Predicting Exclusive Enteral Nutrition Induction Therapy Efficacy in Pediatric Crohn Disease from Clinical Data

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Background

- Exclusive enteral nutrition (**EEN**) is a first line therapy for the **induction of remission** in luminal pediatric Crohn Disease (**pCD**) [1], but 20% of patients do not respond to EEN induction [2].
- These unresponsive patients endure significant physical, psychological, and financial burden and spend weeks consuming an unpalatable diet before being switched to an alternative treatment regimen.

Our objective: Identify EEN non-responders from clinical data routinely collected at the time of diagnosis to allow for more personalized treatment plans.

Methodology

- A prospectively-followed cohort of pediatric patients, who were **prescribed EEN as their first treatment** after being diagnosed with CD was collected through the Canadian Children Inflammatory Bowel Disease Network **(CIDsCaNN) inception cohort** (2013-2020).
- Inclusion criteria is outlined in Figure 1. Figure 2 lists the baseline clinical data used.
- Some patients were prescribed other therapeutics for part of their EEN induction. The classes of other prescribed therapeutics and the prescription duration (represented as a percentage of the induction period) were used as additional features in the dataset.
- Pediatric Ulcerative Colitis Activity Indexes (PUCAI) were included as a feature in the dataset. While not traditionally associated with CD, PUCAI scores were used as a surrogate measure for colonic CD.
- **Unadjusted odds ratios** were calculated to determine whether any **features correlated** with response to **EEN induction**.
- A **machine learning model for predicting response to EEN** induction was also built. Maximum relevance minimum redundancy (MRMR) feature selection [4] and a nested cross-validation scheme were used to optimize the model.

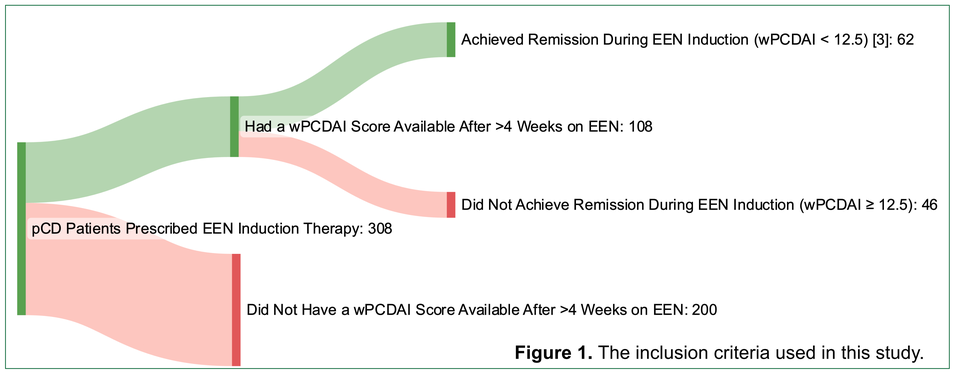

Figure 1. The inclusion criteria used in this study.

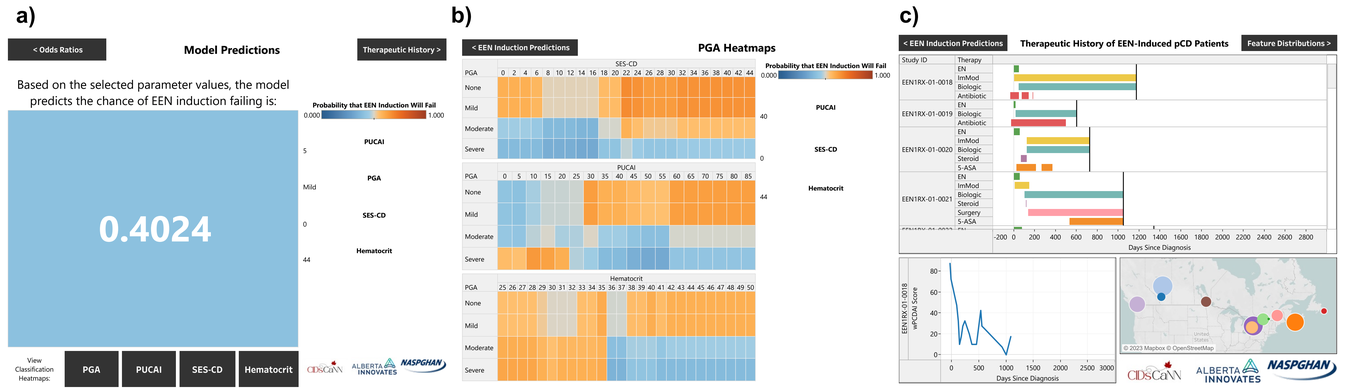

Figure 4. An interactive dashboard has been created to explore the dataset, including a) an interface to see the model's EEN induction failure predictions for different hypothetical patients, b) a heatmap to explore how variables influence the model's predictions, and c) a Gantt chart showing the therapeutic history and disease progression of each patient, and more. Want to explore the data for yourself? Scan the QR code!

