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Factors Predicting Visual Acuity Outcome in Intermediate, Posterior and Panuveitis: *The Multicenter Uveitis Steroid Treatment (MUST) Trial*

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Abstract

Purpose—To identify factors associated with best-corrected visual acuity (BCVA) presentation and two-year outcome in 479 intermediate, posterior, and panuveitic eyes.

Design—Cohort study using randomized controlled trial data

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*The Credit Roster for the Multicenter Uveitis Steroid Treatment (MUST) Trial Research Group appears in Appendix 1, available at http://www.ajo.com.

Supplemental Material: Supplemental Material available at AJO.com includes Supplemental Tables 1 and 2, and Appendices 1 and 2.

ClinicalTrials.gov **Identifier:** NCT00132691

Disclosure

Dr. Dunn report no relationships that might be perceived as conflicts of interest.

Methods—Multicenter Uveitis Steroid Treatment (MUST) Trial masked BCVA measurements at baseline and 2 years' follow-up used gold standard methods. Twenty-three clinical centers documented characteristics per protocol, which were evaluated as potential predictive factors for baseline BCVA and two-year change in BCVA.

Results—Baseline factors significantly associated with reduced BCVA included: age ≥50 vs. <50 years; posterior vs. intermediate uveitis; uveitis duration >10 vs. <6 years; anterior chamber (AC) flare > grade 0; cataract; macular thickening; and exudative retinal detachment. Over two years, eyes better than 20/50 and 20/50 or worse at baseline improved, on average, by 1 letter (p=0.52) and 10 letters (p<0.001) respectively. Both treatment groups and all sites of uveitis improved similarly. Factors associated with improved BCVA included resolution of active AC cells, of macular thickening, and cataract surgery in an initially cataractous eye. Factors associated with worsening BCVA included longer duration of uveitis (6–10 or >10 vs. <6 years), incident AC flare, cataract at both baseline and follow-up, pseudophakia at baseline, persistence or incidence of vitreous haze, and incidence of macular thickening.

Conclusions—Intermediate, posterior and panuveitis have a similarly favorable prognosis with both systemic and fluocinolone acetonide implant treatment. Eyes with more prolonged/severe inflammatory damage and/or inflammatory findings initially or during follow-up have a worse visual acuity prognosis. The results indicate the value of implementing best practices in managing inflammation.

Uveitis has been reported to be the fifth to seventh leading cause of blindness in developed countries.[1] The incidence has been estimated at 17–52 new cases/100,000/year and the prevalence at 58 to 115/100,000);[2–5] it causes several-fold more years of potential vision lost per case than age-related diseases, due to an average age of onset decades earlier in life.[6] The economic impact per case of uveitis-induced visual loss is correspondingly high, potentially on par with that for diabetic retinopathy.[6]

For many cases, treatment is able to mitigate vision loss.[7] However, treatment is potentially expensive,[8] and complicated to administer. Identification of factors predictive of a poorer visual outcome and comparison of outcomes in patients treated with either systemic or "local" therapy with a fluocinolone acentonide implant would help guide clinicians in making treatment decisions.

As part of the Multicenter Uveitis Steroid Treatment (MUST) Trial, 479 eyes of 255 patients were followed longitudinally for two years, with protocol-driven collection of best-corrected visual acuity (BCVA) using gold standard methods. Standardized data collection regarding a wide variety of characteristics potentially predictive of visual outcome was undertaken. Here we report results regarding factors predictive of visual outcome from this cohort.

Methods

The Multicenter Uveitis Steroid Treatment (MUST) Trial—a comparative effectiveness trial comparing fluocinolone acetonide 0.59 mg implant therapy versus systemic therapy with corticosteroids supplemented in most cases with immunosuppression—randomized subjects having active or recently active (within 60 days) intermediate, posterior or panuveitis to the

alternative treatments. The MUST Trial (ClinicalTrials.gov **Identifier:** NCT00132691) was approved by governing institutional review boards at all participating clinical centers and at the Coordinating and Reading Centers (see Appendix 1 for a list of study participants, and Appendix 2 for list of institutional review boards, each available online at www.ajo.com); approval was maintained throughout the study. The protocol[9] and primary outcomes[7] of the study have been described previously. In brief, eligibility was based on presenting with at least one uveitic eye for which systemic corticosteroid therapy would be indicated, and absence of characteristics suggesting one of the alternative treatments would be contraindicated. In the systemic therapy arm, subjects were assigned systemic corticosteroid therapy supplemented by systemic immunosuppressive therapy when indicated, following guidelines for such therapy developed by an expert panel.[10] In the implant therapy arm, subjects were assigned to initial quieting of the anterior chamber using topical, injected, and/or oral corticosteroid therapy following by implantation of a fluocinolone acetonide implant[11;12] in each eye for which study treatment was indicated. Both groups were permitted use of topical corticosteroids without restriction, on grounds that such treatment would have limited impact on the posterior segment, and for ethical reasons. In addition to use for quieting the anterior chamber prior to implant surgery, periocular and intravitreous injections were indicated in the trial for treatment of residual complications of uveitis—e.g., macular edema[13–15]—rather than as a primary anti-inflammatory treatment. All subjects provided informed consent.

