Determinants of Glycemic Response to Add-On Therapy with a Dipeptidyl Peptidase-4 Inhibitor.

Mamza J, Mehta R, Donnelly R, Idris I.Diabetes TechnolTher. 2016 Feb;18(2):85-92. doi: 10.1089/dia.2015.0052. Epub 2016 Jan 11.

Data on 25,386 patients with type 2 diabetes, newly treated with a DPP4 inhibitor (2007-2013), were sourced from a United Kingdom general practice database via the Health Improvement Network database. Baseline clinical parameters of patients (n = 13,525) for whom a DPP4 inhibitor was added because of suboptimal glucose control (HbA1c >7%) were compared with 12-month follow-up data. An optimum response to the DPP4 inhibitor was defined as an HbA1c level of <7.0% at 12 months. Descriptive analyses and unadjusted comparisons using ÷(2) and t tests were carried out to ascertain glycemic and body weight responses to treatment intensification with a DPP4 inhibitor. Predictor of response analyses were performed using multivariate logistic regression.

Overall, 1,708 (13%) of the study population achieved an HbA1c level of <7%. Intensification with a DPP4 inhibitor was associated with significant reductions in HbA1c (-0.5%), body weight (-0.9 kg), and total cholesterol (-0.1 mmol/L) (P < 0.001). Independent predictors of achieving optimal HbA1c target of <7% included the use of metformin (adjusted odds ratio [OR] = 2.58; 95% confidence interval [CI], 2.18-3.04) and use of metformin plus sulfonylurea (1.42; 95% CI, 1.21-1.68) as opposed to no use. The independent predictors of suboptimal glucose control included a higher baseline HbA1c level (OR = 0.64; 95% CI, 0.61-0.68) (i.e., 1% increase in HbA1c was associated with a 36% reduced likelihood of response), longer diabetes duration (per every year increase) (OR = 0.85; 95% CI, 0.83-0.88), and intensification therapy below 9 months compared with 9-12 months.

Editor's comment

Other than baseline glycated hemoglobin (HbA1c), we know little about clinical parameters that affect glycemic response to a dipeptidyl peptidase-4 (DPP4) inhibitor when used in routine clinical practice. There is a significant variability in glycemic response to a DPP4 inhibitor in routine practice. The study used a large primary care database to assess the variability in response to a DPP4 inhibitor when used as add-on therapy.

The best effect is seen when gliptins were used as add-on to metformin and metformin plus sulfonylurea, but responses are significantly lower with increased diabetes duration and among patients with high HbA1c levels at baseline

Heart Failure Outcomes with Empagliflozin in Patients with Type 2 Diabetes at High Cardiovascular Risk: Results of the EMPA-REG OUTCOME® Trial.

D Fitchett, B Zinman, C Wanner, JM Lachin, S Hantel, A Salsali, OE Johansen, HJ Woerle, UC Broedl, SE Inzucchi. Eur Heart J 2016 Jan 26; [EPub Ahead of Print

The researchers previously reported that in the EMPA-REG OUTCOME(®) trial, empagliflozin added to standard of care reduced the risk of 3-point major adverse cardiovascular events, cardiovascular and all-cause death, and hospitalization for heart failure in patients with type 2 diabetes and high cardiovascular risk. They further investigated heart failure outcomes in all patients and in subgroups, including patients with or without baseline heart failure.

Patients were randomized to receive empagliflozin 10 mg, empagliflozin 25 mg, or placebo. Seven thousand and twenty patients were treated; 706 (10.1%) had heart failure at baseline. Heart failure hospitalization or cardiovascular death occurred in a significantly lower percentage of patients treated with empagliflozin [265/4687 patients (5.7%)] than with placebo [198/2333 patients (8.5%)] [hazard ratio, HR: 0.66 (95% confidence interval: 0.55-0.79); $P < 0.001$], corresponding to a number needed to treat to prevent one heart failure hospitalization or cardiovascular death of 35 over 3 years. Consistent effects of empagliflozin were observed across subgroups defined by baseline characteristics, including patients with vs. without heart failure, and across categories of medications to treat diabetes and/or heart failure. Empagliflozin improved other heart failure outcomes, including hospitalization for or death from heart failure [2.8 vs. 4.5%; HR: 0.61 (0.47-0.79); $P < 0.001$] and was associated with a reduction in all-cause hospitalization [36.8 vs. 39.6%; HR: 0.89 (0.82-0.96); $P = 0.003$]. Serious adverse events and adverse events leading to discontinuation were reported by a higher proportion of patients with vs. without heart failure at baseline in both treatment groups, but were no more common with empagliflozin than with placebo.

Editor's comment

The EMPA-REG OUTCOME trial was designed as a randomized controlled trial of empagliflozin 10 mg, empagliflozin 25 mg, or placebo for patients with type 2 diabetes and high cardiovascular risk. In this analysis, heart failure hospitalization, all-cause hospitalization, and cardiovascular death were seen to happen less frequently in empagliflozin-treated patients than placebo-treated patients. Empagliflozin treatment effects were consistent across subgroups with and without heart failure. Without any relation to the baseline heart failure, empagliflozin reduced heart failure hospitalization, indicating that the SGLT2 inhibitor not only prevents or delays the progression of clinical heart failure in patients already affected but may also prevent the development of heart failure in those not affected.

Protein Preload Enhances the Glucose-Lowering Efficacy of Vildagliptin in Type 2 Diabetes.

Wu T, Little TJ, Bound MJ, et al. Diabetes Care. 2016. doi:10.2337/dc15-2298.

A protein preload consisting of whey protein enhances the glucose-lowering efficacy of vildagliptin in type 2 diabetes, in 22 patients with type 2 diabetes treated with metforminas per a study published in Diabetes Care. Patients were treated with 50 mg of vildagliptin or placebo on both the evening before and the morning of each study day. A preload drink containing either 25 g of whey protein or control flavour was given 60 minutes after the latter dose. Then, after another 30 minutes, patients received a 13C-octanoate-labeled mashed potato meal.

The researchers found that placebo/whey group reduced postprandial peak glycemia; increased plasma insulin, glucagon, and incretin hormones (total and intact); and slowed gastric emptying compared with placebo/control. In contrast, vildagliptin/control reduced both the peak and area under the curve for glucose, increased plasma intact incretins, and slowed gastric emptying but suppressed plasma glucagon and total incretins.

