
†Mean ± standard deviation (range).
‡Difference = Snellen - ETDRS in logMAR.

A Bland-Altman analysis evaluating differences between visual acuity scores between the Snellen and ETDRS chart starting at 4 meters (Figure 6) plotted against their mean indicated that as the visual acuity worsened, there was a larger variability between the two charts. In eyes with better visual acuity, the difference was not as disparate. The mean difference was -0.13 logMAR (95% CI, -0.4742 to 0.2229). This was further analyzed by looking at the mean difference between Snellen and ETDRS charts for various average vision score samples in the same eye (Table 3). As average acuity worsened on the Snellen chart, the average discrepancy between the charts

in general also increased. This was especially true for eyes with visual acuity that could not be accurately measured on the Snellen chart (<20/400), where on average there was a difference of over 4 lines between the charts. Figure 7 shows the relationship between visual acuity scores measured on the two charts for all study eyes. A significant correlation was observed (R^2 = 0.8839). The regression slope was significantly different from 1.0 (P < .00001).

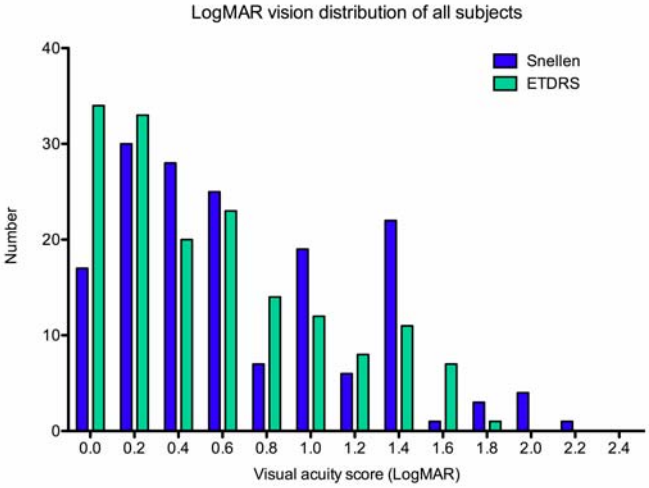

FIGURE 4

Frequency distribution of logarithm of the minimum angle of resolution (logMAR) vision scores for all patients in the clinical study.

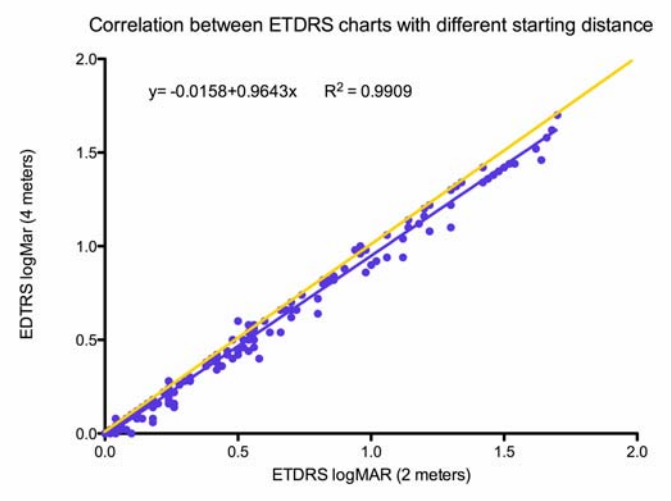

FIGURE 5

Correlation between logarithm of the minimum angle of resolution (logMAR) visual acuity scores on Early Treatment Diabetic Retinopathy Study (ETDRS) charts starting testing at either 4 meters or 2 meters from the patient. The x-axis and y-axis are the logMAR visual acuity scores. The yellow line represents the equivalence line, and the blue line represents the regression line.

