SUPPLEMENTARY MATERIAL

OCT macular volume as a predictor of vascular leakage in uveitis

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Leakage and OCT metrics

The objective of the analysis of longitudinal leakage scores was to characterise the relationship between leakage scores and each of the OCT metrics. We conducted a complete case analysis, which is a valid approach to handle missing data when the missing data does not depend on the outcome. Multiple imputation was not considered due to lack of auxiliary data, and imputation model could introduce bias if miss-specified.

To model the longitudinal leakage score, GLMM with negative binomial link was considered because the leakage score is an over-dispersed count data. The independent variables were selected based on background knowledge, including reviewing literature and consulting clinical experts. Inclusion of the interaction term is based on data visualisation and by performing likelihood ratio tests to compare goodness of fit of the models. In the GLMM models with negative binomial link, independent variables were standardised, which mitigate the model convergence and multi-collinearity problem as the final model contained interaction term between time and OCT metrics.

Appendix table 1 shows the fixed effects of the (final) GLMM model for leakage scores with each of the three OCT metrics, i.e., MV in 6mm, MV in 3mm and CST, as covariate of interest. The corresponding random effects are reported in Appendix Table 2, which considered the inter-eye correlation and between patient variability. Appendix Table 3 reports the Akaike Information Criteria (AIC), Bayesian Information Criteria (BIC) and deviance value, which compares the goodness of fit of the three GLMM models. The smaller the AIC or BIC or deviance, the better the fit of the model is.

Appendix Table 1: Estimates of the fixed effects from the GLMM models for leakage scores, with each of the three OCT metrics as covariate of interest

	MV in 6mm		**MV in 3mm**		**CST**	
	Estimate (SD)	**p value**	**Estimate (SD)**	**p value**	**Estimate (SD)**	**p value**
Intercept	1.150 (0.125)	<0.001	1.107 (0.132)	<0.001	1.075 (0.137)	<0.001
Time	-0.128 (0.030)	<0.001	-0.156 (0.028)	<0.001	-0.181 (0.027)	<0.001
OCT metrics	0.414 (0.028)	<0.001	0.274 (0.022)	<0.001	0.226 (0.021)	<0.001
Gender (Male vs Female)	-0.164 (0.139)	0.237	-0.232 (0.144)	0.107	-0.261 (0.150)	0.082
Age	0.008 (0.069)	0.905	-0.099 (0.071)	0.162	-0.117 (0.074)	0.112
VA	0.128 (0.033)	<0.001	0.193 (0.033)	<0.001	0.209 (0.034)	<0.001
Local enhancement (Yes vs No)	0.150 (0.122)	0.221	0.241 (0.130)	0.065	0.296 (0.137)	0.030
Interaction term between Time and OCT metrics	0.103 (0.022)	<0.001	0.104 (0.019)	<0.001	0.092 (0.019)	<0.001

SD: standard deviation

Appendix Table 2: Estimates of the random effects from the GLMM models for leakage scores, with each of the three OCT metrics as covariate of interest

Variance for random effects	**MV in 6mm**	**MV in 3mm**	**CST**
Eye level	0.076	0.098	0.118
Patient level	0.214	0.224	0.240

Appendix Table 3: Comparisons of AIC, BIC and deviance of GLMM models for leakage scores, with each of the three OCT metrics as covariate of interest

	MV in 6mm	**MV in 3mm**	**CST**
AIC	2896.3	2947.6	2985.2
BIC	2946.0	2997.3	3034.9
Deviance	2874.3	2925.6	2963.2

AIC: Akaike Information Criteria; BIC: Bayesian Information Criteria

Vitreous haze and leakage

The objective of the analysis of vitreous haze was to characterise the relationship between vitreous haze and leakage scores, and to investigate whether leakage score is able to predict the presence of vitreous haze. GLMM with binomial link was considered because the outcome variable is a binary variable, i.e, presence of vitreous haze or not. Interaction term was not included in the final based on likelihood ratio test, and the independent variables were not standardised. Appendix Table 4 shows the fixed effects of the (final) GLMM model for vitreous haze. The variance for random effects are 0.578 and 5.778 respectively for eye level and patient level.

Appendix Table 4: Estimates of the fixed effects from the GLMM model for vitreous haze, with leakage score as covariate of interest

	Estimate (SD)	**Exp (Estimate)**	**p value**
Intercept	-2.011 (1.160)	0.134	0.083
Time	-0.091 (0.022)	0.913	<0.001
Leakage score	0.989 (0.101)	2.689	<0.001
Gender (Male vs Female)	-0.084 (0.751)	0.919	0.911
Age	-0.012 (0.029)	0.988	0.673
VA	0.325 (0.958)	1.384	0.734
Local enhancement (Yes vs No)	-1.064 (0.702)	0.345	0.130

SD: standard deviation

Furthermore, we conducted ROC analysis using the predicted outcomes of the fitted GLMM model for vitreous haze. The AUC is 0.906 (95% Delong's CI: 0.884-0.927). We used the Youden's index method to choose the optimal cut-off point, which is equivalent to the cut-off point that has the highest sum of sensitivity and specificity. The optimal sensitivity value is 0.868 (95% CI 0.833-0.903), and the optimal specificity is 0.783 (95% CI: 0.738-0.828). The corresponding negative predictive value (NPV, which is the proportion of those that are predicted as without vitreous haze who indeed do not have vitreous haze) is 0.843 (95% CI: 0.802-0.884), and the positive predictive value (PPV, which is the proportion of those that are predicted as presence of vitreous haze who indeed have vitreous haze) is 0.815 (95% CI: 0.776-0.854). The 95% CI for sensitivity, specificity, PPV and NPV were calculated based on the simple asymptotic method.