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Cardiovascular risk according to add-on therapy in patients with type 2 diabetes

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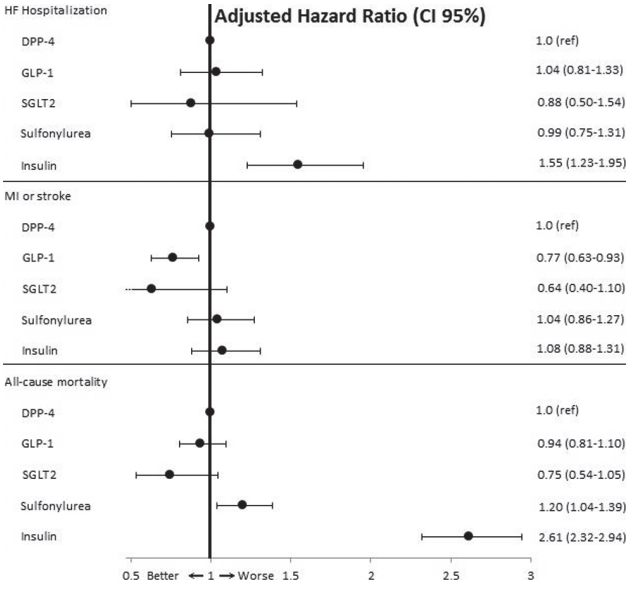
Background: Clinical trials have demonstrated lower risk of cardiovascular events in high-risk patients with type 2 diabetes (T2D) receiving glucagon like peptide 1 (GLP-1) analogues and sodium/glucose transporter 2 (SGLT2) inhibitors. However, whether these drugs are associated with similar benefits in a real world cohort of patients with T2D initiating add-on therapy is unclear.
Purpose: To investigate the cardiovascular risk associated with different glucose-lowering agents in addition to metformin in a real-world cohort of T2D patients.
Method: By use of Danish nationwide health- and administrative registries we included patients with T2D with no prior history of heart failure (HF), myocardial infarction (MI) or stroke, initiating add-on therapy on top of metformin in the period 2010–2016. Patients were grouped according to add-on therapy (dipeptidyl peptidase-4 [DPP-4] inhibitors, GLP-1 analogues, SGLT-2 inhibitors, sulfonylurea or insulin). Patients were followed for up to two years for the outcomes of heart failure (HF) hospitalization, myocardial infarction (MI) or stroke and death. Cox regression models adjusted for age, sex, duration of T2D and comorbidity were used to estimate the risks of outcomes with DPP-4 inhibitors as reference.
Results: The study included 46,215 patients with T2D, with a median age of 61 years, 59% men and median duration of T2D of 4.2 years prior to inclusion. A total number of 15,054 (32%) initiated DPP4 treatment, 13,211 (29%) GLP-1, 2,065 (5%) SGLT2, 8,775 (19%) sulfonylurea and 7,110 (15%) insulin. During follow-up 1,753 (4%) died (range across groups 2–9%), 511 (1%) were hospitalized for HF (range 0.5–2%), and 829 (2%) had an MI or a stroke (range 1.0–2.2%). In adjusted Cox regression models with DPP4 group as reference, insulin or sulfonylurea therapy was associated with a higher risk of death and HF hospitalization (only insulin) (Figure). The risk of MI or stroke was lower in patients treated with GLP-1 analogues, and a trend toward a similar reduction in those treated with SGLT inhibitors.



Conclusion: In a nationwide cohort of patients with T2D treated with metformin, add-on therapy with insulin and sulfonylurea was associated with higher risk of death compared to DPP-4 inhibitors. GLP-1 analogues and SGLT2 inhibitors were not associated with any significant differences in risk of death or HF hospitalization compared to DPP4 inhibitors; although both drugs appeared to be associated with a lower risk of MI or stroke. Our findings suggest that the guidelines ought to highlight use of newer anti-diabetic therapies.
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Lentiviral transfer of interleukin 4 gene to 3T3-L1 adipocytes prevents development of lipid-induced insulin resistance