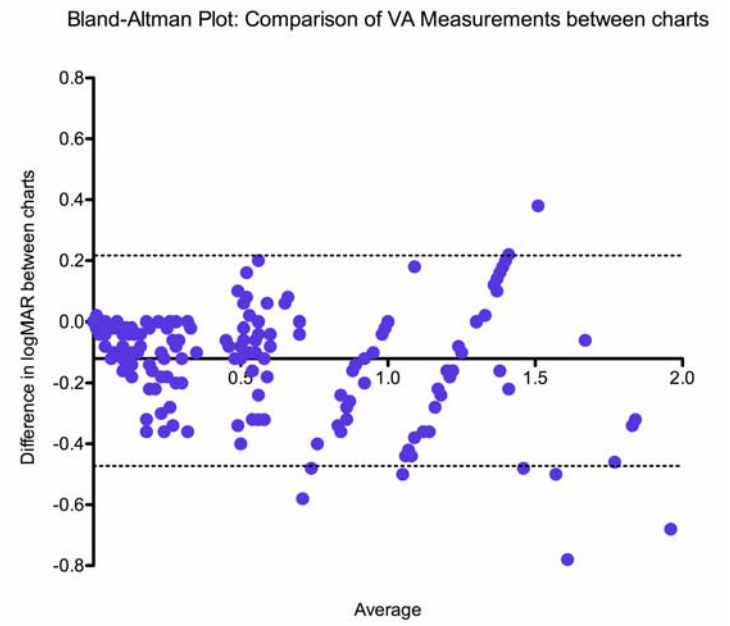

FIGURE 6

Bland-Altman plot of the differences in logarithm of the minimum angle of resolution (logMAR) visual acuity scores between Snellen and Early Treatment Diabetic Retinopathy Study (ETDRS) charts. The y-axis displays the difference between measurements on both charts, and the x-axis displays the mean vision score value between the charts. All values represent the logMAR visual acuity scores. The solid line is the mean difference in logMAR acuity (-0.13), and the area within the dotted lines equals 95% limits of agreement between logMAR vision between the two charts. All points below the solid line reflect Snellen scores worse than ETDRS scores in the same eye.

TABLE 3. AVERAGE DISCREPANCY BETWEEN LOGMAR VISUAL ACUITY SCORES FOR SNELLEN AND ETDRS CHARTS

N	MEAN SNELLEN VA	MEAN SNELLEN VA (logMAR)	MEAN CORRESPONDING ETDRS VA (logMAR)	MEAN DISCREPANCY (logMAR)	MEAN DISCREPANCY (LETTERS)*
10	<20/400	1.85	1.44	0.41	20.5
27	20/400	1.3	1.19	0.11	5.5
19	20/200	1	0.79	0.2	10
10	20/100	0.7	0.45	0.25	12.5
11	20/80	0.6	0.54	0.06	3
8	20/70	0.54	0.47	0.07	3.5
9	20/60	0.48	0.47	0.01	0.5
8	20/50	0.4	0.22	0.18	9
21	20/40	0.3	0.19	0.11	5.5
16	20/30	0.18	0.11	0.07	3.5
24	≤20/25	0.06	0.03	0.03	1.5

ETDRS, Early Treatment Diabetic Retinopathy Study; logMAR, logarithm of the minimum angle of resolution; N, number of eyes, VA, visual acuity.
*Letters on an ETDRS chart.