At baseline, demographic data and clinical characteristics were collected for all patients (see Tables 1 and Supplemental Table 1, the latter available online at http://www.ajo.com). These included age, sex, race/ethnicity, smoking status, presence of an associated systemic inflammatory disease, diagnosis with diabetes mellitus, bilaterality vs unilaterality of uveitis, years between diagnosis with uveitis and enrollment, and site of inflammation as defined by the Standardization of Uveitis Nomenclature (SUN) Working Group modification of International Uveitis Study Group criteria (anterior plus intermediate uveitis, intermediate uveitis, posterior uveitis or panuveitis).[16;17]

After the baseline visit, patients had study visits at one month, three months, and quarterly thereafter through two years. BCVA, the primary outcome of the study, was measured at all visits using gold standard methods,[18] which involved a protocol-driven refraction under standardized lighting conditions[19] using a logarithmic visual acuity chart.[20] BCVA was measured prior to randomization at baseline, and was measured by masked examiners at baseline, six months and thereafter. The BCVA at one and three months was measured by unmasked examiners, to avoid unmasking (due to visible postoperative changes in implant-treated eyes at these relatively early postoperative visits). The visual acuity measurement protocol was enforced by a visual function quality assurance committee which that certified all examiners and conducted regular site visits for protocol enforcement. Additional clinical information collected at all visits by study-certified ophthalmologists included the presence of posterior synechiae, anterior chamber cells and flare (each measured per SUN guidelines[16]), lens status (clear or trivial opacities, cataract, pseudophakia or aphakia), and the presence of choroidal neovascularization, retinal vascular sheathing and/or retinal detachment. During the MUST Trial, vitreous haze was measured using a modification of

the SUN-endorsed National Eye Institute scale[16;21] in which 0.5+ haze was omitted. The presence of peripheral anterior synechiae was assessed by annual gonioscopy. In addition, Goldmann applanation tonometry measurement of intraocular pressure (the median of three measurements) was conducted at every visit. Macular thickness was determined by masked Reading Center gradings of macular thickness based on time-domain (Zeiss Stratus 3, Carl Zeiss AG, Oberkochen, Germany) optical coherence tomography (OCT) images.

Baseline characteristics were compared across the four sites of uveitis inflammation using multinomial regression with generalized estimating equations to account for correlation due to patients with two affected eyes. Visual acuity in each eye was dichotomized as better than >20/50 Snellen equivalent or 20/50 or worse. Logistic regression with generalized estimating equations was used to assess the association of baseline characteristics with dichotomized visual acuity at baseline. Baseline BCVA also was modeled continuously. Because of the left-skewness of the distribution due to observations with poor visual acuity, robust linear regression was used to downweight outliers and bootstrapping with 2,000 repetitions clustering on patient was used to obtain valid estimates of the standard error. The adjusted model included all baseline predictive factors. Because missingness was informative, vitreous haze, OCT retinal thickness, and retinal sheathing included a category for “missing.” Seven observations with missing data in other variables were excluded from the multiple regression analysis. Change in visual acuity at 2 years was modeled using robust linear regression and bootstrapping with 2,000 repetitions clustering on patient and adjusted for baseline visual acuity. Analyses were stratified by visual acuity at baseline into better than 20/50 Snellen equivalent or 20/50 or worse. Patient-level predictive factors were modeled as time-independent and eye-level predictive factors were categorized into one of four categories: normal at both baseline and two years; normal at baseline and abnormal at two years; abnormal at baseline and normal at two years; or abnormal at both baseline and two years. Wald’s test was used to assess whether the relationship of change in visual acuity at two years with the predictive factor varied by baseline visual acuity subgroup. Statistical analyses were done with SAS (SAS Institute 2011, Base SAS 9.3 Procedures Guide) and Stata (StataCorp 2013, Stata Statistical Software: release 13).

Results

Among the 479 uveitic eyes of 255 patients enrolled in the MUST Trial, 475 eyes of 254 patients had complete visual acuity information at baseline and were assessed for the presenting visual acuity analyses. Characteristics of this population have been reported previously.[7;9] Four hundred twenty-nine eyes of 231 patients had complete visual acuity at the two year follow-up visit (excluding two eyes with no light perception at baseline which could not have changed), and were used in the incidence analyses (Figure 1). At baseline, BCVA was distributed widely, from better than 20/20 to no light perception, with a skew toward better vision and a median BCVA=20/40 (See Figure 2).

Factors Predictive of Reduced Mean Visual Acuity at Baseline

Factors significantly associated with differences in mean BCVA at baseline are summarized in Table 1 (a focused excerpt of a complete summary of all factors studied which is

available as Supplemental Table 1 online at http://www.ajo.com). Age >50 years was associated with poorer baseline BCVA (mean BCVA four letters worse (−4 letters), adjusted model p=0.05). Sex, race, smoking status, presence of diabetes mellitus, and presence of a systemic inflammatory disease associated with uveitis were not significantly related to baseline visual acuity status. With respect to intermediate uveitis, posterior uveitis (−6 letters, p=0.02) was associated with significantly lower BCVA, whereas panuveitis (−3 letters, p=0.26) and anterior and intermediate uveitis had fairly similar BCVA (−1 letters, p=0.82). With respect to eyes with uveitis diagnosed fewer than six years before baseline, eyes with uveitis diagnosed >10 years prior to baseline had significantly worse BCVA (−10 letters, p=0.005), whereas those diagnosed 6–10 years earlier had similar BCVA (−1 letters, p=0.78). After adjusting for other factors (including pathologies complicating inflammation), anterior cell count and the level of vitreous haze were not significantly associated with baseline BCVA, although vitreous haze 2+ or worse tended to be associated with lower BCVA (−4 letters, p=0.06). Detectable anterior chamber flare was associated with worse baseline BCVA (grade 1+: −7 letters, p=0.01; grade 2+ or worse: −12 letters, p=0.01).

