

A Personalized Approach to Asthma Control Over Time: Discovering Phenotypes Using Machine Learning

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Rationale

Over 22 million people suffer from asthma in the United States. Up to 30% of cases are difficult-to-treat and the poor treatment response is thought due to differences in underlying pathophysiology. The variation in pathophysiology is reflected by recently described granular phenotypes (endotypes). It is not known which medication each endotype best responds to. In order to address this knowledge gap, we applied our novel machine learning approach (Predictor Pursuit)¹ to identify endotypes and response to medication over time. The discoveries can be used to provide real-time decision support to clinicians to personalized asthma treatment recommendations for their patients.

Methods

We studied 1,019 patients enrolled in the Childhood Asthma Management Program (CAMP) Trial who had >4 clinical follow-ups documented. Asthma “severity” and “control” were determined using features from the 2007 NAEPP Asthma Guideline criteria. We defined “controlled” patients as those whose last three visits met criteria for “well-controlled” from the guideline. We defined overweight as body mass index >85 percentile for age. We evaluated differences in response to medication with a statistical method (proportionality test) with a significance level of 0.05.

Results

Patients were equally distributed in terms of asthma severity level: intermittent (23.6%), mild (23.1%), moderate (24.3%), and severe (29.1%) persistent. For the entire study population, we did not find a statistical difference in the level of control between the budesonide group as compared to the nedocromil group (34.4% (Bud) vs 32.3% (Ned), p-value=0.28). However; our method was able to discover the obese-asthma endotype, which had a significant difference in asthma control. More specifically, the obese asthma patients were more controlled with nedocromil (20.3% vs 37.9%, p-value<0.015) as compared to non-obese asthma patients who responded more favorably to budesonide (38.2% vs 30.9%, p-value<0.044).

Conclusion

These methods successfully described asthma control over time in a protocolled trial. The findings of our algorithm also support the clinical construct that obese-asthma patients have a more neutrophilic inflammation profile and are at risk to respond less favorably to corticosteroids.² In future work, we will apply Predictor Pursuit methods to a larger clinical data from the EHR. We will focus on time analysis of asthma control over time as applied to fine-grained asthma phenotypes. Our eventual goal is automated real-time clinical decision support for asthma management.

¹ <http://medianetlab.ee.ucla.edu/papers/PredictPursuit.pdf>

² Telenga, et al. Obesity in asthma: more neutrophilic inflammation as a possible explanation for a reduced treatment response. *Allergy* 2012; Aug;67(8):1060-8.

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