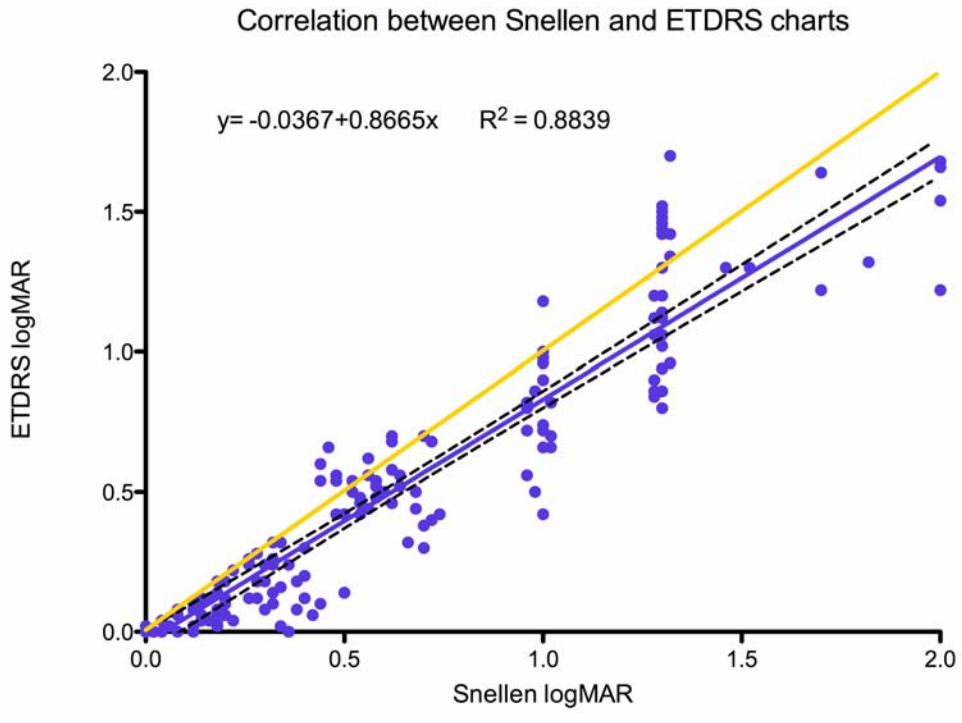

FIGURE 7

Correlation between visual acuity scores measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) and Snellen charts. The x-axis and y-axis are the logarithm of the minimum angle of resolution (logMAR) visual acuity scores. The yellow line represents the equivalence line, and the blue line represents the regression line. The dotted lines represent the 95% confidence intervals of the regression line.

VISION SUBGROUPS

Since it has been suggested that patients with worse visual acuity may have greater visual acuity differences when measured on Snellen vs ETDRS charts, the patients were retrospectively split into subgroups based on their Snellen vision score: good vision (20/20 to 20/50), intermediate vision (<20/50 to 20/200), and poor vision (<20/200) (Table 1). The good vision subgroup (20/20 to 20/50) contained 69 eyes of 69 patients with a mean age of 64.8 ± 19.9 years. The mean visual acuity score with the Snellen chart was 0.20 ± 0.13 logMAR (20/32) and 0.12 ± 0.11 logMAR (Snellen equivalent 20/26) on the ETDRS chart starting at 4 meters. Visual acuity was significantly better on the ETDRS chart with a mean difference of 0.08 logMAR or 4 letters (P = .000000001). The intermediate vision subgroup (<20/50 to 20/200) contained 38 eyes of 38 patients with a mean age of 52.0 ± 19.1 years. The mean visual acuity score with the Snellen chart was 0.59 ± 0.09 logMAR (20/78) and 0.49 ± 0.13 logMAR (Snellen equivalent 20/62) on the ETDRS chart starting at 4 meters. Visual acuity was again significantly better on the ETDRS chart with a mean difference of 0.10 logMAR or 1 line (5 letters, P = .00026). The greatest difference between charts was seen in the poor vision subgroup (<20/200) that contained 56 eyes of 56 patients with a mean age of 75.4 ± 10.1 years. The mean visual acuity score with the Snellen chart was 1.29 ± 0.31 logMAR (20/390) and 1.10 ± 0.33 logMAR (Snellen equivalent 20/252) on the ETDRS chart starting at 4 meters. Visual acuity was significantly better on the ETDRS chart with a difference of 0.2 logMAR or 2 lines (10 letters; P = .0000002).

DIAGNOSIS SUBGROUPS

Patients with different diagnoses were included in this study (Table 4). The most common diagnosis was exudative AMD, seen in 68 eyes (42%), followed by diabetic retinopathy (53 eyes), nonexudative AMD (31 eyes), posterior vitreous separation (5 eyes), cataract with no retinal pathology (3 eyes), and epiretinal membrane (3 eyes). The difference in visual acuity scores based on diagnosis is shown in Table 5. Except for the "Other" subgroup, visual acuity scores for all the other diagnoses were significantly better on the ETDRS charts. The greatest mean difference was seen in patients with exudative AMD, with an 8.5-letter difference between charts (P = .00000007).

