Assessment of Macular Function Using the SKILL Card in Adults With Type 2 Diabetes Mellitus

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Purpose. To evaluate the impact of reduced contrast and reduced luminance on visual acuity (VA) using the Smith–Kettlewell Institute Low Luminance (SKILL) Card in patients with type 2 diabetes mellitus (T2DM).

Methods. We studied adults aged 27 to 65 years, 32 with T2DM and no retinopathy (NoRet group), 22 with T2DM and nonproliferative diabetic retinopathy (NPDR group), and 38 healthy control subjects. Monocular high-contrast (SKILL light) and low-contrast, low-luminance (SKILL dark) near visual acuities were tested. The SKILL score was calculated as the difference between dark chart and light chart acuities and was corrected for age. Contrast sensitivity (CS) was also measured. Subject group differences were examined using ANOVA and Tukey honestly significant difference test. Receiver operating characteristic curve analysis was used to assess the ability of the SKILL Card and CS to discriminate the subject groups.

Results. The SKILL score and CS were significantly worse in both diabetes groups compared with the controls ($P < 0.01$). SKILL scores in the NPDR group were poorest (highest) and significantly worse than those in the NoRet group ($P < 0.05$). SKILL scores discriminated NPDR and NoRet patients from the controls with high accuracy (99% and 88%, respectively), which was significantly ($P < 0.03$) better than CS (78% and 74%, respectively).

Conclusions. The SKILL Card demonstrated vision function changes in diabetes even in the absence of clinically evident retinopathy. Diabetic retinopathy led to a further increase in the SKILL score, while high-contrast VA remained unchanged.

Keywords: diabetes, diabetic retinopathy, visual acuity

As type 2 diabetes mellitus (T2DM) has reached epidemic proportions over the last two decades, the number of patients at risk of vision-threatening retinal changes due to diabetes has also increased dramatically. Diabetic retinopathy, present in 40% of people with diabetes, continues to be the primary cause of blindness in working-age adults and remains an unresolved therapeutic challenge.[1–3] The risk of developing diabetic retinopathy and eventually losing vision increases with disease duration.[4] It has long been reported that early detection and appropriate treatment can reduce the vision loss and blindness associated with diabetes.[5] Almost one-third of patients with diabetic retinopathy and a few with evidently advanced stages have no symptoms or signs of reduced vision detected in visual screening in clinics using standard visual acuity (VA).[6] As a result, these patients may remain unidentified as at risk and not followed up appropriately. This translates into a demand for more sensitive and specific methods that can detect the early changes to retinal function in diabetes.

Currently, clinical assessment of retinal function loss in patients with diabetes relies heavily on VA. The decision about how frequently to follow up these patients rests upon their VA and retinopathy status.[7–10] Unfortunately, by the time VA is reduced, the signs of retinal damage are already present. Many studies, including investigations from our laboratory, have shown that there are other psychophysical[11–15] and electrophysiological[16,17] tests that are highly sensitive to identify and predict[18] early retinal changes in diabetes. In this study, we continue to explore subtle effects of diabetes on macular function using a psychophysical task that has potential as an addition to a screening protocol in patients with diabetes.

The Smith–Kettlewell Institute Low Luminance (SKILL) Card (Figs. 1A, 1B) was designed to provide a simple, rapid, and inexpensive test to assess near spatial vision at high and low contrasts and luminances.[19] The test uses a card with a high-contrast black-on-white letter chart on one side and a low-contrast chart of dark letters on a dark gray background, designed to simulate a reduced luminance condition, on the reverse side. The SKILL Card has been shown to detect changes to visual function in aging[20] and in diseases such as optic neuritis and age-related maculopathy[19] and cortical abnormalities.[21] SKILL test results are reproducible.[19]

In this study, we examine the sensitivity of the SKILL Card to detect subclinical vision changes in adult patients with T2DM. We investigate the potential effects of age and diabetes control (glycated hemoglobin [HbA_{1c}] concentration and random blood glucose level [BGL] at the time of examination) on SKILL Card performance.