Uveitic complications associated with decreased BCVA included cataract (−6 letters, p=0.01), retinal detachment (−10 letters, p=0.03) and macular thickening by OCT.[22] Eyes that had undergone cataract surgery prior to baseline tended to have reduced mean BCVA compared with eyes with clear lenses (−5 letters, p=0.07). The degree of macular thickening was associated with lower mean BCVA in a dose-response relationship (240–339 μm: −4 letters, p=0.08; ≥340 μm: − 16 letters, p<0.001, each compared with “normal” thickness ≤239 μm). With respect to normal intraocular pressure (IOP) (8–20 mmHg), neither low IOP (≤7 mmHg: −8 letters, p=0.36) nor high IOP (≥21 mmHg: −5 letters, p=0.12) was associated with significantly different presenting mean BCVA, although both tended to present with worse BCVA than normotensive eyes.

Loss of Visual Acuity During Follow-up

The relationship between baseline BCVA and BCVA at two years is plotted as Figure 3. Among the 429 eyes with BCVA measurements at both baseline and two years, 38 (9%) worsened by ≥ 3 lines, 71 (16%) improved by ≥ 3 lines and 320 (75%) had baseline and two-year visual acuity within three lines of each other. Eyes with worse baseline BCVA tended to show more improvement than eyes presenting with better BCVA. Among 62 eyes presenting with BCVA of 20/200 or worse, only six (10%) experienced a loss of more than three lines of VA whereas 30 (48%) and 21 (34%) respectively gained ≥3 and ≥6 lines respectively, with a mean gain in BCVA of 20.2 letters. For those presenting with BCVA of 20/50 or worse but better than 20/200, eight (7%) and five (4%) respectively lost ≥3 and ≥6 lines whereas 33 (30%) and 12 (11%) respectively gained ≥3 and ≥6 lines, with an overall net mean gain of 9.9 letters. Among eyes presenting with BCVA better than 20/50, potential for improvement was limited, but most eyes retained similar or better BCVA, with only 24 (9%) losing ≥3 lines and 12 (5%) losing ≥6 lines of BCVA, with an overall median improvement of +1.0 letters (interquartile range −5.0, +6.0).

Evaluation of factors potentially related to the two-year change in BCVA reconfirmed that treatment assignment to systemic or implant therapy was not a significant predictor[7] (see Table 2; a complete list of factors studied is available as Supplemental Table 2 at http://www.ajo.com). Age, sex, race, diabetes mellitus status, smoking status, and laterality of uveitis were not associated with mean change in BCVA outcome at two years. The presence of an associated systemic immune-mediated disease was associated with a slightly more favorable mean change in BCVA outcome (+3 letters, p=0.04). Cases of anterior and intermediate, intermediate, posterior, and panuveitis all had a similar degree of improvement during follow-up (from different baselines). Compared with <6 years' duration of uveitis, increased duration of uveitis was associated with relative worsening in BCVA during follow-up, with a dose-response relationship [6–10 years' duration (−3 letters, p=0.03), >10 years' duration (−8 letters, p<001)]. Occurrence of cataract surgery during follow-up was associated with visual improvement (+5 letters, p=0.02); resolution of posterior synechiae during follow-up (implying occurrence of cataract surgery) had a similar effect. In contrast, presence of a cataract at two years that had been present at baseline (−6 letters, p=0.01) and pseudophakia at baseline (−5 letters, p=0.03) both were associated with worsening of BCVA over two years' follow-up. Regarding inflammatory clinical signs, resolution of anterior chamber cells present at baseline was associated with BCVA improvement (+4 letters, p=0.02), whereas incidence of anterior chamber flare (≥1+ vs zero at baseline, −7 letters, p=0.04), incidence of vitreous haze (1+ or worse, grade 0 at baseline: −30 letters, p<0.001) and persistence of vitreous haze (presence at both baseline and two years; −15 letters, p=0.04) were associated with worsening of mean BCVA over two years. Incidence of macular edema was associated with worsening of BCVA (−11, p=0.001), whereas resolution of macular edema was associated with improvement of BCVA (+5, p=0.04). Other ocular characteristics, including IOP fluctuations, were not associated with significant mean changes in BCVA over two years.

Discussion

Our results demonstrate in a detailed fashion that most uveitic eyes of participants in the MUST Trial had favorable visual outcomes, suggesting that severe cases of uveitis for which systemic corticosteroid therapy is indicated have a generally favorable prognosis under best practices systemic[10] or implant[11;12] therapy in a subspecialty setting. Many more of the eyes intially 20/50 or worse improved than worsened, especially eyes with baseline BCVA of 20/200 or worse. The latter eyes often experienced a large improvement in BCVA over time. Eyes presenting with BCVA of better than 20/50 at baseline did not improve on average, reflecting a "ceiling effect" because of limited room for improvement in this group (see Figure 1), but few worsened. However, some eyes worsened, indicating that the prognosis of patients is heterogeneous, which to some extent is predicted by predictive factors identified here.