Vildagliptin/whey was associated with higher plasma intact glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide, slower gastric emptying, and lower postprandial glycemia compared with both placebo/whey and vildagliptin/control.

In metformin-treated type 2 diabetes, a protein preload has the capacity to enhance the efficacy of vildagliptin to slow gastric emptying, increase plasma intact incretins, and reduce postprandial glycemia.

Editor's comment

This is a unique study which shows favourable effect of dietary elementwhey protein to enhance the efficacy of a costly antidiabetic drug Vildagliptin. It is too early to comment on this trial .Let us wait for future trials.

Effect of Atorvastatin on Glycemia Progression in Patients with Diabetes:

An Analysis From the Collaborative Atorvastatin in Diabetes Trial (CARDS). SJ Livingstone, HC Looker, T Akbar, DJ Betteridge, PN Durrington, GA Hitman, HA Neil, JH Fuller, HM Colhoun.Diabetologia 2016 Feb 01;59(2)299-306.

While atorvastatin use was associated with an increase in glycemia, the effect was small (0.14%) and did not have much impact on the substantial CVD risk reduction associated with statin use.In an individual-level analysis we examined the effect of atorvastatin on glycaemia progression in type 2 diabetes and whether glycaemia effects reduce the prevention of cardiovascular disease (CVD) with atorvastatin.

The study population comprised 2,739 people taking part in the Collaborative Atorvastatin Diabetes Study (CARDS) who were randomised to receive atorvastatin 10 mg or placebo and who had post-randomisation HbA1c data. This secondary analysis used Cox regression to estimate the effect of atorvastatin on glycaemia progression, defined as an increase in HbA1c of e"0.5% (5.5 mmol/mol) or intensification of diabetes therapy. Mixed models were used to estimate the effect of atorvastatin on HbA1c as a continuous endpoint.

Glycaemia progression occurred in 73.6% of participants allocated placebo and 78.1% of those allocated atorvastatin (HR 1.18 [95% CI 1.08, 1.29], $p < 0.001$) by the end of follow-up. The HR was 1.22 (95% CI 1.19, 1.35) in men and 1.11 (95% CI 0.95, 1.29) in women ($p = 0.098$ for the sex interaction). A similar effect was seen in on-treatment analyses: HR 1.20 (95% CI 1.07, 1.35), $p = 0.001$. The net mean treatment effect on HbA1c was 0.14% (95% CI 0.08, 0.21) (1.5 mmol/mol). The effect did not increase through time. Diabetes treatment intensification alone did not differ with statin allocation. Neither baseline nor 1-year-attained HbA1c predicted subsequent CVD, and the atorvastatin effect on CVD did not vary by HbA1c change (interaction p value 0.229).

Editor's comment

This is a secondary analysis of data from the randomized Collaborative Atorvastatin Diabetes Study. The effect of atorvastatin 10 mg was compared with that of placebo on glycemia progression in 2739 patients with type 2 diabetes.The effect of atorvastatin 10 mg on glycaemia progression among those with diabetes was statistically significant but very small. There is no significant difference between sexes, no increase with duration of statin and does not have an impact on the magnitude of CVD risk reduction with atorvastatin. Considering the reasonable benefits of statin therapy on vascular wall it should not be avoided in the treatment of Diabetes.

Breaking Up Prolonged Sitting With Standing or Walking Attenuates the Postprandial Metabolic Response in Postmenopausal Women

A Randomized Acute Study. J Henson, MJ Davies, DH Bodicoat, CL Edwardson, JM Gill, DJ Stensel, K Tolfrey, DW Dunstan, K Khunti, T Yates. Diabetes Care 2016 Jan 01;39(1)1130-1138.

In postmenopausal women, standing or walking for 5 minutes intermittently during periods of prolonged sitting had beneficial effects on postprandial glucose, insulin, and non-esterified fatty acid responses, and public health interventions could encourage simple behavioral changes.

This study determined whether breaking up prolonged sitting with short bouts of standing or walking improves postprandial markers of cardiometabolic health in women at high risk of type 2 diabetes.

Twenty-two overweight/obese, dysglycemic, postmenopausal women (mean ± SD age 66.6 ± 4.7 years) each participated in two of the following treatments: prolonged, unbroken sitting (7.5 h) or prolonged sitting broken up with either standing or walking at a self-perceived light intensity (for 5 min every 30 min). Both allocation and treatment order were randomized. The incremental area under the curves (iAUCs) for glucose, insulin, nonesterified fatty acids (NEFA), and triglycerides were calculated for each treatment condition (mean ± SEM). The following day, all participants underwent the 7.5-h sitting protocol.

Compared with a prolonged bout of sitting (iAUC 5.3 ± 0.8 mmol/L · h), both standing (3.5 ± 0.8 mmol/L · h) and walking (3.8 ± 0.7 mmol/L · h) significantly reduced the glucose iAUC (both $P < 0.05$). When compared with prolonged sitting (548.2 ± 71.8 mU/L · h), insulin was also reduced for both activity conditions (standing, 437.2 ± 73.5 mU/L · h; walking, 347.9 ± 78.7 mU/L · h; both $P < 0.05$). Both standing (-1.0 ± 0.2 mmol/L · h) and walking (-0.8 ± 0.2 mmol/L · h) attenuated the suppression of NEFA compared with prolonged sitting (-1.5 ± 0.2 mmol/L · h) (both $P < 0.05$). There was no significant effect on triglyceride iAUC. The effects on glucose (standing and walking) and insulin (walking only) persisted into the following day.

Breaking up prolonged sitting with 5-min bouts of standing or walking at a self-perceived light intensity reduced postprandial glucose, insulin, and NEFA responses in women at high risk of type 2 diabetes. This simple, behavioral approach could inform future public health interventions aimed at improving the metabolic profile of postmenopausal, dysglycemic women.

Editor's comment

To determine the effect on postprandial cardio-metabolic markers, postmenopausal women were evaluated while participating in either prolonged, unbroken sitting or prolonged sitting disrupted by 5 minutes of standing or light-intensity walking every 30 minutes. Both standing and walking significantly reduced the incremental Area Under Curve (AUC) for glucose and insulin, and the effect continued into the next day. Compared with prolonged sitting, suppression of non-esterified fatty acids was diminished by standing and walking. There was no effect seen on the incremental AUC for triglycerides.

Can Slight Glucose Intolerance During Pregnancy Predict Future Maternal Atherosclerotic Morbidity?

