

Supplementary Material

Prediction Models for Recurrence of Retinopathy of Prematurity after Intravitreal Ranibizumab or Laser Photocoagulation Treatment: A Multicenter Cohort Study

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Table S1. Comparison between the ROP infants treated with intravitreal injection of Ranibizumab or laser photocoagulation.

Table S2. Comparison between the ROP infants with recurrence and non-recurrence after intravitreal injection of Ranibizumab or laser photocoagulation treatment.

Figure S1. Weight ratios of each characteristic in different machine learning models.

Figure S2. Binary comparison evaluating the concordance between the prediction models and retinal specialists using the test dataset.

Table S1. Comparison between the ROP infants treated with intravitreal injection of Ranibizumab or laser photocoagulation.

Baseline characteristics	IVR group (n=344)	LP group (n=96)	<i>P value</i>
Gender (No, female%)	129 (37.5)	32 (33.3)	0.559
Gestational age, mean (SD), weeks	28.2 (2.5)	28.2 (2.1)	0.951
Birth weight, mean (SD), kg	1.2 (0.4)	1.1 (0.3)	0.368
Birth head circumference, mean (SD), cm	28.2 (2.8)	26.8 (3.0)	0.061
Stage, (%)			
Stage 2	55 (16.0)	8 (8.3)	0.92
Stage 3	268 (77.9)	80 (83.3)	0.231
Stage 4A	21 (6.1)	8 (8.3)	0.140
Zone, (%)			
Zone I	98 (28.5)	14 (14.6)	0.090
Zone II	246 (71.5)	82 (85.4)	0.300
Plus disease, (%)	224 (65.1)	88 (91.7)	0.948
AP-ROP, (%)	48 (14.40)	4 (4.2)	0.053
Recurrence, (%)	62 (18.0)	7 (7.3)	0.002*
1 min Apgar scoring, mean (SD)	7.7 (2.2)	7.4 (1.8)	0.262
5 min Apgar scoring, mean (SD)	9.0 (1.6)	8.7 (1.4)	0.129
10 min Apgar scoring, mean (SD)	9.2 (1.1)	9.0 (1.0)	0.096
Neonatal pneumonia, (%)	134 (41.9)	56 (58.3)	0.050
Septicemia, (%)	56 (16.3)	31 (32.3)	0.054
Catheter arteriosus, (%)	101 (29.4)	32 (33.3)	0.563
Respiratory distress, (%)	60 (17.4)	20 (20.8)	0.210
Bronchial dysplasia, (%)	170 (49.4)	67 (69.8)	<0.001*
Anemia, (%)	53 (15.4)	50 (52.1)	0.040*
Total bilirubin, mean (SD), µmol/L	65.2 (47.9)	70.5 (53.7)	0.492
Red blood cell count, mean (SD), T/L	4.0 (0.8)	4.0 (1.0)	0.634
White blood cell count, mean (SD), G/L	8.3 (5.3)	10.1 (6.6)	0.208
Platelet count, mean (SD), G/L	246.7(88.7)	263.6 (37.0)	0.511

Table S1. Comparison between the ROP infants treated with intravitreal injection of Ranibizumab or laser photocoagulation (continued).

Baseline characteristics	IVR group (n=344)	LP group (n=96)	<i>P</i> value
Neutrophil count, mean (SD), G/L	3.3 (3.1)	5.1 (5.5)	0.084
Lymphocyte count, mean (SD), G/L	3.5 (1.7)	3.2 (1.5)	0.333
Maternal age, mean (SD), years	29.0 (5.1)	31.2 (5.1)	0.528
IVF-ET, (%)	35 (10.2)	22 (22.9)	0.314
Maternal uterine infection, (%)	18 (5.2)	20 (20.8)	0.060
Gestational hypertension, (%)	25 (7.3)	10 (10.4)	0.582
Gestational diabetes, (%)	31 (9.0)	11 (11.5)	0.737
Glucocorticoid therapy, (%)	163 (47.4)	43 (44.8)	0.163

*The *P* values were obtained by comparing the two groups above. Continuous variables groups were analyzed by ANOVA. Categorical variables groups were analyzed by Chi-square test. Nonparametric variables were analyzed using Mann-Whitney Test. The *P* values have been corrected and verified.

Abbreviations: ROP: retinopathy of prematurity, IVR: intravitreal injection of ranibizumab, LP: laser photocoagulation, SD: standard deviation, AP-ROP: acute posterior polar retinopathy of prematurity, IVF-ET: In vitro fertilization and embryo transfer.