Contrast sensitivity (CS) testing has been reported to be a rapid and sensitive vision assessment tool in patients having diabetes with normal VA.[11,12] Therefore, we compare the ability of the SKILL Card and CS to discriminate among nondiabetic control subjects, T2DM patients without retinopathy, and T2DM patients with nonproliferative diabetic retinopathy

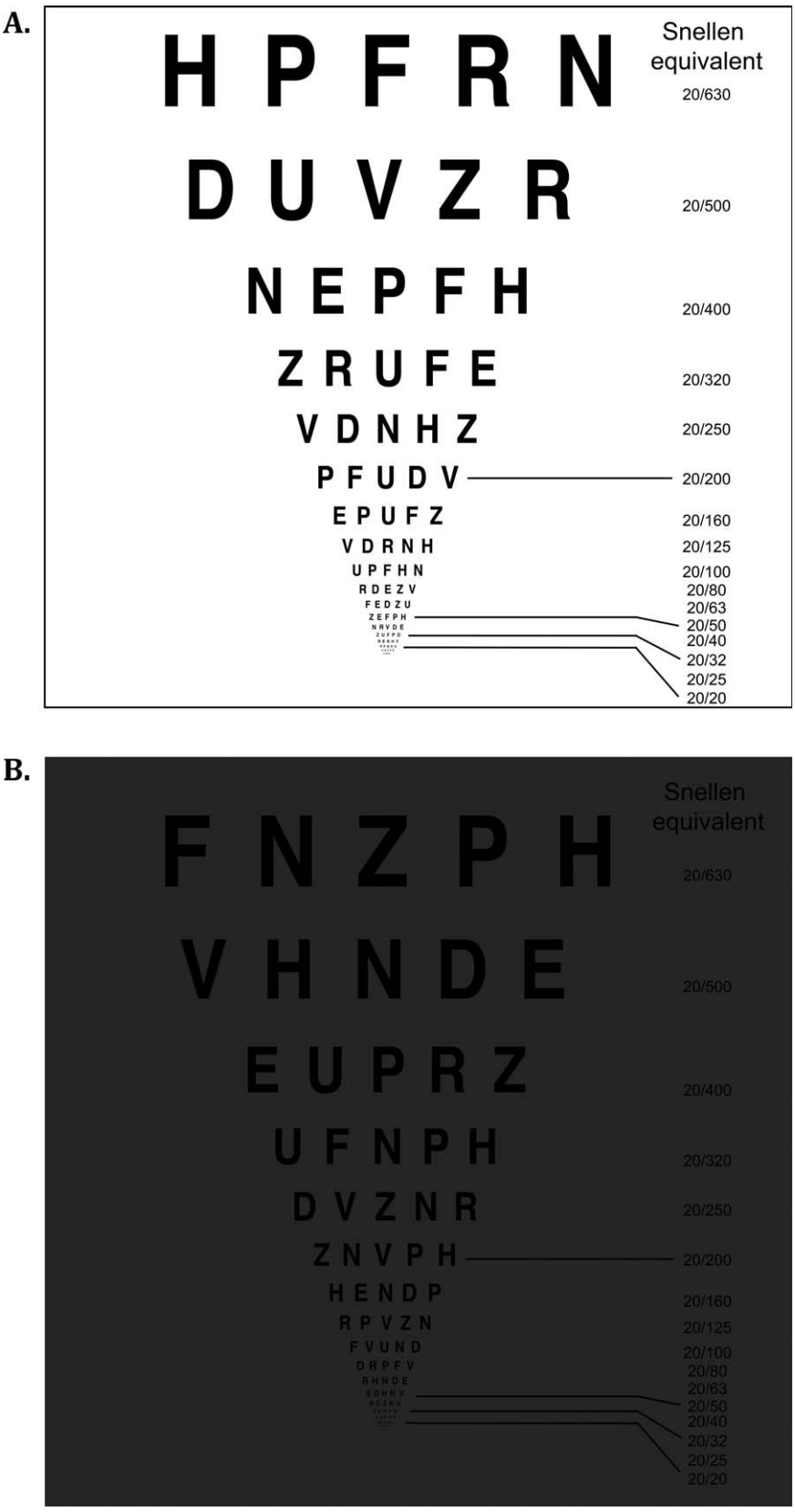

Figure 1. (**A**) Rendition of the SKILL light chart: *black letters* on a *white background*, with letter size ranging from 20/12.5 to 20/630 Snellen equivalents. (**B**) Rendition of the SKILL dark chart: *black letters* on a *gray background*, with letter size ranging from 20/20 to 20/630 Snellen equivalents. The dark chart in the figure is not calibrated. The figure was adapted from *Invest Ophthalmol Vis Sci*. 1997;38:207–218 by Haegerstrom-Portnoy et al.[19]