Our results confirmed that more posteriorly located uveitis tended to have worse visual acuity than intermediate or anterior/intermediate uveitis cases. On average, posterior uveitis cases presented with the worst visual acuity, whereas intermediate uveitis without accompanying anterior uveitis had the best initial visual acuity and the other groups not significantly worse than intermediate. Posterior uveitis cases may suffer irrecoverable visual

loss from retinal damage near the onset of the disease, which may explain the difference. Regardless, eyes in all categories of uveitis tended to improve equally from their baseline state while under the study treatments.

Among the demographic characteristics, higher age was associated marginally with lower visual acuity at presentation—probably reflecting general population associations between greater age and worse mean visual acuity[23]—but did not affect change in visual acuity over the two years of follow-up under treatment. Sex, race, smoking status, diabetes status, and bilaterality of uveitis were not associated with significant differences in presenting visual acuity or visual acuity outcome over a two-year period in this population. While prior reports have found smokers have a higher risk of macular edema among intermediate uveitis cases,[24] and more recurrences in a broader population of ocular inflammation patients,[25] no direct association between smoking and visual acuity outcome was observed in this population of intermediate, posterior, and panuveitis cases.

Regarding our observations that eyes with longstanding uveitis tended to have a worse visual outcome while participating in the trial, there are a number of potential explanations. One possibility is that there is some tipping point of cumulative exposure to inflammation after which an eye is destined to do worse over time. Another possibility is that such eyes may have been less well managed before the trial than during it, which somehow may have perpetuated a worse clinical course even during the trial. In either case, the results suggest there is value with early institution of appropriate treatment. Such appropriate treatment could be accomplished either via early subspecialty care or care following published guidelines[10–12] administered by other ophthalmologists.

In general, we found that most markers of ocular inflammatory activity at baseline tended to be associated with worse presenting visual acuity, as were several inflammatory complications, consistent with expectations. Abnormal IOP during follow-up was not a predictor of visual acuity outcome, suggesting that eyes with initially abnormal IOP were able to be stabilized enough to avoid loss of visual acuity on average (at least over two years), despite a high risk of glaucoma during this period.[26] Further observation will be needed to determine whether the high incidence of glaucoma in this population (especially in the implant arm) is associated with long-term adverse visual outcomes. Macular edema as measured by OCT was associated with worse presenting visual acuity, worse outcome when it was incident during follow-up, and improvement in visual acuity outcome when it was observed to resolve, consistent with expectations.[27;28] Exudative retinal detachment was associated with worse presenting visual acuity, but the visual improvement associated with resolution thereof was modest—not a statistically significant change. Cataract was associated with lower visual acuity at presentation, persistence of cataract during follow-up was associated with further worsening, and cataract surgery during follow-up among eyes presenting with cataract was associated with visual acuity improvement, as expected. However, eyes that had undergone cataract surgery prior to presentation presented with lower visual acuity, and also had significantly less favorable visual acuity outcome during follow-up despite clinical management under a common study protocol utilizing state of the art practices. The latter observation may reflect a greater severity of disease in cases requiring early cataract surgery, or could suggest that there is an advantage to undergoing

cataract surgery while under treatment according to the study protocol, based on recommended standards for systemic[10] or implant[11;12] therapy. Further data will be needed to evaluate this issue.

As with all human studies, these results must be interpreted in the context of their methodological limitations. Cases were enrolled based on eligibility at the time they were encountered. The clinical history of such cases is unknown, making it harder to evaluate the meaning of prevalent reductions in visual acuity and the factors associated therewith. As is typical in exploratory epidemiological studies, P-values presented in the manuscript are nominal and have not been adjusted for multiple comparisons. Because of the large number of tests and associated increase in Type I error, replication is needed, and may fail to confirm some of the associations. Nevertheless, most observations were strong and consistent with inferences that make sense from a clinical perspective. It is important to note that factors associated with poorer or better visual acuity at presentation do not have an identical meaning to factors associated with poorer or better visual outcome under therapy. The former may reflect a scenario where inflammation may or may not have been managed optimally, whereas the latter would reflect outcomes under standard of care treatment. When similar predictive factors are identified in both analyses, it is most likely that such factors are predictive of visual outcome across a variety of clinical scenarios. Other limitations include enrollment of subjects at tertiary centers; results should be generalizable to the tertiary setting, but may represent expected outcomes in patients more severe on average than encountered in a general ophthalmology setting. In addition, intermediate uveitis cases often do not require long-term, aggressive treatment;[29] the results reported here would apply to the minority who do require such treatment. Strengths of the study include ascertainment of visual acuity using well-established, gold-standard techniques following a rigorous common clinical trial protocol; ascertainment of clinical characteristics of interest by MUST-certified expert uveitis specialists; favorable sample size; and a reasonably favorable length of follow-up (two years).