Table S2. Comparison between the ROP infants with recurrence and non-recurrence after intravitreal injection of Ranibizumab or laser photocoagulation treatment.

Baseline characteristics	IVR group (n=344)			LP group (n=96)		
	Non-recurrence (n=282)	Recurrence (n=62)	<i>P</i> <i>value</i>	Non-recurrence (n=89)	Recurrence (n=7)	<i>P</i> <i>value</i>
Gender (No, female%)	51 (36.4)	15 (48.4)	0.060	28 (54.9)	2 (50.0)	0.165
Gestational age, mean (SD), weeks	28.4 (2.5)	27.3 (2.4)	0.263	28.1 (2.1)	30.0 (1.7)	0.166
Birth weight, mean (SD), kg	1.2 (0.4)	1.0 (0.4)	0.230	1.1 (0.4)	1.1 (0.7)	0.891
Birth head circumference, mean (SD), cm	28.2 (2.3)	28.1 (4.5)	0.951	26.8 (3.1)	26.0 (3.0)	0.720
Stage, (%)						
Stage 2	20 (14.3)	2 (6.3)	0.026*	3 (5.9)	0	0.054
Stage 3	115 (82.1)	23 (71.9)	0.035*	41 (80.4)	3 (75.0)	0.028*
Stage 4A	5 (3.6)	7 (21.9)	0.012*	7 (13.7)	1 (25.0)	0.003*
Zone, (%)						
Zone I	33 (23.6)	11 (34.4)	0.011*	10 (19.6)	2 (50.0)	0.005*
Zone II	107 (76.4)	21 (65.6)	0.023*	41 (80.4)	2 (50.0)	0.021*
Plus disease, (%)	106 (75.7)	23 (71.9)	0.332	49 (95.8)	4 (100)	0.725
AP-ROP, (%)	17 (12.1)	9 (28.1)	0.003*	4 (7.8)	0	0.557
1 min Apgar scoring, mean (SD)	7.9 (2.1)	7.0 (2.8)	0.001*	7.4 (1.9)	8.0 (1.0)	0.140
5 min Apgar scoring, mean (SD)	9.0 (1.5)	8.6(1.9)	0.046*	8.7 (1.4)	8.2 (1.6)	0.025*
10 min Apgar scoring, mean (SD)	9.3 (1.0)	9.0 (1.3)	0.020*	9.0 (1.0)	9.0 (1.2)	0.024*
Neonatal pneumonia, (%)	49 (35.0)	17 (53.1)	0.013*	27 (52.9)	3 (75.0)	0.026*
Septicemia, (%)	21 (15.0)	3 (9.4)	0.081	14 (28.1)	3 (75.0)	0.015*
Catheter arteriosus, (%)	74 (52.9)	14 (43.8)	0.071	16 (32.2)	1 (25.0)	0.240
Respiratory distress, (%)	20 (14.3)	18 (56.3)	0.009*	11 (20.8)	3 (75.0)	0.033*
Bronchial dysplasia, (%)	65 (46.2)	20 (62.5)	0.024*	17 (33.3)	1 (25.0)	0.679
Anemia, (%)	44 (31.4)	9 (28.1)	0.210	26 (51.4)	2 (50.0)	0.339
Total bilirubin, mean (SD), $\mu\text{mol/L}$	59.5 (44.8)	87.7 (54.4)	0.040*	67.5 (52.4)	121.1 (57.8)	0.052
RBC, mean (SD), T/L	4.0 (0.8)	4.1 (0.8)	0.639	4.0 (1.0)	3.7 (1.3)	0.497

Table S2. Comparison between the ROP infants with recurrence and non-recurrence after intravitreal injection of Ranibizumab or laser photocoagulation treatment (continued).