TABLE. Participant Characteristics

Subject Group	Sex		Mean (SD) Age, y	Mean (SD) T2DM Duration, y	Mean (SD) HbA_{1c} Concentration, %
	Male	Female			
NoRet	15	17	55.0 (9.6)	9.8 (4.6)	8.1 (1.9)
NPDR	12	10	54.4 (8.7)	11.9 (4.8)	8.5 (1.5)
Control	13	25	39.5 (12.0)	NA	NA

NA, not applicable.

(NPDR). We also evaluate correlations of SKILL Card performance with CS and low-contrast VA (LCVA).

METHODS

Participants

This was an observational cross-sectional study that tested 92 participants (age range, 27–65 years). Fifty-four participants with T2DM were enrolled in the study and were divided into two groups based on the presence or absence of NPDR. Thirty-two participants with no retinopathy comprised the NoRet group, and 22 participants with mild to severe NPDR and no edema comprised the NPDR group. In total, 64% of the eyes in the NPDR group had mild NPDR, and only two of the 22 patients (9%) had severe NPDR. Thirty-eight healthy individuals without diabetes were included in the control group. The mean (SD) ages were 55.0 (9.6), 54.4 (8.7), and 39.5 (12.0) years for the NoRet, NPDR, and control groups, respectively. The mean (SD) durations of diabetes were 9.8 (4.6) and 11.9 (4.8) years, and the mean (SD) HbA_{1c} concentrations were 8.1% (1.9%) and 8.5% (1.5%) for the NoRet and for the NPDR groups, respectively (Table). One eye from each participant was included in the analyses. The eye having better distance VA was selected.

Inclusion criteria were age between 25 and 65 years, refractive error within ±6 diopter (D) spherical equivalent, a habitually corrected high-contrast distance VA of 20/25 or better, the presence of mild to severe NPDR for the NPDR group, and the absence of clinical signs of retinopathy for the NoRet group. The exclusion criteria were media opacification (including any cataract [nuclear sclerosis >1]), any systemic conditions that could affect the visual system (apart from T2DM for the patient groups), and a history of ocular trauma, concomitant ocular diseases, ocular or retinal surgery, and intravitreal injections. The difference between high-contrast distance and near VA was calculated. To minimize the impact of uncorrected refractive error, any subject having distance and near VA that differed by more than five letters (0.10 log unit) was excluded as potentially having an improper refractive correction.

All procedures adhered to the tenets of the Declaration of Helsinki, and the University of California, Berkeley, Committee for Protection of Human Subjects approved the experimental protocol. All subjects provided informed consent to participate in the study and underwent visual function evaluation after examination of the pupil and angle of anterior chamber using a penlight.

Procedures

Each eye's habitually corrected distance high-contrast and low-contrast visual acuities were assessed at 10 ft using the Bailey-Lovie chart.[22] Contrast sensitivity was measured using the Pelli-Robson chart[23] at 10 ft, and SKILL card performance was measured. Contrast sensitivity was tested at 10 ft rather than at 1 m to avoid the need of an addition over the habitual correction of participants. In people with good VA, there is no difference in Pelli-Robson CS tested at 3 m compared with at 1 m.[24]

The vision testing was followed by pupil dilation (using 1% tropicamide and 2.5% phenylephrine eyedrops) and retinal imaging using stereo fundus photography (Zeiss Visucam Pro NM; Carl Zeiss Meditec, Inc., Dublin, CA, USA). A retina specialist (SB) examined central 45° fundus photographs to determine the presence or absence of retinopathy and to grade the retinopathy. The study participants were evaluated using biomicroscopy for lens opacification according to the Lens Opacities Classification System III.[25] The HbA_{1c} concentration and BGL were determined.