R Charach, T Wolak, I Shoham-Vardi, R Sergienko, E Shiener .Diabet. Med. 2015 Dec 24;[EPub Ahead of Print]

This study examined the association between glucose level during pregnancy and the subsequent development of long-term maternal atherosclerotic morbidity.A retrospective case-control study was conducted. The study included all women who had at least one glucose measurement during their pregnancies. Cases were all women who delivered between the years 2000-2012 and subsequently developed atherosclerotic morbidity (n = 815).

Controls were randomly matched by age and year of delivery (n = 6065). The atherosclerotic morbidity group was further divided by severity: major events (cardiovascular, cerebrovascular disease, chronic renal failure), minor events (hypertension, diabetes mellitus and hyperlipidaemia without target organ damage or complications) and cardiac evaluation tests (such as coronary angiography without records of atherosclerosis, cardiac scan and stress test). The mean follow-up duration for the study group was 74 months. Cox proportional hazards model was used to control for confounders.

A significant linear association was found between glucose levels during pregnancy and long-term maternal atherosclerotic morbidity. Among the cases with severe atherosclerotic morbidity, the proportion of women with a high glucose level (> 5.5 mmol/l) was the highest, whereas in controls it was the lowest ($P < 0.001$). In a Cox proportional hazard model, adjusted for atherosclerotic confounders such as gestational diabetes, pre-eclampsia and obesity, a glucose level of > 5.5 mmol/l was noted as an independent risk factor for hospitalizations later in non-pregnant life (hazard ratio = 1.3, 95% confidence interval 1.1-1.5, $P < 0.003$).

Editor's comment

The authors of this retrospective study evaluated the association between glucose intolerance during pregnancy and the future development of maternal atherosclerotic disease. They found that there was a direct, linear relationship between glucose levels in pregnancy and development of maternal atherosclerotic disease, and glucose level >5.5 mmol/L was an independent predictor of hospitalization later in life.A high glucose level during pregnancy, even if within the range of slight glucose intolerance, may serve as a marker for future maternal atherosclerotic morbidity. Further long-term studies are needed.

Variations in Metformin Prescribing for Type 2 Diabetes

Tiffany Goldberg, PharmD; Miranda E. Kroehl, MS, PhD; Kathleen Heist Suddarth, MD; Katy E. Trinkley, PharmD.J Am Board Fam Med. 2015;28(6):777-784.

Reasons for suboptimal metformin prescribing are unclear, but may be due to perceived risk of lactic acidosis. The purpose of this study is to describe provider attitudes regarding metformin prescribing in various patient situations.An anonymous, electronic survey was distributed electronically to 76 health care providers across the nation. The 14-item survey contained demographic questions and questions related to prescribing of metformin for T2DM in various patient situations, including suboptimal glycemic control, alcohol use, history of lactic acidosis, and varying degrees of severity for certain health conditions, including renal and hepatic dysfunction, chronic obstructive pulmonary disease, and heart failure.

There were a total of 100 respondents. For suboptimal glycemic control, most providers (75%) would increase metformin from 1500 to 2000 mg daily; however, 25% would add an alternate agent, such as a sulfonylurea (18%) or dipeptidyl peptidase-4 inhibitor (7%). Although 51% of providers would stop metformin based on serum creatinine thresholds, the remainder would rely on glomerular filtration rate thresholds of <60 mL/min (15%), <30 mL/

min (33%), or <15 mL/min (1%) to determine when to stop metformin. For heart failure, 45% of providers would continue metformin as currently prescribed regardless of severity. Most providers would adjust metformin for varying severity of hepatic dysfunction (74%) and alcohol abuse (40%).

Editor's comment

The current evidences are supporting the cardiovascular benefits of metformin.The indications and contraindications for metformin use are all changing and favouring it's more and more use. But provider attitudes toward prescribing metformin are suboptimal in certain patient situations and vary greatly by provider.

Treatment with Diet and Exercise for Women With Gestational Diabetes Mellitus Diagnosed Using IADPSG Criteria

O Kgosidialwa, AM Egan, L Carmody, B Kirwan, P Gunning, FP Dunne. J. Clin. Endocrinol. Metab. 2015 Dec 01;100(12)4629-4636.

Prevalence of gestational diabetes mellitus (GDM) and obesity continue to increase.This study aimed to ascertain whether diet and exercise is a successful intervention for women with GDM and whether a subset of these women have comparable outcomes to those with normal glucose tolerance (NGT).

This was a retrospective cohort study of five antenatal centers along the Irish Atlantic seaboard of 567 women diagnosed with GDM and 2499 women with NGT during pregnancy.Diet and exercise therapy on diagnosis of GDM were prescribed and multiple maternal and neonatal outcomes were examined.

Infants of women with GDM were more likely to be hypoglycemic (adjusted odds ratio [aOR], 7.25; 95% confidence interval [CI], 2.94-17.9) at birth. They were more likely to be admitted to the neonatal intensive care unit (aOR, 2.16; 95% CI, 1.60-2.91). Macrosomia and large-for-gestational-age rates were lower in the GDM group (aOR, 0.48; 95% CI, 0.37-0.64 and aOR, 0.61; 95% CI, 0.46-0.82, respectively). There was no increase in small for gestational age among offspring of women with GDM (aOR, 0.81; 95% CI, 0.49-1.34). Women with diet-treated GDM and body mass index (BMI) < 25 kg/m(2) had similar outcomes to those with NGT of the same BMI group. Obesity increased risk for poor pregnancy outcomes regardless of diabetes status.

Women with gestational diabetes and a BMI <25 kg/m2 have outcomes similar to those with normal glucose tolerance, while obesity increases the risk of poor pregnancy outcomes regardless of diabetic status.

Editor's Comment

The research group of this retrospective cohort study evaluated the effect of diet and exercise intervention in women diagnosed with gestational diabetes compared with those with normal glucose tolerance. Infants of the women with gestational diabetes were more likely to be hypoglycemic and admitted to the neonatal intensive care unit, but macrosomia and large-for-gestational-age rates were lower in this group, without an increase in small-for-gestational-age infants.

Medical nutritional therapy and exercise for women with GDM are probably successful in lowering rates of large for gestational age and macrosomia without increasing small-for-gestational-age rates. Women with GDM and a BMI less than 25kg/m(2) had outcomes similar to those with NGT suggesting that these women could potentially be treated in a less resource intensive setting.

Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis

Dena Ettehad, Connor A Emdin, Amit Kiran, Simon G Anderson, Thomas Callender, Jonathan Emberson, Prof John Chalmers, Prof Anthony Rodgers, Prof KazemRahimi.Published Online: 23 December 2015,Lancet. 2015;doi:10.1016/S0140-6736(15)01225-8.

The benefits of blood pressure lowering treatment for prevention of cardiovascular disease are well established. However, the extent to which these effects differ by baseline blood pressure, presence of comorbidities, or drug class is less clear. The study group made a systematic review and meta-analysis to clarify these differences.

For this systematic review and meta-analysis, they searched MEDLINE for large-scale blood pressure lowering trials, published between Jan 1, 1966, and July 7, 2015, and we searched the medical literature to identify trials up to Nov 9, 2015. All randomised controlled trials of blood pressure lowering treatment were eligible for inclusion if they included a minimum of 1000 patient-years of follow-up in each study arm. No trials were excluded because of presence of baseline comorbidities, and trials of antihypertensive drugs for indications other than hypertension were eligible. They extracted summary-level data about study characteristics and the outcomes of major cardiovascular disease events, coronary heart disease, stroke, heart failure, renal failure, and all-cause mortality. Inverse variance weighted fixed-effects meta-analyses to pool the estimates were used.

They identified 123 studies with 613 815 participants for the tabular meta-analysis. Meta-regression analyses showed relative risk reductions proportional to the magnitude of the blood pressure reductions achieved. Every 10 mm Hg reduction in systolic blood pressure significantly reduced the risk of major cardiovascular disease events (relative risk [RR] 0·80, 95% CI 0·77–0·83), coronary heart disease (0·83, 0·78–0·88), stroke (0·73, 0·68–0·77), and heart failure (0·72, 0·67–0·78), which, in the populations studied, led to a significant 13% reduction in all-cause mortality (0·87, 0·84–0·91). However, the effect on renal failure was not significant (0·95, 0·84–1·07). Similar proportional risk reductions (per 10 mm Hg lower systolic blood pressure) were noted in trials with higher mean baseline systolic blood pressure and trials with lower mean baseline systolic blood pressure (all ptrend>0·05). There was no clear evidence that proportional risk reductions in major cardiovascular disease differed by baseline disease history, except for diabetes and chronic kidney disease, for which smaller, but significant, risk reductions were detected.

The β blockers were inferior to other drugs for the prevention of major cardiovascular disease events, stroke, and renal failure. Calcium channel blockers were superior to other drugs for the prevention of stroke. For the prevention of heart failure, calcium channel blockers were inferior and diuretics were superior to other drug classes. Risk of bias was judged to be low for 113 trials and unclear for 10 trials. Heterogeneity for outcomes was low to moderate; the I2 statistic for heterogeneity for major cardiovascular disease events was 41%, for coronary heart disease 25%, for stroke 26%, for heart failure 37%, for renal failure 28%, and for all-cause mortality 35%.

Editor's comment

Blood pressure lowering significantly lowers vascular risk across various baseline blood pressure levels and comorbidities. The results provide strong support for lowering blood pressure to systolic blood pressures less than 130 mm Hg and providing blood pressure lowering treatment to individuals with a history of cardiovascular disease, coronary heart disease, stroke, diabetes, heart failure, and chronic kidney disease. Complications development depend upon the nature of antihypertensive drugs.

Ethnic Disparities in Risk of Cardiovascular Disease, End-Stage Renal Disease and All-Cause Mortality: A Prospective Study among Asian People with Type 2 Diabetes

JJ Liu, SC Lim, LY Yeoh, C Su, BC Tai, S Low, S Fun, S Tavintharan, KS Chia, ES Tai, CF Sum.Diabet. Med. 2015 Dec 08;[EPub Ahead of Print]

Ethnicity appears to affect the risk of developing CVD and ESRD, but not the risk of mortality, in an Asian population with T2DM. This study prospectively assessed the ethnic-specific risks of cardiovascular disease, end-stage renal disease and all-cause mortality in patients with Type 2 diabetes mellitus among native Asian subpopulations.A total of 2337 subjects with Type 2 diabetes (70% Chinese, 17% Malay and 13% Asian-Indian) were followed for a median of 4.0 years. Time-to-event analysis was used to study the association of ethnicity with adverse outcomes.

Age- and gender-adjusted hazard ratios for cardiovascular disease in ethnic Malay and Asian-Indian subjects were 2.01 (1.40-2.88; P<0.0001) and 1.60 (1.07-2.41; P=0.022) as compared with Chinese subjects. Adjustment for conventional cardiovascular disease risk factors, including HbA1c , blood pressure and lipid profile, slightly attenuated the hazards in Malay (1.82, 1.23-2.71; P=0.003) and Asian-Indian subjects (1.47, 0.95-2.30; P=0.086); however, further adjustment for baseline renal function (estimated GFR) and albuminuria weakened the cardiovascular disease risks in Malay (1.48, 0.98-2.26; P=0.065) but strengthened that in Asian-Indian subjects (1.81, 1.14-2.87; P=0.012). Competing-risk regression showed that the age- and gender-adjusted sub-distribution hazard ratio for end-stage renal disease was 1.87 (1.27-2.73; P=0.001) in Malay and 0.39 (0.18-0.83; P=0.015) in Asian-Indian subjects. Notably, the difference in end-stage renal disease risk among the three ethnic groups was abolished after further adjustment for baseline estimated GFR and albuminuria. There was no significant difference in risk of all-cause mortality among the three ethnic groups.

Risks of cardiovascular and end-stage renal disease in native Asian subjects with Type 2 diabetes vary substantially among different ethnic groups. Differences in prevalence of diabetic kidney disease may partially explain the ethnic disparities.

Editor's comment

In this prospective study evaluation of the association between ethnicity and cardiovascular disease (CVD), end-stage renal disease (ESRD), and all-cause mortality among 2337 Chinese, Malay, and Asian-Indian adults with type 2 diabetes (T2DM) were attempted.

They found that Malay and Asian-Indian patients had higher risks of CVD compared with Chinese patients. They also found that Malay patients had a higher risk of ESRD and Asian-Indians had a lower risk of ESRD compared with Chinese patients; however, these differences disappeared after adjusting for baseline renal function. They found no difference in mortality among the three groups.

10-Year Observational Follow-Up of PROactive: A Randomized Cardiovascular Outcomes Trial Evaluating Pioglitazone in Type 2 Diabetes.