TABLE 4. DIAGNOSES OF PATIENTS INCLUDED IN THE STUDY

DIAGNOSIS	N
Nonexudative AMD	31
Exudative AMD	68
Diabetic retinopathy	53
Other	11
Epiretinal membrane	3
Posterior vitreous detachment	5
Cataracts	3

AMD, age-related macular degeneration.

TABLE 5. COMPARISON OF LOGMAR VISUAL ACUITY SCORES FOR SNELLEN AND ETDRS CHARTS BASED ON UNDERLYING DIAGNOSIS

N	DIAGNOSIS	SNELLEN VA*	ETDRS VA*	DIFFERENCE†	LETTERS‡	*P* VALUE
31	Nonexudative AMD	0.27±0.15 (0 to 0.56)	0.14±0.12 (0 to 0.56)	0.13±0.11	6.5	.00000008
68	Exudative AMD	1.14±0.43 (0.18 to 2.3)	0.96±0.41 (0 to 1.7)	0.17±0.24	8.5	.00000007
53	Diabetic retinopathy	0.39±0.28 (0.04 to 1.3)	0.3±0.27 (0 to 1.18)	0.08±0.12	4	.0000085
11	Other	0.19±0.14 (0 to 0.32)	0.17±0.13 (0 to 0.32)	0.02±0.02	1	.069

AMD, age-related macular degeneration; ETDRS, Early Treatment Diabetic Retinopathy Study; logMAR, logarithm of the minimum angle of resolution; VA, visual acuity.
*Mean ± standard deviation (range).
†Difference = Snellen - ETDRS in logMAR.
‡Letters on an ETDRS chart.

The relationship between visual acuity and age is shown in Figure 8. As patient age increased, the visual acuity scores worsened on both charts. To evaluate the effects of age, gender, and refraction on the differences seen between the charts, a multivariate ANCOVA was performed, which showed that none of the differences were due to these factors.

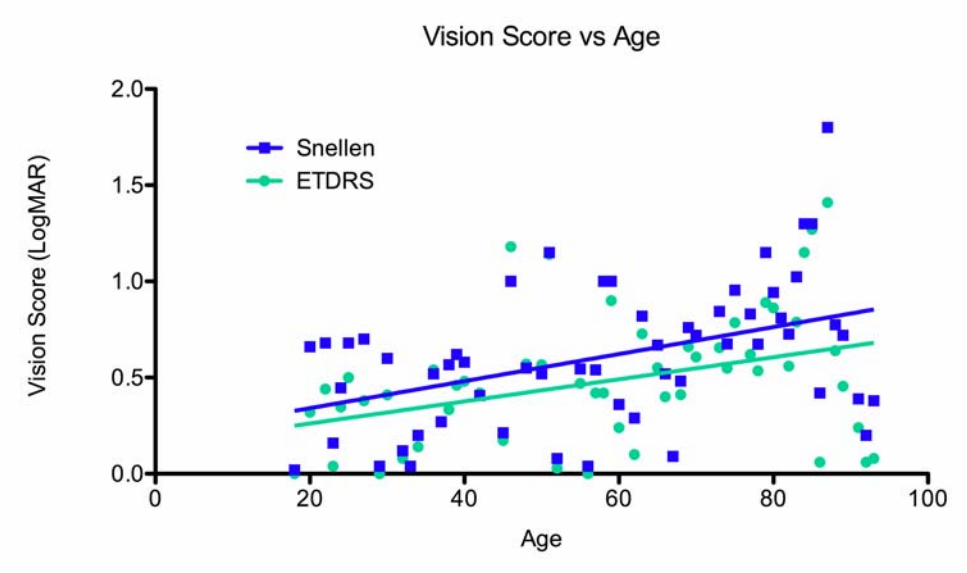

FIGURE 8

Logarithm of the minimum angle of resolution (logMAR) visual acuity scores by age for Snellen and Early Treatment Diabetic Retinopathy Study (ETDRS) charts. The lines represent the regression line for Snellen and ETDRS charts.