SKILL Card Measurements

The SKILL Card (Figs. 1A, 1B), as mentioned above, consists of two near acuity charts mounted back to back.[19] The light chart is a high-contrast (>90%), black-on-white letter chart with logarithmic letter progression. The dark chart has black letters on a dark gray background (approximately 10% of the reflectance of the light chart's) providing lower contrast (14%) and luminance conditions. The letters on the dark chart ranged from Snellen equivalents of 20/20 to 20/630 at the test distance of 40 cm. The light chart contains two extra lines, measuring acuity up to 20/12.5 (logMAR, −0.20). All participants were examined in office lighting (approximately 80 cd/m^2 on the white chart) with habitual correction for near vision.

Because the control group was more than a decade younger than the diabetes groups, we performed regression analysis to examine the association between age and SKILL scores in each of the three subject groups. Only the control group showed a statistically significant age dependence ($P < 0.01$) of the SKILL score. To be conservative, SKILL scores of the diabetes groups were adjusted for age, assuming that once the age factor is subtracted any remaining reduction in SKILL scores could be attributed to the disease effects. This was done by calculating the differences in the mean age between the control group and the two diabetes groups. These differences were then multiplied by the change in SKILL score per year that we obtained from the linear regression performed on the control group data to estimate the age-dependent increases in the SKILL score. These estimates were then subtracted from the raw scores in each group of diabetic subjects. Note that a higher SKILL score is indicative of greater vision function loss at reduced luminance and contrast.

Statistical Analysis

ANOVA, followed by Tukey honestly significant difference test, was used to analyze the differences between subject groups. $P \leq 0.05$ was considered significant. Receiver operating characteristic (ROC) curves were calculated to evaluate the sensitivity and specificity of the SKILL Card and CS to discriminate participants in the three subject groups. Each point on the

ROC curve represents the proportion of subjects in one group (e.g., the control group) exceeding a criterion value and the proportion of subjects in a comparison group (e.g., the NPDR group) exceeding that value. The criterion begins at the maximum data value and is systematically reduced by a fixed amount (step size) until all subjects in both groups have been included. When SKILL scores are analyzed, the step size in this process is the smallest possible difference, a single chart letter. Likewise, when CS is analyzed, the step size is 0.05, which corresponds to one letter on the Pelli-Robson chart. The relative ability of the two tests to accurately identify the groups was assessed by comparing the areas under their ROC curves. Linear regression was performed to examine the association between the SKILL score and the duration of diabetes, age, BGL, HbA_{1c} concentration, LCVA, and CS.

Results

SKILL Card

High-contrast near visual (SKILL light) acuity was significantly lower in both diabetes groups (NoRet and NPDR) compared with the controls ($P < 0.05$) and was similar between the diabetes groups (Fig. 2A), although the mean SKILL light acuity for all groups was better than 20/20 (logMAR, 0.0). Thus, although statistically significant, the difference in acuity between groups is not likely to be clinically meaningful due to the study's inclusion criterion of a minimum VA of 20/25. Low-contrast, low-luminance near visual (SKILL dark) acuity was significantly lower in both diabetes groups compared with the controls ($P < 0.01$) and was lowest in the NPDR group ($P < 0.01$) (Fig. 2B). SKILL scores were significantly worse (higher) in both diabetes groups compared with the controls ($P < 0.01$) and were worse in the NPDR group than in the NoRet group ($P < 0.05$) (Fig. 2C). The two patients with severe NPDR had the worst (highest) SKILL scores.

Other Vision Measures

The CS and LCVA were similar between the diabetic groups (NoRet and NPDR) but were significantly reduced (worse) in both diabetes groups compared with the controls ($P < 0.01$). There were no statistically significant correlations between the SKILL score and the duration of diabetes, BGL, HbA_{1c} concentration, LCVA, or CS ($P > 0.05$ for all) in any group. However, age and the SKILL score were significantly correlated in the control group ($P < 0.01$).

Discrimination Between Subject Groups

The sensitivity, specificity, and overall accuracy of the SKILL score and CS for discriminating the three subject groups (i.e., correctly classifying subjects) were estimated from ROC curve analyses (Figs. 3–5). The sensitivity and specificity are determined by the coordinates of the data point on the ROC curve that is closest to a diagonal line of equal sensitivity and specificity. This line runs from the upper left-hand corner to the lower right-hand corner of the ROC plot. In one case (the discrimination of NoRet patients from NPDR patients using CS), the sensitivity and specificity were estimated where the diagonal line crossed the line connecting the two data points bracketing the diagonal. The area under the curve (AUC) (range, 0.0–1.0 [stated below as percentages]), a measure of the overall accuracy of the SKILL score and CS, was computed for each comparison. The AUC can be interpreted as the average value of the sensitivity for all possible values of the specificity.[26,27]