E Erdmann, S Harding, H Lam, A Perez.DiabetesObesMetab 2015 Nov 23;[EPub Ahead of Print]

Cardiovascular benefits do not appear to persist in patients with T2DM and macrovascular disease who have previously been treated with pioglitazone.PROactive evaluated pioglitazone for secondary prevention of macrovascular events in patients with type 2 diabetes and pre-existing macrovascular disease. A 10-year, observational follow-up of patients completing PROactive investigated whether trends of cardiovascular benefit with

pioglitazone and imbalances in specific malignancies persisted over time.

Macrovascular endpoints and malignancies were compared based on original randomization to pioglitazone or placebo and "Any" versus "No pioglitazone use" for bladder and prostate cancer.

Of 4873 patients completing PROactive, 74% entered the follow-up. During follow-up (mean 7.8 years), there were no statistically significant differences in the primary (all-cause mortality, myocardial infarction [MI], cardiac intervention, stroke, major leg amputation, leg revascularization) or main secondary (death, MI, stroke) endpoints for subjects originally randomized to pioglitazone and placebo, except for leg amputations during follow-up (4.1% pioglitazone, 5.6% placebo; HR=0.74 [95%CI0.55-0.99]; p=0.046). During follow-up, the incidence of total malignancies was similar between groups; bladder cancer was reported in 0.8% of patients (n=14) in the pioglitazone versus 1.2% (n=21) in the placebo group (RR=0.65 [95%CI0.33-1.28]), and prostate cancer was reported in 44 (3.7%) men in the pioglitazone versus 29(2.5%) men in the placebo group (RR=1.47 [95%CI0.93-2.34]).

The trends of macrovascular benefits of pioglitazone compared with placebo during PROactive did not persist in the absence of continued pioglitazone during this 10-year follow-up. Trends of decreased bladder cancer and increased prostate cancer were observed in the pioglitazone group during follow-up; however, these imbalances should be interpreted with caution due to limitations of the observational study design.

Editor's comment

The authors of this 10-year observational follow-up study evaluated whether cardiovascular benefit and increased risk of certain malignancies persisted in patients with type 2 diabetes (T2DM) and macrovascular disease who had been randomized to receive pioglitazone in the original PROactive trial.

After a mean follow-up of 7.8 years, it was found that there are similar rates of mortality, MI, cardiac intervention, stroke, and leg revascularization between patients who had been randomized to receive pioglitazone compared with those who had been randomized to receive placebo in the original trial. They also found similar overall rates of malignancies between the two groups, with trends toward a lower rate of bladder cancer and a higher rate of prostate cancer in the pioglitazone group. This message is totally opposite to the previous alarm raised that pioglitazone increases the rate of bladder cancer.

Contribution of β-Cell Dysfunction and Insulin Resistance to Cirrhosis-Associated Diabetes: Role of Severity of Liver Disease.

V Grancini, M Trombetta, ME Lunati, D Zimbalatti, ML Boselli, S Gatti, MF Donato, V Resi, R D'Ambrosio, A Aghemo, G Pugliese, RC Bonadonna, E Ors .J. Hepatol. 2015 Dec 01;63(6)1484-1490.

This study evaluated the contribution of â-cell dysfunction and insulin resistance to cirrhosis-associated diabetes. One-hundred and sixty cirrhotic patients with normal fasting plasma glucose (FPG), three with impaired fasting glucose and seven with untreated diabetes mellitus (DM) underwent an extended oral glucose tolerance test (OGTT). The OGTT data were analyzed with a Minimal Model to estimate dynamic (derivative) control (DC) and static (proportional) control (PC) of β-cell function, and with the Oral Glucose Insulin Sensitivity (OGIS)-2h index to estimate insulin sensitivity.

Twenty-six patients (15.6%) had normal glucose tolerance (NGT), 60 (35.8%) had impaired glucose tolerance (IGT), and 84 (48.6%) had DM. DC was significantly reduced in DM vs. NGT and IGT patients. PC was significantly impaired in DM and IGT vs. NGT patients and in DM vs. IGT subjects. The OGIS-2h index was significantly reduced to a similar extent in DM and IGT vs. NGT patients. Patients with Child-Pugh class B and C cirrhosis had reduced DC and PC, but not OGIS-2h values, as compared with subjects in class A. Moreover, Child-Pugh class/score was an independent predictor of β-cell function even after adjustment for glucose tolerance.

Abnormalities of glucose tolerance occur frequently in cirrhosis even in patients with normal FPG, thereby supporting the importance of performing an OGTT. Transition from IGT to DM is driven primarily by â-cell dysfunction. Insulin secretion worsens in parallel with the severity of liver disease, thus suggesting a detrimental effect of liver failure on pancreatic islets on its own.

Editor's comment

The authors evaluated the relationships of β-cell dysfunction and insulin resistance to cirrhosis-associated diabetes. OGTT was done with the participants, and the data were analyzed to determine dynamic control (DC) and proportional control (PC) of β-cell function.

Compared with patients with normal glucose tolerance (NGT) and impaired glucose tolerance (IGT), patients with diabetes mellitus (DM) had significantly reduced DC. Compared with NGT patients, DM and IGT patients had significant impairment of PC. DC and PC were reduced in patients with Child-Pugh class B and C cirrhosis compared with class A, and Child-Pugh class independently predicted â-cell function.

Worsening impairment of insulin secretion occurred as the severity of liver disease progressed. This finding suggests declining liver function may directly impact pancreatic β-cell function.

Estimated Global, Regional, and National Disease Burdens Related to Sugar-Sweetened Beverage Consumption in 2010.

Singh GM, Micha R, Khatibzadeh S, et al. Circulation. 2015;132(8):639-666.

There is increasing evidence that sugar-sweetened beverages (SSBs; drinks with added sugars) are a major cause of obesity and increase the risk of type 2 diabetes, even independently of weight gain. Individuals have responded to this information by decreasing consumption of SSBs; but, at times, there has been a backlash against public health or regulatory efforts to limit SSB consumption. In a comprehensive public policy review with lessons for daily practice, Singh and colleagues used national surveys and data to estimate the effects of SSB consumption on diabetes mellitus and BMI-mediated effects of SSB consumption on cardiovascular disease, diabetes mellitus, and cancer in work that represented 63% of the world's adult population as part of the Global Burden of Diseases, Risk Factors, and Injuries 2010 study.