In summary, our results suggest that the average case of anterior & intermediate, intermediate, posterior, or panuveitis tends to remain stable or improve under the standard of care treatment protocols used in the trial.[10–12] Visual acuity outcomes did not differ significantly between the randomized treatment groups. Uveitis primarily affecting the choroid and/or retina tends to be associated with worse visual acuity, but not with worse prognosis for further loss of vision while under standard of care management with implant or systemic therapy. Higher age, longer duration of uveitis, anterior chamber flare, exudative retinal detachment, cataract, and macular edema were associated with lower visual acuity, with the latter two factors largely reversible if they could be resolved by treatment. Successful control of inflammation during the MUST Trial tended to be associated with visual improvement, whereas persistence or incidence of vitreous haze was associated with worsening. The observation that cataract surgery prior to enrollment was associated with both poorer presenting visual acuity and poorer visual acuity outcome during follow-up should be investigated further; it may represent a disease severity indicator. In general, these results attest to the considerable value of prompt, aggressive management of anterior and intermediate, intermediate, posterior, and panuveitis following best practice recommendations as implemented in the MUST Trial.[7;10–12] Appropriate interventions to

address complications of uveitis that may appear over time should be implemented promptly as well. Ophthalmologists prepared to carry out such management should direct management of patients with vision-threatening intermediate, posterior, and panuveitis, to ensure that these therapeutic goals will be achieved.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Biographies

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Mark L. Van Natta is an associate scientist in the Department of Epidemiology at Johns Hopkins Bloomberg School of Public Health. He received a Masters of Health Science in Biostatistics from the School in 1987. He has worked at the Johns Hopkins Center for Clinical Trials since 1985 and was the director of the Coordinating Center for the National Eye Institute-sponsored Studies of Ocular Complications of AIDS from 2013-2015.

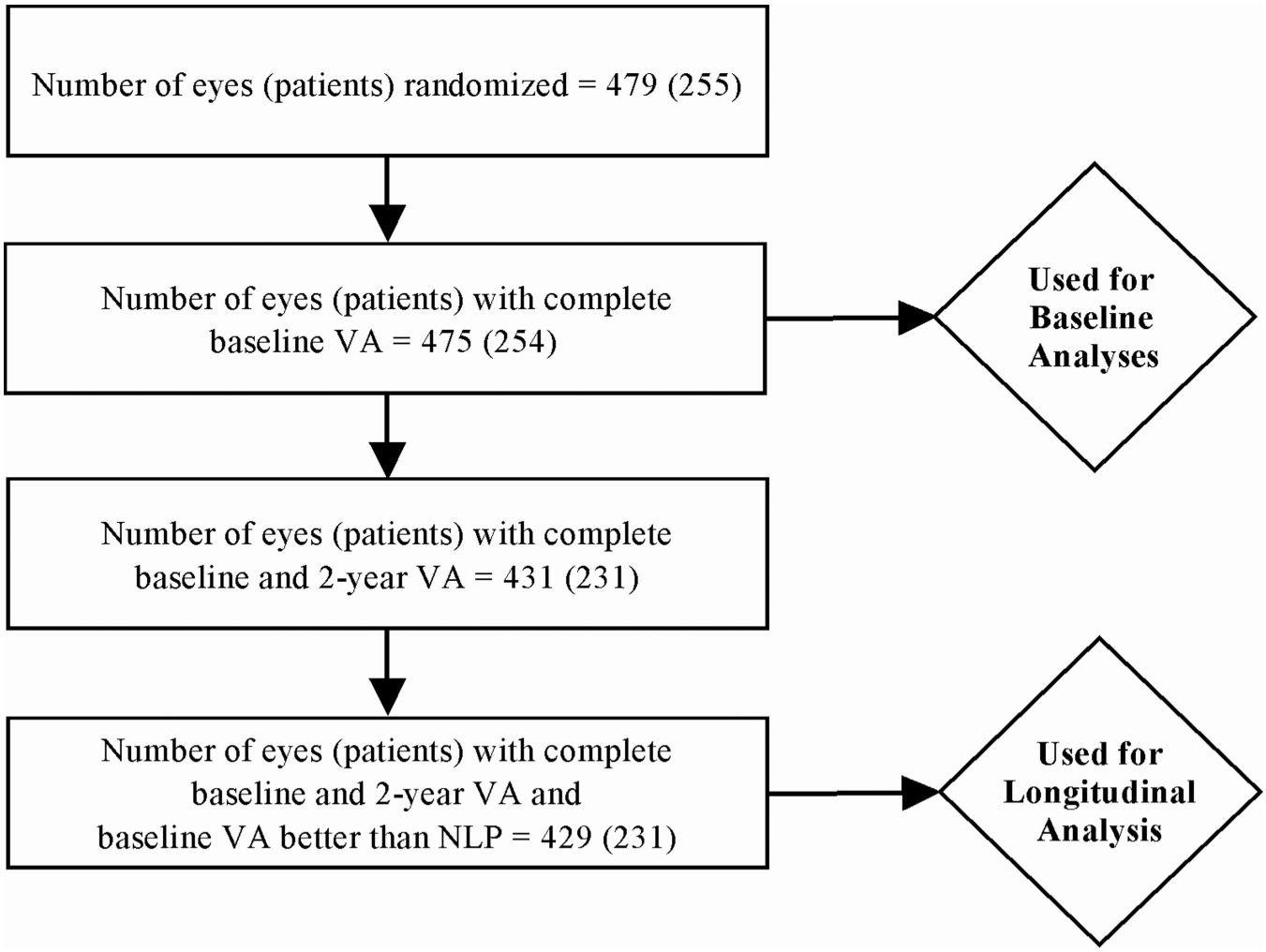

Figure 1.
Flow chart indicating inclusion of uveitic eyes from Multicenter Uveitis Steroid Treatment (MUST) Trial participants in the baseline and longitudinal visual acuity analyses.