DISCUSSION

Vision is one of our most important senses. The measurement of vision is the primary outcome of most clinical trials and all FDA registration trials, and plays a vital role in our ability to perform daily tasks such as driving. Yet, for all its importance, our measurement of visual acuity is relatively crude. This is important since visual acuity is used to measure both disease and change. Not infrequently, we proudly announce to patients that their vision has improved by 1 or 2 Snellen lines, but what does that mean and is this change clinically relevant? Is this difference even real or simply variability inherent to the testing method? Visual acuity is essential for clinical trials to measure treatment response. Accurately ascertaining vision is influenced by several factors, including light intensity; number, size, contrast, and shape of the optotypes; and the design of the test chart. The choice of chart ideally should not influence the outcome of the vision measurement. The Snellen chart has historically been the most popular visual acuity testing measure, but it has considerable flaws. To reduce the variability and enhance the precision of vision testing, newer charts have been proposed. The ETDRS chart based on the Bailey-Lovie chart and tested using the ETDRS protocol, which added a standardized administration and scoring of vision, is the current "gold standard" for vision testing in clinical trials.

This is one of the first studies to directly evaluate the difference in visual acuity between the Snellen and ETDRS charts in a "real world" retina practice with a variety of retinal pathologies using the established testing protocols for each chart. Overall, the ETDRS chart yielded significantly better visual acuity scores than the Snellen chart ($P = .000000001$). The mean difference was 6.5 letters or 1.3 lines. The regression analysis revealed a significant correlation between the visual acuity scores on the 2 charts ($R^2 = 0.8839$) with a slope significantly different from 1 ($P < .0001$). A similar finding was reported by Falkenstein and colleagues,[17] who noted that on average the difference between the charts was 2.5 lines. However, there were several important differences between our study and theirs.

First, Falkenstein and colleagues evaluated only older patients with AMD, whereas this study evaluated patients of all ages with the most common retinal pathologies, including AMD, diabetic retinopathy, and macular pathology such as epiretinal membranes. In the nonexudative AMD subgroup there was a 6.5 letter difference, and in the exudative AMD subgroup, the mean difference was slightly greater, at 8.5 letters or 1.7 lines. Falkenstein and colleagues did not analyze their data based on level of AMD.

Second, Falkenstein and colleagues used different termination rules than this study. Different termination rules can affect the variance between visual acuity measures.[22] In this study, the termination rules for the ETDRS charts were based on a forced-choice paradigm where testing continued until the patient made a complete line of errors, or read all the letters on the chart. In contrast, Falkenstein and colleagues terminated the test when the patient made >2 errors for lines with ≥5 letters, more than 1 error for the lines with 3 or 4 letters, or any errors for a line with ≤2 letters on the Snellen chart or >2 letters on a line on the ETDRS chart. This is

different from the ETDRS protocol and could have led to an artificially larger difference between the charts. Falkenstein and colleagues tested only at 2 meters, whereas we tested the ETDRS charts at both 4-meter and 2-meter starting points. Thus, our study mimics the testing protocol in registration studies (ETDRS protocol) and may be more representative of the true difference between the two charts.