Baseline characteristics	IVR group (n=344)			LP group (n=96)		
	Non-recurrence (n=282)	Recurrence (n=62)	<i>P</i> <i>value</i>	Non-recurrence (n=89)	Recurrence (n=7)	<i>P</i> <i>value</i>
WBC, mean (SD), G/L	8.2 (4.7)	8.6 (7.4)	0.779	10.1 (6.7)	9.7 (5.4)	0.901
Platelet count, mean (SD), G/L	240.1 (84.5)	272.7 (102.4)	0.205	256.6 (102.1)	384.5 (93.0)	0.017*
Neutrophil count, mean (SD), G/L	3.3 (2.8)	3.2 (4.3)	0.901	5.2 (5.6)	4.1 (3.6)	0.692
Lymphocyte count, mean (SD), G/L	3.5 (1.6)	3.7 (2.1)	0.662	3.1 (1.5)	3.9 (0.6)	0.354
Maternal age, mean (SD), years	28.9 (5.4)	29.5 (3.3)	0.700	31.0 (5.1)	34.5 (4.0)	0.183
IVF-ET, (%)	16 (11.4)	4 (12.5)	0.204	21 (41.2)	2 (50.0)	0.195
Maternal uterine infection, (%)	14 (10.0)	5 (15.6)	0.413	16 (31.3)	3 (75.0)	0.025*
Gestational hypertension, (%)	11 (7.9)	2 (6.3)	0.136	5 (9.3)	0	0.155
Gestational diabetes, (%)	13 (9.3)	4 (12.5)	0.309	4 (7.8)	0	0.414
Glucocorticoid therapy, (%)	20 (14.3)	5 (15.6)	0.730	23 (44.8)	2 (50.0)	0.550

*The *P* values were obtained by comparing the two groups above. Continuous variables groups were analyzed by ANOVA. Categorical variables groups were analyzed by Chi-square test.

Abbreviations: ROP: retinopathy of prematurity, IVR: intravitreal injection of ranibizumab, LP: laser photocoagulation, SD: standard deviation, AP-ROP: acute posterior polar retinopathy of prematurity, RBC: red blood cell count, WBC: white blood cell count, IVF-ET: In vitro fertilization and embryo transfer.

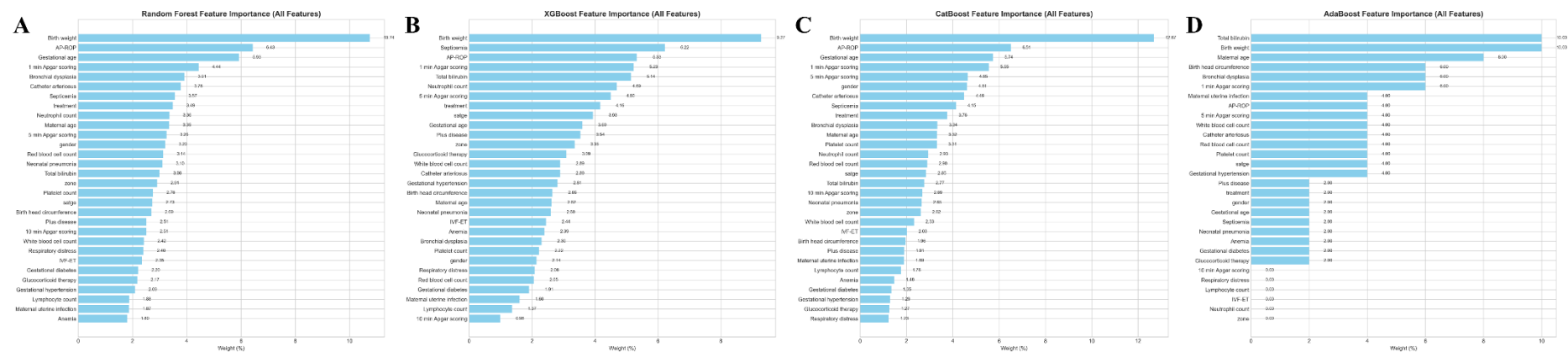


Figure S1. Weight ratios of each characteristic in different machine learning models

The absolute values of the weights of each characteristic in random forest (RF), Extreme Gradient Boosting (XGBoost), Categorical Boosting (CatBoost), and Adaptive Boosting (AdaBoost) models were summed to obtain the corresponding importance factors. Then, the importance factors of all characteristic were normalized to obtain the final weight ratios. The bar of the final weight ratios indicates the importance of different features for the 4 machine learning models. A, The bars represent the weight ratios of the RF model. B, The bars represent the weight ratios of the XGBoost model. C, The bars represent the weight ratios of the CatBoost model. D, The bars represent the weight ratios of the AdaBoost model. The higher the bar is, the more important the corresponding clinical characteristics is for the prediction task. Abbreviations: AP-ROP: AP-ROP: acute posterior polar retinopathy of prematurity, IVF-ET: In vitro fertilization and embryo transfer.