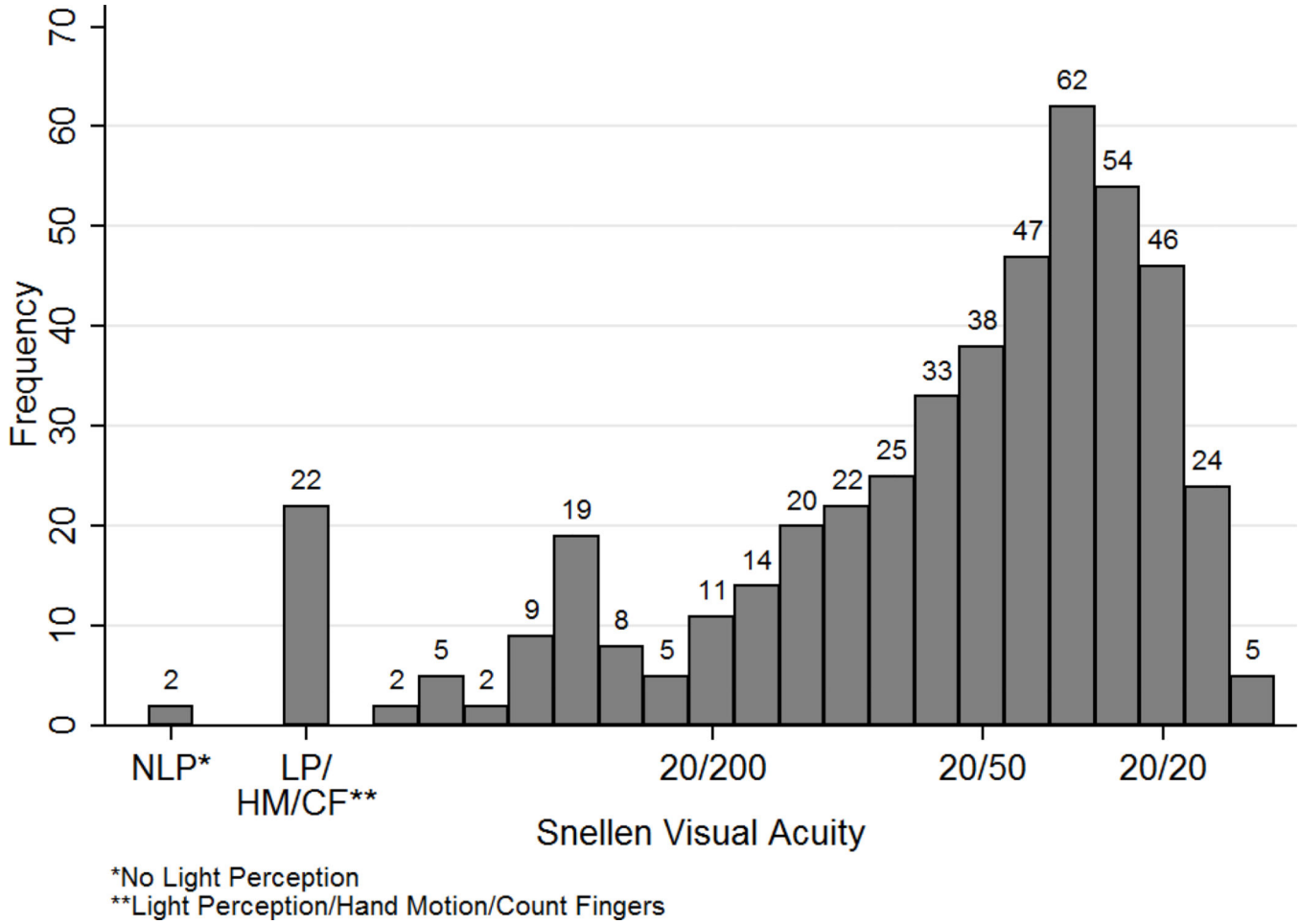

Figure 2.

Distribution of best-corrected visual acuity at the baseline visit, uveitic eyes of participants in the Multicenter Uveitis Steroid Treatment (MUST) Trial.