Third, Falkenstein and colleagues used the line assignment scoring for both the Snellen and ETDRS charts. The line assignment method is considerably faster than the forced-choice paradigm required by the ETDRS protocol.[6] In the line assignment method, the test is terminated when half or more of the letters are misread on a line, unlike the forced-choice paradigm, where testing continues until an entire line is incorrect. Using the line assignment method increases the TRV. A higher TRV has implications for clinical trial design, since increased TRV will necessitate an increased sample size to demonstrate a true clinical change. For the ETDRS chart, the TRV is ±0.18 logMAR.[7,21,26] Thus, a change of at least 0.2 logMAR or 10 letters is necessary to exceed the test's measurement error and be deemed a real change.[26] In contrast, the TRV of a Snellen chart is ±0.29 to 0.33 logMAR.[6,7] Moreover, the scaling problem of the Snellen chart means that the minimum clinically significant change, while almost 50% greater than the ETDRS chart, cannot be defined in terms of a consistent number of letters or lines. In this study, we used the single letter forced-choice paradigm for the ETDRS charts, which likely made the differences between the two charts lower. More important, by following the ETDRS protocol, the differences reported in this study can be used to guide clinicians in interpreting their clinical results on Snellen charts, especially when comparing them to published clinical trials.

For patients with good visual acuity (>20/50), the difference between the Snellen and ETDRS charts was less than 1 line. When looking at the average discrepancy, the differences ranged from 1.5 to 9 letters. This is similar to what Falkenstein and colleagues reported in patients ≥20/30 (3.5 letters).[17] Thus, to answer one question posed in the "Introduction" section of this study, in patients with Snellen acuities of 20/50 to 20/70, it would be reasonable to consider laser photocoagulation for macular edema due to a branch vein occlusion, since the ETDRS protocol cutoff was 20/50 in the BVOS.[25] For clinical trials that call for patients with good vision, it is reasonable to assume that the ETDRS vision will roughly be within 1 line of the Snellen acuity measured in one's office. The one factor that may skew these results is the fact that patients in this study were very motivated and pushed to obtain the best Snellen acuity possible, whereas in clinical practice this is not always the case. Thus, the variability may be slightly greater in clinical practice.

On the other end of the scale, there was a greater variation in the visual acuity scores in eyes with poor visual acuity. In patients with poor acuity (≤20/200), the difference between the two charts was 2 lines. However, in patients who could not read the big "E" (20/400) on the Snellen chart, the variability was huge—up to 5 lines. Falkenstein[17] noted a similar discrepancy of 4 lines, and Dr Gary Abram[27] has suggested 3 to 4 lines in exudative AMD patients. The large difference between charts underscores the fact that the Snellen chart is unsuitable for patients who have severe vision loss or when evaluating low vision patients. The fact that the greatest differences in our study were seen in patients with poor visual acuity is not surprising, since the ETDRS chart can accurately measure low visual acuities, whereas on the Snellen chart a 1- or 2-letter difference can be huge. The implication of this finding is that published case series with low vision patients that use the Snellen chart must show at least a 5-*line* difference for any treatment to have a clinically meaningful result.

Unlike in other studies, patients of all ages were included in this study. As the patients' age increased, the visual acuities worsened; however, the differences between the charts were not significantly different based on age. This is a known fact, as others have reported that logMAR visual acuity testing improves with age up to 29 years; thereafter, there is a loss of 0.029 logMAR per decade.[28] Others have reported similar decay curves with age.[29]

Another goal of this study was to evaluate if there truly was a difference in the visual acuities measured on the ETDRS charts that start testing at either 4 or 2 meters. This is not an issue for most clinicians in practice but has tremendous importance in registration trials, as the FDA now requires all studies to use the 4 meter standard. In the past, 2 meters could be used, which saved time for patients with poorer vision, since they would not see many letters at 4 meters anyhow. The regression analysis revealed a significant correlation between the visual acuity scores between 4 and 2 meters ($R^2 = 0.9909$); however, the slope was significantly different from 1.0, indicating that there is a difference between the measurements at 4 and 2 meters ($P < .0001$). In fact, as visual acuity worsened, the differences between the testing distances increased with the 2 meter distance having better acuities. Others have noted no difference in visual acuity scores on ETDRS charts as the testing distance was varied.[30] One explanation for the differences seen at 4 and 2 meters is that patients get tired, incorrectly identifying letters on the 4 meter chart before it is moved to 2 meters, and thus they do not try as hard at 2 meters. In any case, by requiring all studies to be performed at 4 meters, the FDA may have made the ability to see real change marginally more difficult.

