Predicting time to natural remission in chronic urticaria using random survival forest model

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Background
- Currently available treatments for chronic urticaria (CU) reduce symptoms, but they do not show a disease modification effect.
- Published evidence on the natural remission rates for CU varies widely: 21% to 47% of patients reach remission within 1 year, 33% to 64% within 2 years, and 34% to 45% within 5 years.
- The average disease duration is 3 to 5 years in adults and 20% of patients have persistent symptoms beyond 5 years.

Objective
- Given the large heterogeneity in reported remission rates and time to remission, the objective of the study was to identify natural remission rates and develop a machine-learning model to predict time to natural remission for patients with CU using a large real-world database.

Methods
- The study used Optum Life Science clinical electronic health record (Q1 2007-Q2 2019) US data of adult patients with CU based on 22 relevant ICD-9 and/or ICD-10 codes at least 6 weeks apart.
- Natural remission was defined as ≥12 months free of CU diagnosis or treatment after the last code.
- Kaplan-Meier was used to characterize the observed time to natural remission, while random survival forest was used to predict the time to natural remission for patients with CU using a large real-world database.

Results
- Of the 112,443 patients who met the inclusion criteria, 82,680 reached natural remission. The median observed time to remission in the study cohort was 336 days (Figure 2a).

Figure 1. Study design

Figure 2. Observed (a) and predicted (b) time to remission

Figure 3. Model predictor selection

Table 1. Model Performance Metrics at 12 months

<table>
<thead>
<tr>
<th>Patients observed to reach natural remission within 12 months of CU diagnosis</th>
<th>Patients not observed to reach natural remission within 12 months of CU diagnosis</th>
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<tbody>
<tr>
<td>Patients predicted to reach natural remission within 12 months of CU diagnosis</td>
<td>54,400 (True Positives) 23,776 (False Positives)</td>
</tr>
<tr>
<td>Patients not predicted to reach natural remission within 12 months of CU diagnosis</td>
<td>5,163 (False Negatives) 29,104 (True Negatives)</td>
</tr>
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</table>

Table 1 shows the model performance at 12 months with 70% of the patients predicted to reach natural remission within 12 months of CU diagnosis actually reaching natural remission (precision: 0.70) and 91% of the patients that actually reached remission within 12 months of CU diagnosis being correctly identified (sensitivity 0.91).

Further improvement in model performance was seen over time, for example at year 2 (precision: 0.75 and sensitivity: 0.99) and at year 3 (precision: 0.77 and sensitivity: 1.00).

Figure 4. Comparison of model calibration (a) and discrimination (b) across time intervals

Limitations
- The results of this study were based on patients diagnosed with CU in a US database, thus the generalizability to the overall population of patients with CU or to other non-US databases may be limited requiring further refinement.

Conclusions
- This is the first study to successfully leverage machine-learning techniques to predict time to natural remission in CU using real-world medical data among a cohort of patients with known status.
- Future development of this model could assist clinicians in identifying chances of remission for each patient and potentially support an optimized, personalized disease management.
- Ongoing work aims to integrate these findings into clinical applications for CU management.

References

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