A bioinformatic approach to predicting HIE following perinatal asphyxia

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Introduction

- Hypoxic-ischemic encephalopathy (HIE) remains a major cause of neurological disabilities in term neonates. It is known to cause one million neonatal deaths globally per year and is responsible for 23% of the annual global neonatal deaths[1].
- Early intervention with therapeutic hypothermia improves outcome if commenced within 6 hours of birth, but prediction of HIE is difficult.
- No single clinical marker is reliable in the prediction of HIE.
- Machine Learning algorithms have been shown to create robust prediction models by combining readily available data.

Aims

- To examine the ability of machine learning to predict the occurrence of HIE in a prospective cohort of infants with perinatal asphyxia.
- To identify a clear method of identifying those who will benefit from therapeutic hypothermia within the 6 hour treatment window.

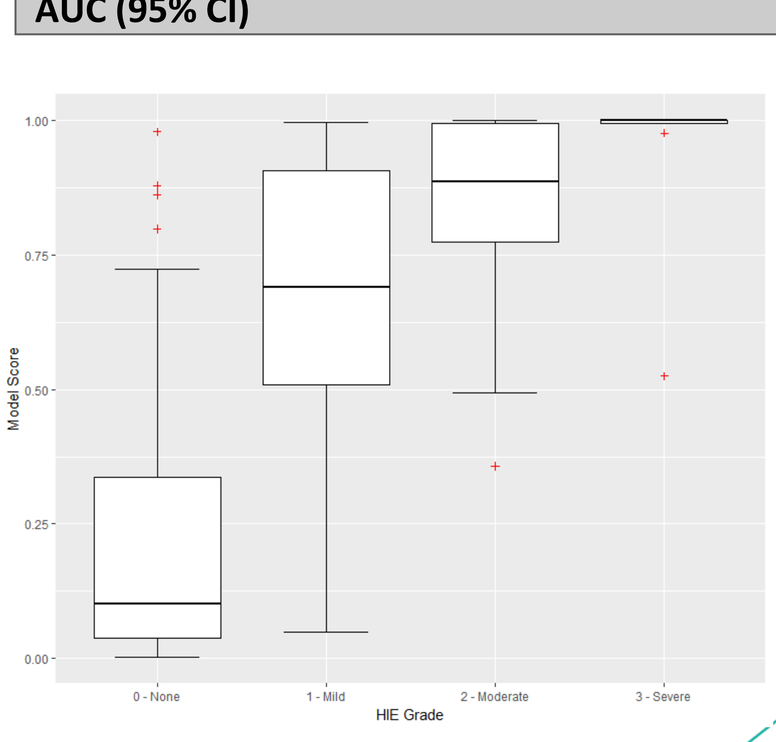
Method

- Infants were part of the BiHiVE and the BiHiVE2 studies at Cork University Maternity Hospital and Karolinska University Hospital. Inclusion criteria were gestation >36 weeks and one or more of the following: Cord pH<7.1, 5-minute Apgar score ≤ 6, and the need for intubation or resuscitation at 10 minutes of age.
- Recursive Feature Elimination (RFE) was conducted to determine the best subset of clinical features for the prediction of HIE.
- Statistical and machine learning modelling was applied to the data and cross validated to ensure robust results.

Results

- Complete data was available for 48 clinically relevant datapoints available immediately after birth in 174 infants (91 perinatal asphyxia without HIE, 82 with HIE).
- The optimum subset of clinical variables for the prediction of HIE was determined to be comprised of Apgar score at 1 and 5 minutes, level of resuscitation required, continued support of ventilation at 10 minutes of age and first post-natal lactate.
- Using the optimum number and selection of predictors an AUC of 91% (95% CI: 88.97% - 92.35%) was achieved using the clinical predictors. The model performed well with a sensitivity of 76% and a specificity of 96%. Positive Predictive Value (PPV) was 81% and Negative Predictive Value (NPV) was 96%. Overall balanced accuracy for the Random Forest model was 86%.

Accuracy (95% CI)	**86.36% (72.65% - 94.83%)**
Sensitivity	76.19%
Specificity	95.65%
Positive Predictive Value	81.48%
Negative Predictive Value	94.12%
AUC (95% CI)	91% (88.97-92.35%)



Conclusions

- The strongest predictors for the development of HIE were the infant's condition at birth, need, and response to resuscitation. Lactate was the strongest biochemical marker.
- Applying machine learning algorithms to readily available clinical data may support clinicians in the early and accurate identification of infants who will develop HIE.
- This technique has the potential to improve patient outcomes through improved identification of those who will benefit from therapeutic hypothermia within the 6 hour treatment window.

References

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