In the study, SSBs were defined as any sugar-sweetened sodas, fruit drinks, sports/energy drinks, sweetened iced tea, and homemade SSBs that contained at least 50 kcal per 8-oz serving; 100% fruit juice was excluded. Using large observational studies, trials, and meta-analyses, the research team used the following assumptions, which also serve as helpful clinical pearls for counseling patients in the clinic.

Each serving-per-day increase in SSB intake was associated with a 0.10-kg/m2 increase in BMI in individuals with BMI <25 kg/m2 and a 0.23-kg/m2 increase in BMI in individuals with BMI e"25 kg/m2.Those who consumed 1 to 2 servings/day had a 26% greater risk of developing type 2 diabetes in comparison with those in the lowest category of SSB intake.

For reference, at the median age of 60 years, the relative risk of cardiovascular disease such as ischemic heart disease, stroke, and hypertensive heart disease ranged from 1.44 to 1.90 per 5-kg/m2 increase in BMI, and the corresponding pooled effect for diabetes mellitus was 2.32 (95% CI, 2.04–2.63).

The results showed that, in 2010, the mean global consumption of SSBs in adults was 0.58 servings/day, to which 184,000 deaths globally could be attributed, including 5.3% of all diabetes deaths, 0.4% of BMI-related cardiovascular deaths, and 0.3% of BMI-related cancer deaths. Of all deaths attributable to SSB consumption, 3 in 4 (75.9%) occurred in low- and middle-income countries. While most of the deaths occurred in older people, a disproportionate rate of death was attributable to SSB consumption among adults aged 20 to 44 years, in whom

14.0% (95% UI, 12.9%–15.0%) of all diabetes mellitus– and adiposity-related deaths were attributable to SSB consumption. Finally, this burden fell highest in low- to middle-income countries where rates of SSB consumption are high, notably Mexico and other Central American and Caribbean countries, as well as other countries around the world.

Editor's comment

The findings highlight that steps should be taken by nations and individuals to decrease the risk of obesity, diabetes, and related mortality, and their likely worldwide impact. While SSBs are only one component of the obesigenic environment, unlike many nutrients, SSBs can be easily identified, isolated, and targeted for elimination from the diet. It is the easiest dietary advice for a clinician to give and a first step that many patients can take to improve their diet and overall health. Children are developing rather addiction for this sweetened beverages. They should be properly counselled against its adverse effects.

Resting metabolic rate varies by race and by sleep duration

Spaeth AM, Dinges DF, Goel N.Obesity (Silver Spring). 2015 Nov 5. doi: 10.1002/oby.21198. [Epub ahead of print]

Short sleep duration is a significant risk factor for weight gain, particularly in African Americans and men. Increased caloric intake underlies this relationship, but it remains unclear whether decreased energy expenditure is a contributory factor. The current study assessed the impact of sleep restriction and recovery sleep on energy expenditure in African American and Caucasian men and women.

Healthy adults participated in a controlled laboratory study. After two baseline sleep nights, subjects were randomized to an experimental (n = 36; 4 h sleep/night for five nights followed by one night with 12 h recovery sleep) or control condition (n = 11; 10 h sleep/night). Resting metabolic rate and respiratory quotient were measured using indirect calorimetry in the morning after overnight fasting.

Resting metabolic rate-the largest component of energy expenditure-decreased after sleep restriction (-2.6%, P = 0.032) and returned to baseline levels after recovery sleep. No changes in resting metabolic rate were observed in control subjects. Relative to Caucasians (n = 14), African Americans (n = 22) exhibited comparable daily caloric intake but a lower resting metabolic rate (P = 0.043) and higher respiratory quotient (P = 0.013) regardless of sleep duration.

Editor's comment

Normal duration and quality of sleep are essential for ideal metabolic rate and body weight. This study shows that. Sleep restriction decreased morning resting metabolic rate in healthy adults, suggesting that sleep loss leads to metabolic changes aimed at conserving energy.

Effect of Low-Fat Diet Interventions Versus Other Diet Interventions on Long-Term Weight Change in Adults: A Systematic Review and Meta-Analysis

DK Tobias, M Chen, JE Manson, DS Ludwig, W Willett, FB Hu.Lancet Diabetes Endocrinol 2015 Dec 01; 3(12) 968–979

The authors examined the outcomes of a systematic review and meta-analysis of randomized controlled trials (N = 53) evaluating the long-term (≥1 year) effectiveness of low-fat diets on weight loss in adults. 35 weight-loss trials were reviewed, 13 trials that were not designed for weight loss, and 5 weight-maintenance trials. In weight-loss trials (18 comparisons), the low-carbohydrate diets resulted in an average 1.5 kg greater weight loss than the

low-fat diets. No differences in weight change from low-fat diets compared with higher-fat diets (19 comparisons) were reported.

However, when compared with usual diets (8 comparisons), the low-fat diets showed a greater weight loss of 5.41 kg. Non–weight loss trials and weight-maintenance trials also reported a significant but smaller weight loss from low-fat diets compared with usual diets (2.2 kg and .70 kg, respectively) and no differences in weight loss between low-fat and higher-fat diets. The limitation of the studies was the significant dropout and lost to follow-up in most trials—perhaps illustrating the difficulty many individuals experience when trying to change their dietary intake long-term.

The effectiveness of low-fat diets for long-term weight loss is debatable for decades, with many randomised controlled trials (RCTs) and recent reviews giving mixed results. They planned to summarise the large body of evidence from RCTs to determine whether low-fat diets contribute to greater weight loss than participants' usual diet, low-carbohydrate diets, and other higher-fat dietary interventions.

The workers did a systematic review and random effects meta-analysis of RCTs comparing the long-term effect (e"1 year) of low-fat and higher-fat dietary interventions on weight loss by searching MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and Cochrane Database of Systematic Reviews to identify eligible trials published from database inception up until July 31, 2014. They excluded trials if one intervention group included a non-dietary weight loss component but the other did not, and trials of dietary supplements or meal replacement drink interventions. Data including the main outcome measure of mean difference in weight change between interventions, and whether interventions were intended to lead to weight loss, weight maintenance, or neither, were extracted from published reports. The pooled weighted mean difference (WMD) with a DerSimonian and Laird random effects method was estimated.