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Obesity-associated latent inflammation in adipose tissue leads to development of insulin resistance (IR) and metabolic disorders such as type 2 diabetes mellitus (T2DM) and metabolic syndrome. While current strategy of anti-inflammatory therapy of T2DM is focused on suppressing inflammatory signaling in cells, little attention is paid to the opposite way, i.e. activation of anti-inflammatory signaling. Some studies have shown that activation of anti-inflammatory mechanisms by the cytokine interleukin 4 (IL-4) improves insulin sensitivity in the high fat diet animal model, the effect attributed to the action of IL-4 on immune cells.
We hypothesized that IL-4 may influence adipocytes directly and restore their insulin pathway activity in insulin resistant states. We studied the effect of recombinant IL-4 on insulin signaling in the IR model of 3T3-L1 adipocytes treated with palmitic acid. We also generated adipocytes expressing IL-4 following lentiviral delivery of IL-4 gene and determined their susceptibility to develop IR.
Recombinant IL-4 restored insulin-dependent phosphorylation of IRS-1 (Y612), Akt (S473, T308), AS160 (S318) in insulin-resistant 3T3-L1 adipocytes, and 50 ng/ml of IL-4 was most effective. IL-4 had no effect on adipogenic differentiation of 3T3-L1. Lentiviral delivery of IL-4 resulted in high expression (70 ng/ml) of this cytokine in 3T3-L1 adipocytes, while no detectable expression of IL-4 was observed in the control cells. The insulin sensitivity of IL-4 expressing adipocytes was restored similarly to those treated by the recombinant cytokine.
Our results indicate that anti-inflammatory cytokine IL-4 improves insulin sensitivity of adipocytes through direct effects on insulin signaling. We suggest that IL-4 inhibits inflammation-associated kinases that impair insulin cascade in adipocytes under dyslipidemic conditions. These findings indicate the potential use of IL-4 for the IR treatment. In view of this, further investigations should be aimed at creation of adipocyte-specific gene therapy approach based on IL-4.
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Diagnostic performance of electrocardiogram in detection of left ventricular hypertrophy in Asian population with different degree of abdominal obesity

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Background: According to 2017 ACC/AHA hypertension guideline, the decision pathway for stage 1 hypertensives is determined by the presence of left ventricular hypertrophy (LVH). The varying degree of diagnostic accuracy of LVH criteria across spectrum of body mass index (BMI) is well described in Caucasian. Whilst Asian have unalike body frame, we test the effect of abdominal obesity on diagnostic accuracy of LVH criteria in this population.
Objective: To investigate the relationship between abdominal obesity and diagnostic performance of LVH by voltage criteria in a Thai population.
Methods: Data are retrieved from participants who entered the Electricity Generating Authority of Thailand study in 2012. Electrocardiogram and echocardiogram were done in a same day. Two standard ECG criteria for LVH; Sokolow-Lyon and Cornell voltage are read. Echocardiographic LV mass index defines true LVH. Body anthropometry are BMI, waist to height ratio (WHtR), percent body fat (PBF) and appendicular skeletal mass index (ASMi). Sensitivity, specificity, and receiver operating characteristic (ROC) curve are used to compare the performance of two criteria in the different groups of body habitus.
Result: One thousand and seven participants are eligible (mean age 68.6±4.5 year, 60.4% are male). LVH by LV mass criteria are identified in 235 subjects (23%). BMI are categorized as underweight (3.3%), normal weight (30.4%), overweight (24.3%) and obesity (42%). There is no difference in the performance of two ECG criteria for detection of LVH amongst BMI categories [Sokolow-Lyon; AUC 0.67, 0.54, 0.51 and 0.51 respectively (P=0.32): Cornell voltage; AUC 0.67, 0.49, 0.51 and 0.51 respectively (P=0.25)], nor WHtR categories (>0.5 vs ≤ 0.5); [Sokolow-Lyon; AUC 0.55 vs 0.52 respectively (P=0.30): Cornell voltage; AUC 0.52 vs 0.51 respectively (P=0.55)]. Percent body fat and appendicular skeletal mass index also show no effect on performance. These findings are not changed after stratified by sex.
Conclusion: In contrast with Caucasian studies, the diagnostic performance of ECG criteria for detect left ventricular hypertrophy (LVH) are not affected by abdominal obesity or BMI in a Thai population.

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Rosuvastatin dose-dependently improves flow-mediated dilation, but reduces adiponectin levels and insulin sensitivity in hypercholesterolemic patients

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Background: Increased risk of type 2 diabetes noted with statins is at least partially explained by HMG-coenzyme A reductase inhibition. We investigated vascular and metabolic phenotypes of different dosages of rosuvastatin in hypercholesterolemic patients.
Methods: This was a randomized, single-blind, placebo-controlled, parallel study. Age, sex, and BMI were matched among groups. Forty-eight patients were given placebo, and 47, 48, and 47 patients given rosuvastatin 5,10, and 20 mg, respectively daily during a 2 month treatment period.