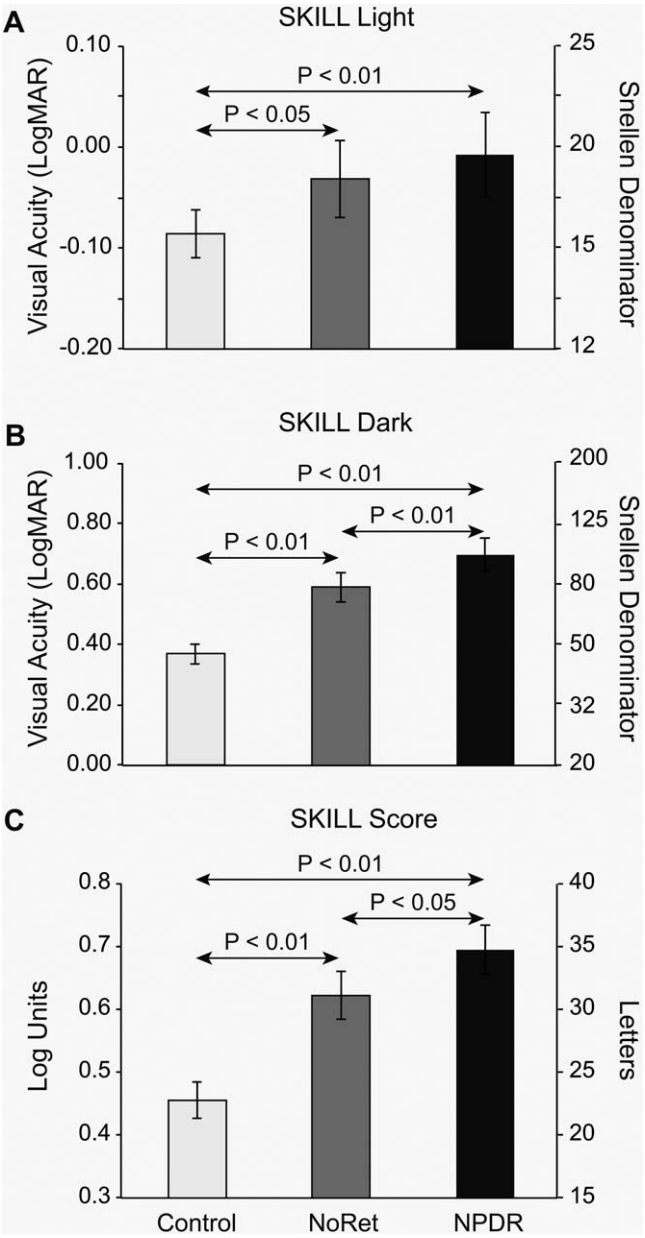

Figure 2. The mean high-contrast, high-luminance near VA measured with the SKILL light chart (**A**), the mean low-contrast, low-luminance near VA measured with the SKILL dark chart (**B**), and the mean SKILL scores (**C**) of the three subject groups. *Error bars* denote ±2 SEM.

The SKILL score is most sensitive (96%), specific (92%), and accurate (99%) in distinguishing NPDR patients from control subjects (Fig. 3). These values correspond to SKILL scores exceeding 29. The test is relatively less but still highly accurate (88%), sensitive (81%), and specific (79%) for discriminating control subjects from NoRet patients (Fig. 4). These values correspond to SKILL scores exceeding 26. The SKILL score is much less sensitive (59%), specific (56%), and accurate (70%) but better than chance in distinguishing NPDR patients from NoRet patients using a SKILL score criterion of greater than 32 (Fig. 5).