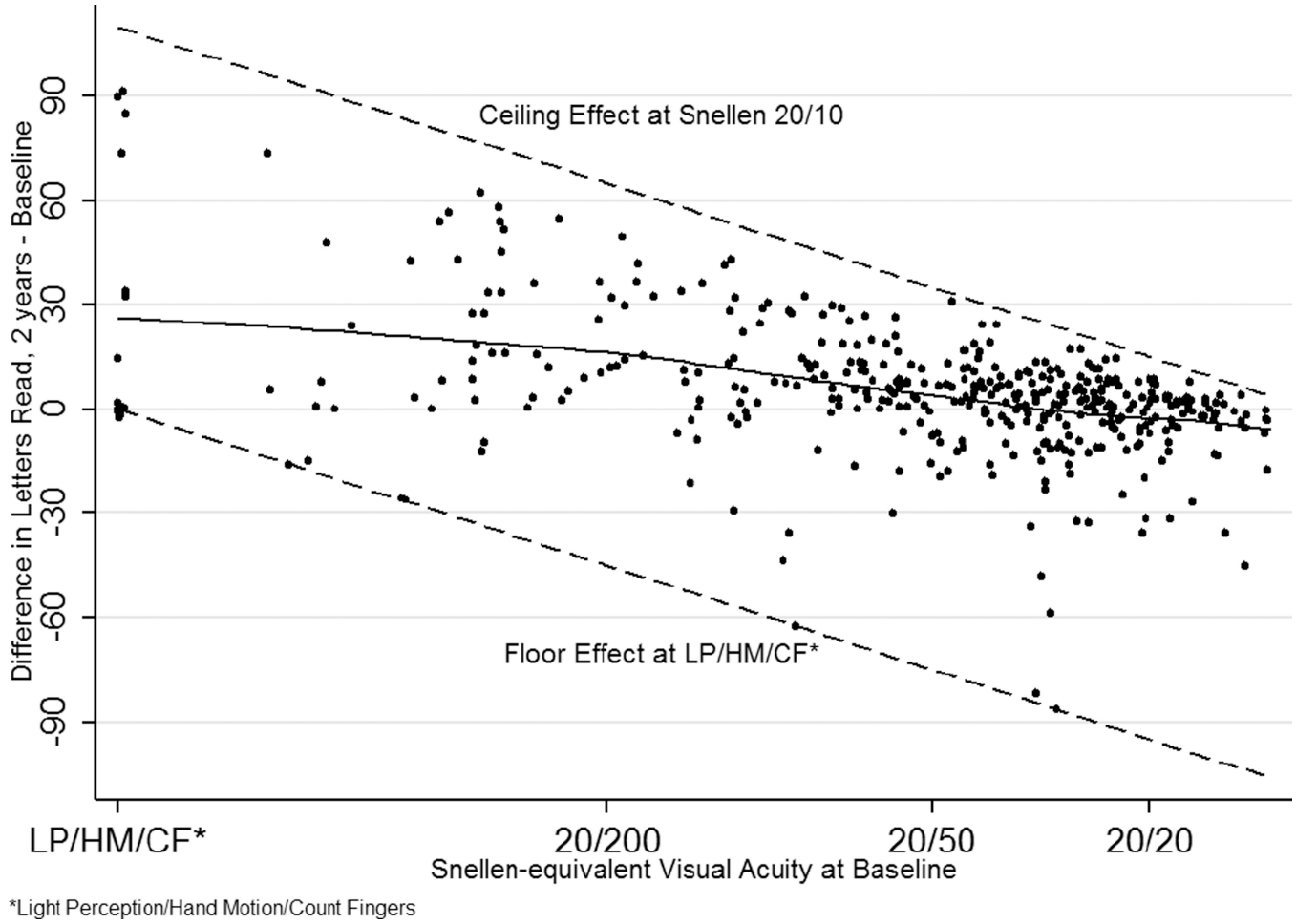

Figure 3.

Change in visual acuity between baseline and two years, by baseline visual acuity status, uveitic eyes of participants in the Multicenter Uveitis Steroid Treatment (MUST) Trial. Floor and Ceiling lines are given indicating LP (Light Perception Only)/HM (Hand Movements only)/CF (Counting Fingers only) and 20/10 best-corrected visual acuity. A lowess curve demonstrates the average change across a range of baseline Snellen-equivalent visual acuity scores.

Table 1

Crude and adjusted association between patient-specific and eye-specific factors and visual acuity at baseline in 475 uveitic eyes enrolled in the Multicenter Uveitis Steroid Treatment Trial*

	Baseline visual acuity			
Baseline factor	**Crude**		**Adjusted***	
	Mean Difference±SE (letters)	**P-value**	**Mean Difference±SE (letters)**	**P-value**
Patient-specific				
Type of uveitis				
Anterior/intermediate vs. intermediate	−7±4	0.11	−1±3	0.82
Posterior vs. intermediate	−3±3	0.30	−6±3	0.02
Panuveitis vs. intermediate	−6±3	0.04	−3±3	0.26
Age 50+ vs. <50 yrs	−7±2	0.002	−4±2	0.05
Years since uveitis diagnosis				
6–10 vs <6	−5±3	0.10	−1±3	0.78
>10 vs <6	−17±4	<0.001	−10±4	0.005
Eye-specific				
IOP (mmHg)				
≤7 vs. 8–20	−40±9	<0.001	−8±9	0.36
21+ vs. 8–20	2±3	0.52	−5±4	0.12
Anterior chamber cells				
0.5+ vs. none	0±2	0.87	0±3	0.86
1+ vs. none	−11±4	0.02	−3±4	0.34
>1+ vs none	−12±8	0.12	6±5	0.26
Anterior chamber flare				
1+ vs. 0	−6±3	0.02	−7±3	0.01
2+ or more vs. 0	−26±6	<0.001	−12±5	0.01
Lens status				
Cataract vs. normal	−13±3	<0.001	−6±2	0.01
Pseudophakic/aphakic vs. normal	−17±2	<0.001	−5±3	0.07
Vitreous haze				
1+ vs. clear	0±2	0.88	2±2	0.20
>1+ vs. clear	−17±3	<0.001	−4±3	0.12
Missing vs. clear	−52±12	<0.001	1±14	0.97
OCT retinal thickness (μm)				
240–339 vs. <240	−7±2	<0.001	−4±2	0.08
340+ vs. <240	−22±3	<0.001	−16±3	<0.001
Missing vs. <240	−59±11	<0.001	−36±11	0.001
Exudative retinal detachment: Yes vs. No	−2±9	0.80	−10±4	0.03