3517 citations were identified by the search and 53 studies met our inclusion criteria, including 68 128 participants (69 comparisons). In weight loss trials, low-carbohydrate interventions led to significantly greater weight loss than did low-fat interventions (18 comparisons; WMD 1·15 kg [95% CI 0·52 to 1·79]; I(2)=10%). Low-fat interventions did not lead to differences in weight change compared with other higher-fat weight loss interventions (19 comparisons; WMD 0·36 kg [-0·66 to 1·37; I(2)=82%), and led to a greater weight decrease only when compared with a usual diet (eight comparisons; -5·41 kg [-7·29 to -3·54]; I(2)=68%). Similarly, results of non-weight-loss trials and weight maintenance trials, for which no low-carbohydrate comparisons were made, showed that low-fat versus higher-fat interventions have a similar effect on weight loss, and that low-fat interventions led to greater weight loss only when compared with usual diet. In weight loss trials, higher-fat weight loss interventions led to significantly greater weight loss than low-fat interventions when groups differed by more than 5% of calories obtained from fat at follow-up (18 comparisons; WMD 1·04 kg [95% CI 0·06 to 2·03]; I(2)=78%), and when the difference in serum triglycerides between the two interventions at follow-up was at least 0·06 mmol/L (17 comparisons; 1·38 kg [0·50 to 2·25]; I(2)=62%).

These findings suggest that the long-term effect of low-fat diet intervention on bodyweight depends on the intensity of the intervention in the comparison group. When compared with dietary interventions of similar intensity, evidence from RCTs does not support low-fat diets over other dietary interventions for long-term weight loss.

Editor's comment

The authors of this meta-analysis of 53 randomized, controlled trials evaluated the effectiveness of low-fat diets for long-term weight loss, finding that low-carbohydrate diets led to more weight loss.Low-fat diets led to greater weight loss compared with usual diets but not compared with other higher-fat weight-loss interventions.The authors are of the opinion that, the systematic review and meta-analysis of randomized controlled trials does not support the efficacy of low-fat diet interventions over higher-fat diet interventions of similar intensity for significant, long-term, clinically meaningful weight control. They claim that "health and nutrition guidelines should cease recommending low-fat diets for weight loss." The study suggests that the effectiveness of weight-loss diets on long-term weight loss and weight maintenance is more likely determined by total energy intake than by macronutrient composition.

Changes in Glucose Metabolism in People with Different Glucose Metabolism Disorders at Baseline: Follow-Up Results of a Finnish National Diabetes Prevention Programme

N Rautio, J Jokelainen, H Oksa, T Saaristo, M Peltonen, H Puolijoki, J Tuomilehto, M Vanhala, L Moilanen, M Uusitupa, S Keinänen-Kiukaanniemi.Diabet. Med. 2015 Dec 01;32(12)1611-1616.

This Finnish study showed that variations in 2-hour and fasting glucose concentrations differ depending on the particular type of glucose metabolism disorder the individual has.The study examined the changes in glucose metabolism (fasting and 2-h glucose) during follow-up in people with impaired fasting glucose in comparison with changes in people with isolated impaired glucose tolerance, people with impaired fasting glucose and impaired glucose tolerance combined and people with screening-detected Type 2 diabetes at baseline, among those who participated in a diabetes prevention programme conducted in Finland.

A total of 10 149 people at high risk of Type 2 diabetes took part in baseline examination. Of 5351 individuals with follow-up e" 9 months, 1727 had impaired glucose metabolism at baseline and completed at least one lifestyle intervention visit. Most of them (94.6%) were overweight/obese.

Fasting glucose decreased during follow-up among overweight/obese people in the combined impaired fasting glucose and impaired glucose tolerance group (P = 0.044), as did 2-h glucose in people in the isolated impaired glucose tolerance group (P = 0.0014) after adjustment for age, sex, medication and weight at baseline, follow-up time and changes in weight, physical activity and diet. When comparing changes in glucose metabolism among people with different degrees of glucose metabolism impairment, fasting glucose concentration was found to have increased in those with isolated impaired glucose tolerance (0.12 mmol/l, 95% Cl 0.05 to 0.19) and it decreased to a greater extent in those with screening-detected Type 2 diabetes (-0.54 mmol/l, 95% Cl -0.69 to -0.39) compared with those with impaired fasting glucose (-0.21 mmol/l, 95% Cl -0.27 to -0.15). Furthermore, 2-h glucose concentration decreased in the isolated impaired glucose tolerance group (-0.82 mmol/l, 95% Cl -1.04 to -0.60), in the combined impaired fasting glucose and impaired glucose tolerance group (-0.82 mmol/l, 95% Cl -1.07 to -0.58) and in the screening-detected Type 2 diabetes group (-1.52, 95% Cl -1.96 to -1.08) compared with those in the impaired fasting glucose group (0.26 mmol/l, 95% Cl 0.10 to 0.43). Results were statistically significant even after adjustment for covariates (P < 0.001 in all models).

Changes in glucose metabolism differ in people with impaired fasting glucose from those in people with isolated impaired glucose tolerance, people with impaired fasting glucose and impaired glucose tolerance combined and people with screening-detected Type 2 diabetes.

Editor's comment

This study involved participants in a diabetes prevention program and examined the variations in fasting glucose and 2-hour glucose concentrations during follow up of people with impaired fasting glucose compared with people with type 2 diabetes detected on screening, people with isolated compromised glucose tolerance, and people with a combination of impaired fasting glucose and impaired glucose tolerance. Participants were followed up over a period of at least 9 months. Even though the participants with isolated compromised glucose tolerance had reduced 2-hour glucose concentrations, they had increased fasting glucose. Compared with the participants with impaired fasting glucose, those whose diabetes was detected on screening had a greater reduction in fasting glucose. Additionally, compared with the participants with impaired fasting glucose, those with isolated impaired glucose tolerance, with diabetes detected on screening, and with combined impaired fasting glucose and impaired glucose tolerance had a drop in 2-hour glucose concentration.

The Frequency and Impact of Hypoglycemia among Hospitalized Patients with Diabetes: A Population-Based Study

R Gómez-Huelgas, R Guijarro-Merino, A Zapatero, R Barba, A Guijarro-Contreras, F Tinahones, R Bernal-LópezJ. Diabetes Complicat. 2015 Nov 01;29(8)1050-1055.