Contrast sensitivity is also most sensitive (73%), specific (71%), and accurate (78%) in distinguishing NPDR patients from control subjects (Fig. 3). These values correspond to a log CS of less than 1.70. It is less sensitive (66%) but equally

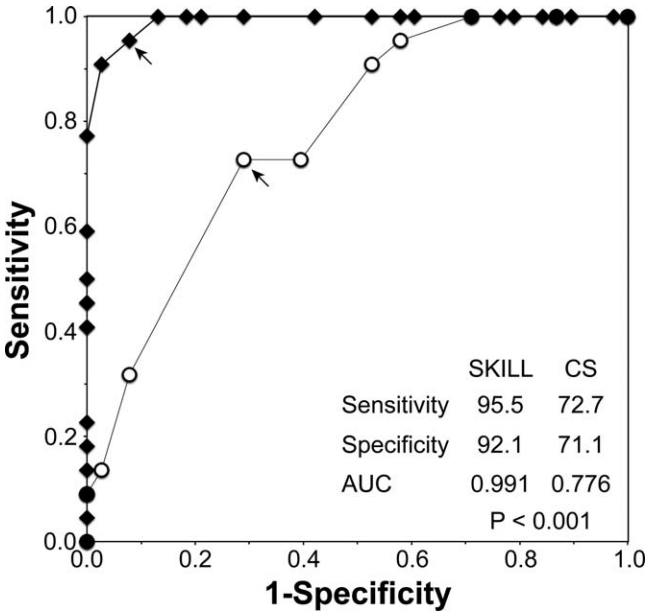

Figure 3. The ROC curves for discriminating NPDR patients from control subjects. *x-axis*: 1 minus the specificity (proportion of false positives [i.e., classifying a control as an NPDR patient]). *y-axis*: the sensitivity (proportion of true positives [i.e., correct detection of an NPDR patient]). *Black diamonds* represent SKILL scores, and *unfilled circles* represent CS. *Arrows* indicate where the sensitivity and specificity were determined. *P* value is for the difference in AUC between the SKILL Card and CS.

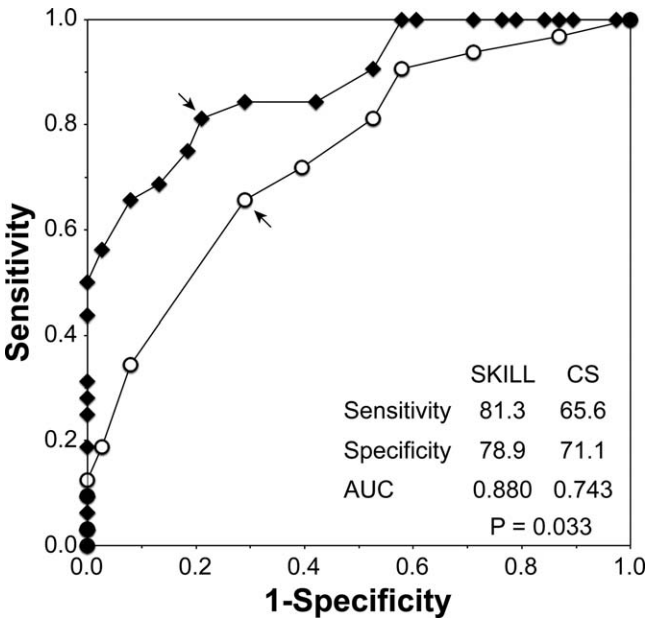

Figure 4. The ROC curves for discriminating NoRet patients from control subjects. *x-axis*: 1 minus the specificity (proportion of false positives [i.e., classifying a control as a NoRet patient]). *y-axis*: the sensitivity (proportion of true positives [i.e., correct detection of a NoRet patient]). *Black diamonds* represent SKILL scores, and *unfilled circles* represent CS. *Arrows* indicate where the sensitivity and specificity were determined. *P* value is for the difference in AUC between the SKILL Card and CS.