Why is all this important? With the increasing reliance on evidenced-based medicine to guide treatment decisions, it is imperative to be able to compare clinical studies to our own practice. Unfortunately, the measurement of visual acuity in terms of chart type and testing method can bias outcomes in clinical studies. For example, most phase III clinical studies rely on ETDRS charts and protocol acuity examinations, whereas most published case series rely on Snellen charts and variable vision testing protocols.[22,31] For example, in 128 reports using vision as an outcome in the 5 major ophthalmology journals in 2005, only 58.6% gave the chart design and, of these, 44% used the Snellen chart.[22] Another study found that Snellen vision was used in 118 (74%) of 160 studies in the US and United Kingdom literature.[31] It is important to remember that one cannot describe Snellen visual results in numbers of lines or fractions of lines, yet this is done routinely in the ophthalmic literature. In many of the reports evaluated in these studies, the methods to determine visual acuity were so poorly described that replication of the studies could not be performed.[22] Some reports converted and discussed the results in logMAR format, while others converted and discussed the results in decimal format, which is even more confusing given the use of logMAR in most reports. Thus, one cannot easily compare the visual outcomes between these studies.

An example of where this issue may affect clinical practice is in the field of retina, where numerous studies of bevacizumab

(Avastin; Genentech, South San Francisco, California) have touted similar visual results as the published phase III ranibizumab (Lucentis; Genentech) studies.[32-36] Many Medicare payers have offered to pay for the off-label use of bevacizumab in diagnoses such as AMD, diabetic retinopathy, and vein occlusions based on these small case series. The thinking is that since the drug is very similar to ranibizumab, the phase III ranibizumab results with significant improvements in ETDRS protocol vision are proof that bevacizumab also works. In contrast, the case series with bevacizumab were largely performed with Snellen charts. This study indicates that one cannot compare the results of the bevacizumab literature with Snellen acuity and ranibizumab trials measured with ETDRS protocol vision. Moreover, Falkenstein has suggested that Snellen charts are not as sensitive at detecting visual change after treatment with anti–vascular endothelial growth factor agents as ETDRS charts.[17] Thus, while the drugs may indeed be similar, until we have studies that measure acuity with ETDRS charts, Medicare's decision may be premature. A 3-line improvement in vision on a Snellen chart may be real or may be due to the variability of the chart, especially for small case series in patients with poor baseline vision, and cannot be compared to a 3-line improvement in vision in a registration trial or a National Institutes of Health study such as the ETDRS. Another example is the numerous reports touting the greater proportion of patients gaining 3 lines of vision after intravitreal triamcinolone acetonide measured on Snellen charts vs the visual acuity results in the ETDRS when laser was used.[37-39] When intravitreal triamcinolone acetonide was directly compared to laser photocoagulation using ETDRS protocol vision in the Diabetic Retinopathy Clinical Research Network study, the results showed that laser worked significantly better.[40] The significant differences between vision measured on the ETDRS and Snellen charts in this study should help clinicians incorporate clinical trial data into their clinical practice and compare case series with Snellen to large randomized studies with ETDRS protocol visual acuities. It also underscores the importance of critically evaluating the published literature before incorporating therapies into one's practice.

Snellen visual acuity has historically been used to evaluate medicolegal decisions, including legal blindness and the ability to drive a car.[5] In most states, 20/50 Snellen vision in at least one eye is the required standard for driving; however; when measured on a Snellen chart, this cutoff encompasses a wide variety of acuities, some of which could prevent a patient from safely driving a car.[41] The visual acuity variability of Snellen charts is exceedingly high when patients have poor vision (20/200 and 20/400). This is noteworthy because 20/200 is the legal limit for blindness and many statutes rely on demonstrating better or worse vision than this standard. Compounding this problem is that low vision patients exhibit a large variability in acuity differences.[42,43] Although we did not analyze TRV, patients with poor vision in this study were significantly more likely to have better vision on the ETDRS chart compared to Snellen charts. Thus, to improve the accuracy of determination of legal blindness or whether a patient can drive, we may want to consider a switch to ETDRS charts.