The researchers aimed to evaluate the frequency of hypoglycemia and its impact on the length of stay and all-cause in-hospital mortality in hospitalized patients with diabetes. They used data from the Basic Minimum Data Set of the Spanish National Health System. Hypoglycemia was defined as having an ICD-9-CM code 250.8, 251.0, 251.1, and 251.2, and categorized as primary if it was the main cause of admission and secondary if it occurred during the hospital stay. The association between hypoglycemia and the study outcomes was evaluated in two cohorts - with and without secondary hypoglycemia - matched by propensity scores and using multivariate models. Among the 5,447,725 discharges with a diagnosis of diabetes recorded from January 1997 to December 2010, there were 92,591 (1.7%) discharges with primary hypoglycemia and 154,510 (2.8%) with secondary hypoglycemia. The prevalence of secondary hypoglycemia increased from 1.1% in 1997 to a peak of 3.8% in 2007, while the prevalence of primary hypoglycemia remained fairly stable. Primary hypoglycemia was associated with reduced in-hospital mortality (Odds ratio [OR] 0.06; 95% Confidence interval [CI], 0.03-0.10) and a significant decrease in time to discharge (Hazard ratio [HR] 2.53; 95% CI, 2.30-2.76), while secondary hypoglycemia was associated with an increased likelihood of in-hospital mortality (OR 1.12; 95% CI, 1.09-1.15) and a significant increase in time to discharge (HR 0.80; 95% CI, 0.79-0.80). In conclusion, the prevalence of secondary hypoglycemia is increasing in patients with diabetes and is associated with an increased likelihood of in-hospital mortality and a longer hospital stay.

Editor's comment

This study examined the impact of hypoglycemia on the amount of time a patient spends in the hospital and number of deaths occurring in the hospital. Over the study period, cases of primary hypoglycemia remained stable, but those of secondary hypoglycemia increased significantly. Additionally, increased amount of time spent in the hospital and higher number of deaths occurring in the hospital were linked with secondary hypoglycemia.Not only the occurrence of secondary hypoglycemia is growing in diabetic patients admitted to the hospital, but it is also linked with poor patient outcomes in the hospital.

Factors Associated With Cardiovascular Events in Patients with Type 2 Diabetes and Acute Myocardial Infarction

K Strojek, I Raz, G Jermendy, AK Gitt, R Liu, Q Zhang, SJ Jacober, Z MilicevicJ. Clin. Endocrinol. Metab. 2015 Nov 23; [EPub Ahead of Print]

The objective was to assess the association between demographic, glycemic, and other clinical factors and cardiovascular (CV) risk in the Hyperglycemia and its effect after acute myocardial infarction on cardiovascular outcomes in patients with Type 2 diabetes mellitus trial.

Design, Settings, Participants and Intervention: We used discrete-time survival tree analysis to examine data collected for up to 4.6 years in 1115 patients with type 2 diabetes mellitus experiencing acute myocardial infarction (MI) ≤ 18 days before enrollment.

The primary objective was to identify demographic, glycemic, and CV risk factors best separating survival curves over time for a composite end point: CV death, nonfatal MI, nonfatal stroke, hospitalization for acute coronary syndromes, or coronary revascularization planned after randomization.

Average change across visits in mean 2-hour blood glucose (BG) level after meals was associated with the greatest difference in event-free survival probability for the primary end point: mean time to 75% event-free survival

for an average change across visits ≤-0.14 mmol/L, 73.48 weeks; for visits with average change >-0.14 mmol/L, 29.10 weeks. An average change across visits in the HbA1c level ≤-0.92% (-10.06 mmol/mol) and the absence of a history of stroke or acute MI increased CV event-free survival time further. Fasting BG and randomized insulin treatment strategy were weak predicting factors of event-free survival.

Postprandial glycemia should be considered a potential target in trials to reduce CV morbidity and mortality in type 2 diabetes mellitus.

Editor's comment

Type 2 diabetes is accepted as a disease of heart.Decreasing risk of cardiovascular disease remains a challenge to survival in type 2 diabetes.This study examined patients with type 2 diabetes mellitus who had suffered a myocardial infarction (MI) within 18 days of study participation.The risk for adverse cardiovascular (CV) events was associated with average postprandial 2-hour blood glucose levels. Prior stroke or acute MI, along with changes in HbA1c level were also adverse CV risk factors.

Effects of Empagliflozin on Blood Pressure and Markers of Arterial Stiffness and Vascular Resistance in Patients with Type 2 Diabetes

R Chilton, I Tikkanen, CP Cannon, S Crowe, HJ Woerle, UC Broedl, OE Johansen .Diabetes ObesMetab 2015 Dec 01;17(12)1180-1193

This study determined the effects of empagliflozin on blood pressure (BP) and markers of arterial stiffness and vascular resistance in patients with type 2 diabetes mellitus (T2DM).

They conducted a post hoc analysis of data from a phase III trial in patients with T2DM and hypertension receiving 12 weeks' empagliflozin and four phase III trials in patients with T2DM receiving 24 weeks' empagliflozin (cohort 1, n = 823; cohort 2, n = 2477). BP was measured using 24-h BP monitoring (cohort 1) or seated office measurements (cohort 2).

Empagliflozin reduced systolic BP (SBP) and diastolic BP in both cohorts ($p < 0.001$ vs placebo), without increasing heart rate. Empagliflozin reduced pulse pressure (PP; adjusted mean difference vs placebo cohort 1: -2.3 mmHg; cohort 2: -2.3 mmHg), mean arterial pressure (MAP; cohort 1, -2.3 mmHg; cohort 2, -2.1 mmHg) and double product (cohort 1, -385 mmHg × bpm; cohort 2, -369 mmHg × bpm) all $p < 0.001$ vs placebo. There was a trend towards a reduction in the ambulatory arterial stiffness index (AASI) with empagliflozin in cohort 1 ($p = 0.059$ vs placebo). AASI was not measured in cohort 2. Subgroup analyses showed that there were greater reductions in PP with increasing baseline SBP in cohort 1 ($p = 0.092$). In cohort 2, greater reductions in MAP were achieved in patients with higher baseline SBP ($p = 0.027$) and greater reductions in PP were observed in older patients ($p = 0.011$). Empagliflozin reduced BP and had favourable effects on markers of arterial stiffness and vascular resistance.

Editor's comment

This study, focused on patients with type 2 diabetes mellitus, examined the impact of empagliflozin on blood pressure, vascular compliance, and resistance. In comparison to placebo, a significant decline in blood pressure, pulse pressure, mean arterial pressure, and double product were noted in patients receiving empagliflozin. This molecule is a unique antidiabetic drug to offer so many favourable cardiovascular effects.