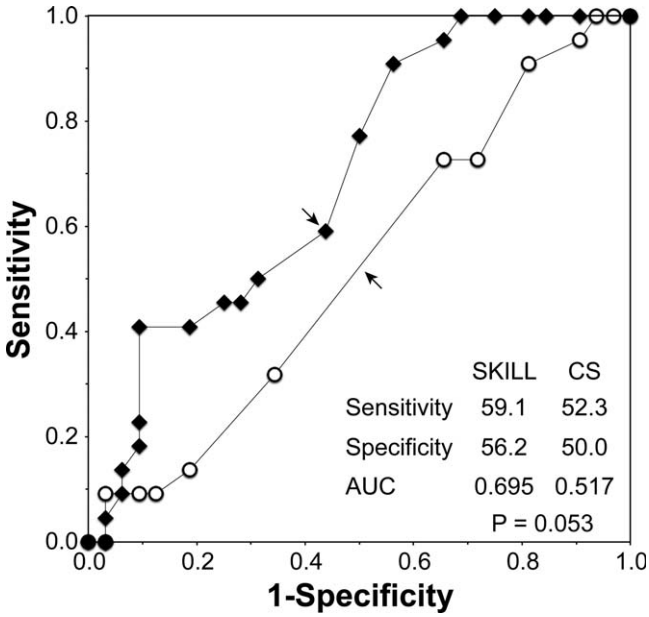

Figure 5. The ROC curves for discriminating NoRet patients from NPDR patients. *x-axis*: 1 minus the specificity (proportion of false positives [i.e., classifying an NPDR patient as a NoRet patient]). *y-axis*: the sensitivity (proportion of true positives [i.e., correct detection of an NPDR patient]). *Black diamonds* represent SKILL scores, and *unfilled circles* represent CS. *Arrows* indicate where the sensitivity and specificity were determined. *P* value is for the difference in AUC between the SKILL Card and CS.

specific (71%) and less accurate (74%) for discriminating control subjects from NoRet patients at the criterion of log CS of less than 1.70 (Fig. 4). Contrast sensitivity is much less sensitive (52%), specific (50%), and accurate (52%) in distinguishing patients with NPDR from NoRet patients at the log CS criterion of less than 1.70 (Fig. 5).

As the text in Figures 3 through 5 indicates, SKILL scores discriminated NPDR patients and NoRet patients from the controls with high accuracy (99% and 88%, respectively), which was significantly ($P < 0.03$ for the AUC difference) better than CS (78% and 74%, respectively), in addition to discriminating NPDR patients from the controls ($P < 0.001$ for the AUC difference). The two vision measures do not differ significantly, however, in their poor ability to discriminate NoRet individuals from NPDR individuals ($P = 0.05$ for the AUC difference).

Discussion

In patients with T2DM who retain good standard VA, the SKILL Card detected vision function changes even in the absence of clinically evident retinopathy. Nonproliferative diabetic retinopathy led to worse (higher) SKILL scores. The increase in SKILL scores reflects a decrease in SKILL dark acuity in diabetes. In this study (in which near VA was similarly good in all participants), the calculation of the SKILL score does not add information beyond that provided by the dark chart. However, this may not be true in other cases in which near VA varies among individuals or between groups (e.g., in a scenario where the SKILL Card might be used as a potential screening test).

The decline in SKILL Card performance in diabetes and diabetic retinopathy may be attributed to several factors. These include pathologic changes in macular function, lenticular

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yellowing, and pupillary miosis, which can affect retinal illumination, as well as postretinal neural changes.

At all ages, pupil size is decreased in diabetes, contributing to differences in pupil size between control and diabetic eyes.[28] Data are not available for the impact of diabetes on pupil size at low photopic light levels, making it difficult to quantify the effect on SKILL Card performance.

The control group was, on average, younger than both patient groups. Therefore, pupil size in the patient groups was likely smaller than that of the controls because pupil size declines with age. Winn et al.[29] measured pupil size across age at a variety of luminance levels in nondiabetic individuals. Based on their data at 9 cd/m^2 (the approximate luminance of the SKILL dark chart as used herein), we calculate that the retinal illuminance of the diabetic groups for the dark chart would be approximately 0.09 log unit lower than that of the control group. It is likely that this small difference would have a negligible effect on the performance on the dark chart. In any case, SKILL scores were adjusted for age in our study.

One might expect that the magnitude of the decline in the SKILL score with age in the patients might be greater than that in the controls. In contrast, as noted earlier, the diabetes groups showed no significant associations of the SKILL score with age, presumably because the effects of diabetes are greater in magnitude than the small age effect.