This study has several limitations, including the fact that the tests were performed only once, so TRV could not be evaluated. Since this study was designed to evaluate vision testing using Snellen vs ETDRS charts and not TRV, repeatability and sensitivity could also not be tested in this study. The same examiner took all measurements in a short period of time under identical conditions using the interpolated scoring method to hopefully reduce the variability as much as possible. Unfortunately, since only one examiner was used, we could not evaluate interobserver variation. Another limitation was that in my clinical practice, there are mainly older patients, and all patients had retinal problems. Thus, evaluation of visual acuity in patients with other ophthalmic problems could not be evaluated in this study, and no children were included in the analysis. Owing to the nature of Snellen acuity testing, there were inexact Snellen measurements beyond 20/400 when a letter "E" card was used to test vision. Certainly, another option would have been to move the patient closer to the Snellen chart, but since the progression is not linear, the patient would have to be continuously moved as he or she read down the chart, and correlating the final vision would have been impractical. The Snellen acuity testing was performed as it is done in clinical practice using the line assignment, not the single letter method (forced-choice). Some reports have shown that Snellen acuity obtained using the single letter method may have a better correlation with ETDRS testing. Unfortunately, this method is slow and impractical, and we wanted to mirror "real world" clinical practice with our Snellen chart testing. The analysis was performed using the logMAR scores instead of comparing the Snellen line assignment scores with the ETDRS chart data rescored using the line assignment method. We did this because some investigators have shown that ETDRS charts scored in this manner are not as reliable.[2] Visual acuity relies on psychological and physiologic factors that cannot be controlled. For example, a patient's level of attention, fatigue, underlying competitiveness, and determination play an important role in measuring visual acuity. To avoid introducing bias from these factors, all patients were given standardized encouragement during vision testing, and the order of charts was changed with each patient to hopefully equalize the chance for bias.

The Snellen chart is the universally accepted method in clinical practice to assess visual acuity despite its known deficiencies, including unreliability and poor reproducibility. It is clearly useful to measure general visual acuity in clinical practice. Unfortunately, Snellen charts are also the "standard" in most retrospective case series and medicolegal decisions. In these areas, the shortcomings of the Snellen chart do not allow appropriate quantification of vision. In contrast, the features of the ETDRS charts allow precise quantification of vision and reliable measures of vision change. As such, it has become the "gold standard" in clinical research and for FDA registration trials in the United States. There are numerous reasons why we have not adopted the ETDRS for clinical practice, including the large size of the chart, the unfamiliarity with the testing and scoring protocol, the time it takes to perform, and the number of letters on the chart. This study was designed to explore the practical differences between visual acuity scores measured on Snellen vs ETDRS charts. It demonstrated that there were significant differences in acuity scores obtained between the two charts in a "real world" academic retina practice. This mirrors what other investigators have found. Why, then, do we continue to use the Snellen chart in practice and, in particular, for most published clinical studies? This is a question that truly perplexes me as a clinical researcher. Time and convenience should not be relevant when testing visual acuity in ways that may guide clinical practice. Precision and accuracy are paramount in this situation, especially when reporting data for public consumption.

After this study was completed, we instituted a system-wide initiative to prospectively follow all our surgical and refractive laser

patients' outcomes with ETDRS protocol visions. This will allow us to precisely evaluate our own clinical outcomes, improve our outcomes over time, and benchmark them against other institutions and the published literature. Moreover, it will hopefully set a standard that others will follow. We hope to expand this initiative in the future to all procedures, in particular intravitreal injections and retinal and glaucoma laser procedures. This is only one institution, and a small start, but hopefully it will begin turning the wheel slowly in the right direction to finally move toward a better measure of visual acuity when we describe outcomes of clinical research.

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