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Subclassification of 3,529 individuals with type 2 diabetes

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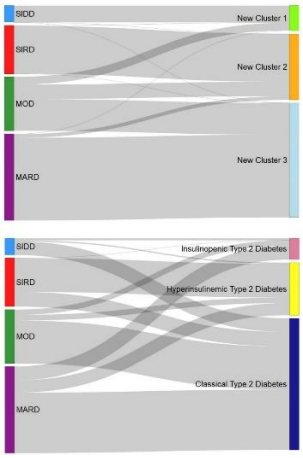
Background and aims: A Swedish data-driven cluster study identified four distinct type 2 diabetes (T2D) clusters based on HbA1c level, BMI, age at diagnosis, and HOMA2 estimates of insulin resistance and beta-cell function. A Danish study suggested three T2D phenotypes (insulinopenic, classical, and hyperinsulinemic) based only on HOMA2 measures. We investigated and compared these two new T2D classifications using the Danish Centre for Strategic Research in Type 2 Diabetes (DD2) cohort.
Materials and methods: In 3,529 individuals recently diagnosed with T2D, we first did a k-means cluster analysis with a *forced* k-value of four in order to replicate the Swedish clusters: severe insulin deficient (SIDD), severe insulin resistant (SIRD), mild obesity-related (MOD), and mild age-related (MARD) diabetes. Next, we performed an analysis open to alternative k-values (i.e. data determined the optimal number of clusters). Lastly, we compared the data-driven clusters with the three Danish T2D phenotypes.
Results: Compared with the Swedish results, the replicated SIDD cluster in DD2 comprised individuals with lower mean HbA1c (86 mmol/mol vs. 101 mmol/mol) and the MOD cluster individuals in DD2 were less obese (mean BMI 32 kg/m2 vs. 36 kg/m2). Our alternative k-value analysis suggested the most optimal number of T2D clusters in the DD2 cohort to be three (i.e. k-value of three), not identifying a MOD-like cluster (Figure, upper panel). When comparing the four replicated Swedish clusters in the DD2 to the three Danish HOMA2-based phenotypes, 81%, 79%, and 69% of the SIDD, MOD, and MARD individuals, respectively, fitted the classical T2D phenotype, whereas 70% of SIRD individuals fitted the hyperinsulinemic phenotype (Figure, lower panel). Among the three clusters identified with the alternative k-value analysis, 60% of individuals in the most insulin-resistant cluster constituted 76% of individuals with a hyperinsulinemic phenotype.
Conclusion: Different classification approaches did not classify T2D patients in a consistent manner. The T2D classes characterized by hyperinsulinemia/high insulin resistance appeared most distinct.



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