Lens density increases with age, and there is evidence of accelerated yellowing of the lens with age in patients with diabetes.[30] To minimize the impact of lens changes, only subjects without nuclear sclerosis (earliest sign of cataract) were included in our study. However, denser lenses in the patients with diabetes, due to their older age and diabetes itself, will affect retinal luminance to some degree. Given that short-wavelength light is most attenuated and that broad-spectrum (white) illumination was used, the impact of increased lens density in the diabetes group on retinal illuminance is also expected to be small.[30]

If we are conservative, allowing for retinal illuminance differences between the control and diabetic groups to be as large as 0.30 log unit, a negligible decline in high-contrast, high-luminance acuity and a larger decline in low-contrast, low-luminance acuity would be predicted to increase the SKILL score by less than 0.10 log unit (five letters).[19] The differences we observed between our diabetes patients and controls in SKILL dark chart acuities and SKILL scores were larger than this, suggesting that retinal functional alterations also contributed to the patients' worse (higher) SKILL scores. Our laboratory and others have revealed alterations in retinal function in the eyes of diabetic subjects both with and without NPDR.[16–18]

The SKILL score demonstrated high sensitivity, specificity, and overall accuracy for discriminating between nondiabetic control subjects and patients having diabetes both with and without NPDR. However, it failed to discriminate with high accuracy the patients with NPDR from the patients without retinopathy. The fact that 64% of the eyes in the NPDR group were diagnosed as having only mild nonproliferative retinopathy may explain this observation. In the NPDR group, only two of the 22 patients had severe NPDR, and those participants had the worst (highest) SKILL scores.

Contrast sensitivity is affected by diabetes before the presence of retinopathy and worsens with the development of retinopathy.[11,12] However, CS and LCVA were not correlated with SKILL scores in any subject group herein. Moreover, the performance of the SKILL Card for discriminating the control subjects from the patients in both diabetes groups was significantly better than CS. The absence of associations between the SKILL score and other sensitive vision measures suggests that the SKILL score may assess a different aspect of macular function. The SKILL Card dark chart is a low-contrast near VA chart that tests at a luminance that is approximately 1.00 log unit lower than that of the high-contrast light chart. These unique features appear to make the SKILL Card more sensitive to vision function changes than standard VA tests and CS.

The SKILL score reflects the impact of both reduced contrast and reduced luminance on VA. We examined the contribution of the two parameters to the SKILL score. The effect of reduced contrast was estimated by comparing, within each individual, standard high-contrast VA with low-contrast VA measured with the Bailey-Lovie chart at the same luminance. The fact that the contrast levels of the SKILL dark chart and the Bailey-Lovie low-contrast chart are very similar (14% and 18% Weber contrast, respectively) permits this approach. The contribution of reduced luminance to the SKILL score was estimated by comparing the low-contrast VA performance with the SKILL dark chart performance. We found for all three subject groups that, on average, approximately 43% of the SKILL score is attributable to reductions in contrast, while luminance reduction contributes approximately 57% of the SKILL score. Although the sizes of the effects of luminance and contrast reduction are larger in patients than in control subjects, the relative contributions of these two to the SKILL score appear to be roughly the same, approximately 50%.

In this study, we used a lower light level (80 cd/m^2 on the light chart) than that used in the original SKILL Card study[19] (150 cd/m^2). As a result, our control subjects had slightly higher (worse) SKILL scores than the published norms.[19] Because reduced luminance has a greater impact on individuals with retinal disease,[31,32] testing at a lower luminance likely increased the sensitivity of the test to the effects of diabetes and diabetic retinopathy.

A potential limitation of the present study was that habitual corrections were used, and it is unknown whether all subjects were appropriately corrected. Thus, it is possible that the habitual correction was not optimal in some instances, leading to defocus that could have affected SKILL scores. It has been shown that 2 to 3 D of blur does not affect the SKILL score significantly but that a large amount of refractive blur may produce an underestimate of the SKILL score.[19] Given the good high-contrast acuities on the light chart of the SKILL Card in all groups, it is doubtful that our subjects had severely uncorrected refractive error. Thus, it is unlikely that the differences in SKILL scores we observed between control subjects and diabetes patients are attributable to refractive error.

In conclusion, the SKILL Card is quick and easy to use, inexpensive, reproducible, and minimally affected by mild refractive blur, and it does not need an expert or a special instrument to administer.[19] Our study shows that it is sensitive to retinal function changes in diabetes. In fact, we find that the SKILL Card is more effective than CS for discriminating between nondiabetic and diabetic individuals with or without NPDR. This test may prove useful in screening patients with diabetes. We are currently assessing SKILL Card performance longitudinally in NoRet patients and in NPDR patients to evaluate whether the SKILL score is predictive of the development of NPDR and/or the development of diabetic macular edema.

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