Type 2 diabetes (T2D) accounts for over 90% of diabetes cases and is heterogeneous in terms of patient’s symptoms, disease progression and response to treatment for the disease. Distinguishing T2D subtypes can be challenging. In contrast to clinical measurements, germline genetic data does not change and can be used to understand T2D heterogeneity. We used k-means clustering to classify UCLA patients into five clusters based on their onset age, BMI and triglyceride, HDL and %HBA1C levels. We extracted loci from an existing genome-wide association study (GWAS) and calculated a polygenic risk score (PRS) for each patient. On average patients of higher risk are more likely found in Cluster 5 but the highest risk patients were found in Cluster 4. Understanding the relationship between genetic risk and clinical measurements in T2D patients could improve our ability to understand and manage the disease.

Results

- Average patient in Cluster 5 had the lowest age of onset
- Average patient in Cluster 2 and average patient in Cluster 4 had the same genetic risk score but average patient in Cluster 4 had a lower age of onset
- Two clusters with overweight BMI and three clusters with obese BMI, one cluster with obese BMI, higher onset age, high triglyceride and low HDL level
- Highest proportion of patients in top decile were from Cluster 4

Table 1: Patient Demographics (Control n=7889, T2D n=1569)

<table>
<thead>
<tr>
<th>Age</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70-79</th>
<th>80-89</th>
<th>90+</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>4479</td>
<td>2097</td>
<td>1258</td>
<td>679</td>
<td>342</td>
<td>145</td>
<td>4502</td>
<td>3387</td>
</tr>
<tr>
<td>T2D</td>
<td>2066</td>
<td>1085</td>
<td>651</td>
<td>351</td>
<td>201</td>
<td>105</td>
<td>1518</td>
<td>1051</td>
</tr>
</tbody>
</table>

Table 2: Average patient in each cluster

Discussion

- On average high triglyceride level, low HDL level and high PRS could be associated with lower age of onset type 2 diabetes
- GWAS based on 62892 cases and 59642 controls of European ancestry
- White people constitute a higher proportion of patients in the control group (45.3%) than in the T2D group (40.6%)
- Only Type 2 diabetes patients with sequencing sample collected and at least 1 clinical measurement post diagnosis were included
- Time series measurements were averaged
- Future directions: incorporating time series measurements and patient medications

References