Results

Unadjusted Odds Ratios

- An **increase in PGA** score (e.g. moving from "mild disease" to "moderate disease") was associated with an increase in the chance of **EEN failure** (Odds Ratio 3.1, 95% CI [1.7,5.8], p=0.0001).
- Higher **PUCAI** scores were associated with an **increased** likelihood of **EEN failure** (Odds Ratio 1.4 for a 10-point PUCAI increase, 95% CI [1.07,1.7], p=0.009).

Machine Learning Model

- The best model for predicting EEN response was a **random forest** consisting of 20 decision trees, each with a maximum depth of 3, using only four features from the dataset: **PGA, PUCAI** and **SES-CD** scores, and **hematocrit**.
- The classifier achieved an **area under the ROC curve** of **0.75 ± 0.07** (Figure 3).

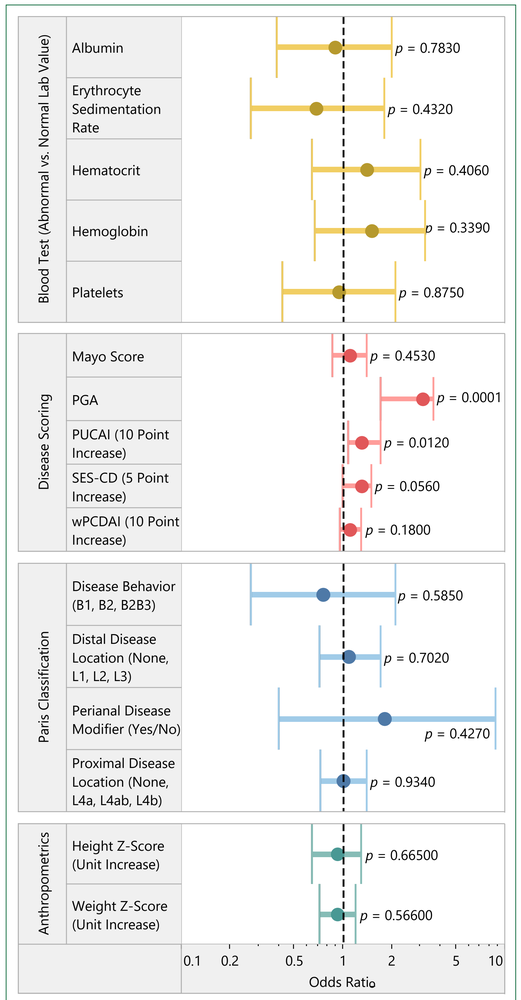

Figure 2. Forest plot showing the effect of the various features on the probability of EEN induction failure. A dashed reference line indicates an odds ratio of 1.

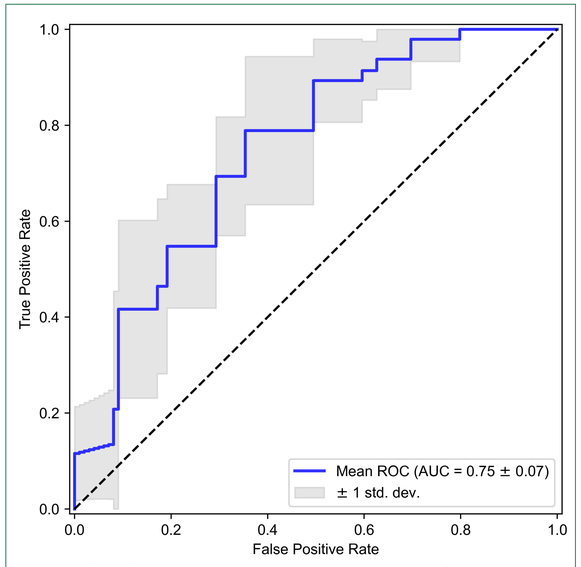

Figure 3. ROC curve showing the performance of the random forest model. A positive label indicates EEN induction failure.

Conclusions

- Higher **PGA, PUCAI, and SES-CD** scores show potential for **predicting** patients less likely to **respond to EEN induction.**
- Higher PUCAI scores may indicate distal colonic CD which is associated with more severe disease phenotypes [5]. Likewise, lower hematocrit levels demonstrate predictive power and have previously been identified as a marker of complicated CD behavior [6].
- These findings suggest **more severe disease activity** at the time of diagnosis is associated with **reduced efficacy** of **EEN** induction therapy.

CIDsCaNN Canadian Children Inflammatory Bowel Disease Network
A Partnership with the Ch.I.L.D Foundation
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This abstract summarizes a summer project done by Daniel McClement with support from NASPGHAN and the NASPGHAN foundation. Data for analysis comes from the Canadian children's IBD network (CIDsCaNN). Contributors from the network will be included in the manuscript to follow this abstract.

References

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