Infection risk is substantially increased in a hyperinsulinaemic type 2 diabetes subgroup: a Danish cohort study

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Background and aims: Type 2 diabetes (T2D) is associated with increased risk of severe infections, but the exact mechanisms are unclear. We hypothesized that the risk of infections is higher in a hyperinsulinemic/insulin resistant T2D subgroup associated with a high burden of adiposity, inflammation, and comorbidity at T2D onset, compared to other T2D subgroups.
Materials and methods: From the Danish Centre for Strategic Research in T2D (DD2) cohort, 4331 persons with recent-onset T2D were divided into three subgroups according to indices of insulin sensitivity and beta-cell function: hyperinsulinemic (HOMA2-S<63.5 and HOMA2-B≥115.5), classical (HOMA2-S<63.5 and HOMA2-B<115.3), and insulinopenic (HOMA2-S≥63.5 and HOMA2-B<115.3). Patients were followed from enrollment until onset of an infection, defined as a community-based antibiotic prescription, or an episode of hospital-treated infection. We used Cox regression to compute confounder-adjusted hazard ratios (HRs).
Results: Among the cohort, 1166 (27%) had hyperinsulinemic, 2737 (63%) classical, and 428 (10%) insulinopenic T2D. Hyperinsulinemic T2D was associated with increased waist circumference ((female/male) ≥88/102 cm in 89% vs 75% vs 39%); higher Charlson comorbidity index (≥2 in 38% vs 29% vs 24%); and low-grade inflammation (median hsCRP 2.5 vs 1.8 vs 0.9 mg/L). The five-year cumulative incidence of hospital-treated infections (treating death as a competing risk) was highest in hyperinsulinemic T2D (Figure 1). Compared with insulinopenic T2D, the HR of hospital-treated infection was 1.86 (95% CI 1.37-2.59) in hyperinsulinemic T2D and 1.45 (95% CI 1.06-1.96) in classical T2D, after adjusting for sex, age, diabetes duration, year of enrollment, glucose-lowering agents, and lifestyle behaviors. Further adjusting for comorbidities, waist circumference, and hsCRP, the HRs of hospital-treated infections decreased to 1.57 (1.13-2.19) for hyperinsulinemic T2D, and 1.28 (95% 0.94-1.75) for classical T2D. The partly and fully adjusted HRs of community-treated infections were 1.28 (95% CI 1.12-1.47) and 1.16 (95% CI 1.01-1.34) for hyperinsulinemic T2D, and 1.10 (95% CI 0.98-1.26) and 1.04 (0.92-1.19) for classical T2D.
Conclusion: Among individuals with recent-onset T2D, those in the hyperinsulinemic/insulin resistant subgroup were at markedly increased risk of severe infections, beyond their excess obesity, inflammation, and comorbidity.

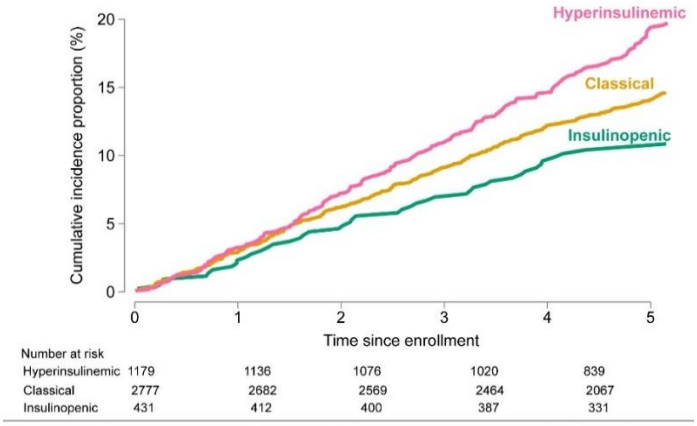

Figure 1. Risk curves for hospital-treated infection according to specific type 2 diabetes subgroups: hyperinsulinemic (red), classical (yellow) and insulinopenic (green)

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