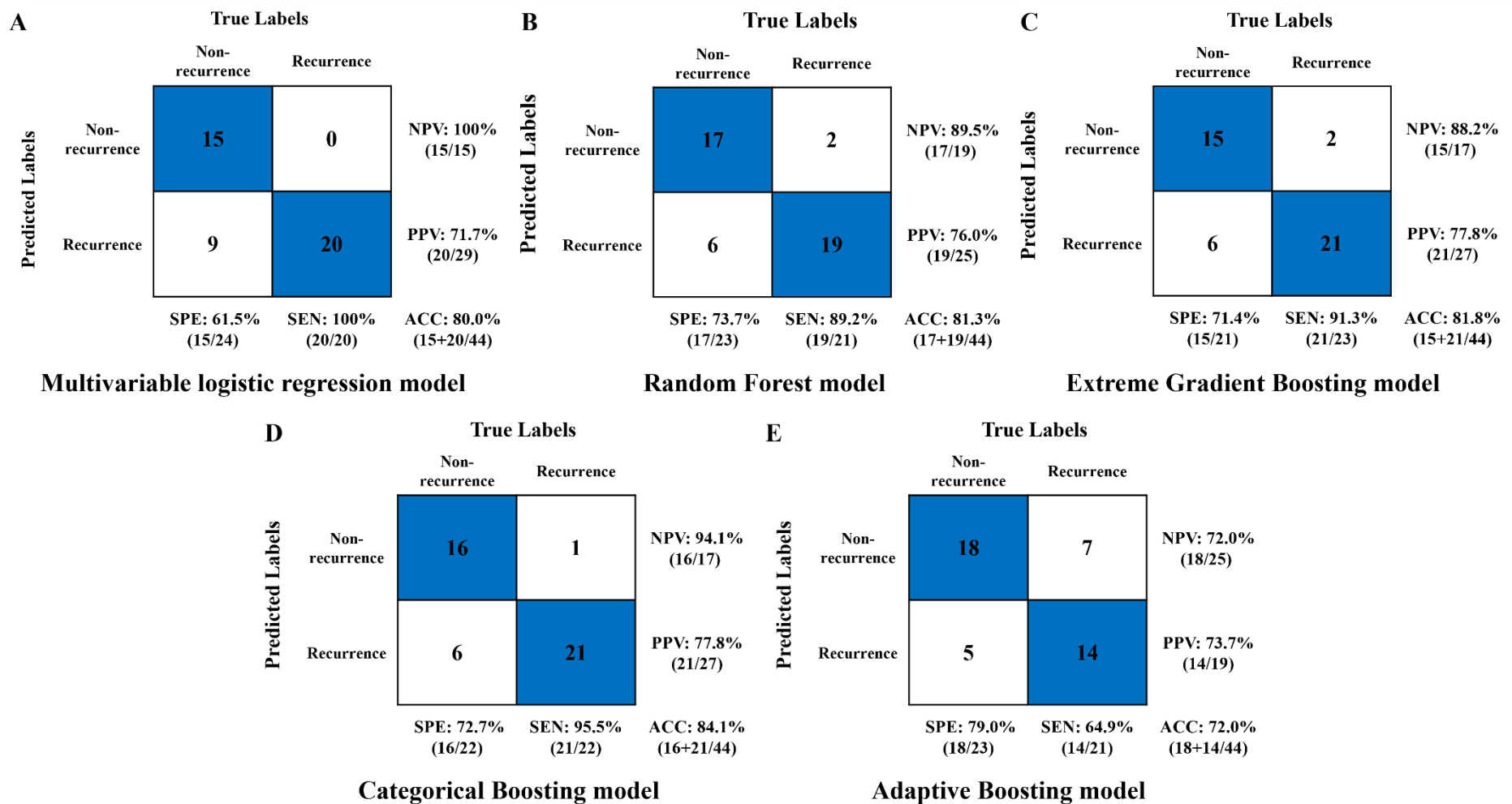


Figure S2. Binary comparison evaluating the concordance between the prediction models and retinal specialists using the test dataset

Confusion matrix of the binary classification for prediction of retinopathy of prematurity recurrence. The column of matrix is the predicted labels obtained from multivariable logistic regression (MLR), random forest (RF), Extreme Gradient Boosting (XGBoost), Categorical Boosting (CatBoost), and Adaptive Boosting (AdaBoost) models. A, The accuracy for MLR model was 80.0%, with a sensitivity of 100% and a specificity of 61.5%. B, The accuracy for RF model was 81.3%, with a sensitivity of 89.2% and a specificity of 73.7%. C, The accuracy for XGBoost model was 81.8%, with a sensitivity of 91.3% and a specificity of 71.4%. D, The accuracy for CatBoost model was 84.1%, with a sensitivity of 95.5% and a specificity of 72.7%. E, The accuracy for AdaBoost model was 72.0%, with a sensitivity of 64.9% and a specificity of 79.0%.