[*] Crude analyses reflect un-adjusted associations between each covariate and best-corrected visual acuity. In the adjusted model, the associations between each covariate and best-corrected visual acuity are adjusted for all of the other variables shown. There were 468 non-missing observations. SE=standard error; IOP=intraocular pressure; OCT=optical coherence tomography. Factors also studied which were not associated with differences in mean best-corrected visual acuity at baseline included: sex, race, smoking status, presence of systemic inflammatory disease, diagnosis with diabetes mellitus, bilaterality of uveitis, and the presence of anterior or posterior synechiae (full details available in Supplemental Table 1, available online at http://www.ajo.com).

Table 2

Risk factors associated with adjusted two-year change in visual acuity, stratified by type of uveitis, uveitic eyes enrolled in the Multicenter Uveitis Steroid Treatment Trial*

	Combined		
	n	**Mean Difference in Letters Read from BL ± Standard Error**	**P**
Overall	429	5±1	<.001
Patient-specific at baseline			
Treatment group			
Implant	217	ref	
Systemic	212	−2±2	0.25
Age			
< 65 yrs	385	ref	
65+ yrs	44	1±3	0.76
Associated systemic disease			
No	307	ref	
Yes	122	3±1	0.04
Years since uveitis diagnosis			
< 6	244	ref	
6–10	101	−3±2	0.03
>10	79	−8±2	<.001
Eye-specific			
Posterior synechiae			
Norm-BL, Norm-2yr	321	ref	
Norm-BL, Abnl-2yr	14	−2±6	0.69
Abnl-BL, Norm-2yr	61	7±3	0.01
Abnl-BL, Abnl-2yr	33	4±3	0.18
Anterior chamber cells			
Norm-BL, Norm-2yr	184	ref	
Norm-BL, Abnl-2yr	36	−1±3	0.72
Abnl-BL, Norm-2yr	125	4±2	0.02
Abnl-BL, Abnl-2yr	83	1±2	0.71
Anterior chamber flare			
Norm-BL, Norm-2yr	206	ref	
Norm-BL, Abnl-2yr	20	−7±3	0.04
Abnl-BL, Norm-2yr	118	3±2	0.06
Abnl-BL, Abnl-2yr	84	−1±2	0.74
Lens status¶			
Norm-BL, Norm-2yr	35	ref	

	Combined		
	n	**Mean Difference in Letters Read from BL ± Standard Error**	**P**
Norm-BL, Cataract-2yr	21	−6±5	0.23
Norm-BL, Pseudophakic-2 yr	43	0±2	0.90
Cataract-BL, Cataract-2yr	44	−6±2	0.01
Cataract-BL, Pseudophakic-2yr	100	5±3	0.02
Pseudophakic-BL & 2 yr	181	−5±2	0.03
Vitreous haze‡			
Norm-BL, Norm-2yr	304	ref	
Norm-BL, Abnl-2yr	5	−30±4	<.001
Abnl-BL, Norm-2yr	79	3±2	0.10
Abnl-BL, Abnl-2yr	7	−15±7	0.04
Missing at BL or 2yr	34	2±13	0.90
OCT re9nal thickness†			
Norm-BL, Norm-2yr	211	ref	
Norm-BL, Abnl-2yr	30	−11±3	0.001
Abnl-BL, Norm-2yr	75	5±2	0.04
Abnl-BL, Abnl-2yr	53	−1±3	0.79
Missing at BL or 2 yr	60	0±5	0.97
Exudative retinal detachment			
Norm-BL, Norm-2yr	413	ref	
Norm-BL, Abnl-2yr	1	NC	
Abnl-BL, Norm-2yr	15	−2±4	0.57
Abnl-BL, Abnl-2yr	0	NC	

*Adjusted for baseline visual acuity. N=number of eyes; BL=baseline; ref=reference group; yr=year; yrs=years; Norm=normal; Abnl=abnormal. Additional variables studied which were not associated with a change in mean best-corrected visual acuity from baseline through two years included: age, race, smoking status, diagnosis with diabetes mellitus, bilateral uveitis, intraocular pressure status, presence of retinal vascular sheathing, or presence/absence of exudative retinal detachment (full details available in Supplemental Table 2, available online at http://www.ajo.com).

†P-value < 0.001 for interaction test of type of uveitis by optical coherence tomography (OCT) retinal thickness category (Missing category not included)

‡Normal defined as 0 or 1+; Abnormal defined as 2+, 3+ or 4+

¶5 eyes that were cataract at BL and normal at 2 yrs were excluded