BAND 30

Diabetes Metabolism and the Heart

Diabetes, Stoffwechsel und Herz

CVOT Summit 2021

FINAL PROGRAMME AND ABSTRACTS

Virtual CVOT Summit 2021, 18–19 November 2021

9 European CME credits (EACCME)

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KIRCHHEIM

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14:00–14:30 CET Discussion round with experts

Chair: Giorgino F (Bari, Italy), Rydén L (Stockholm, Sweden)

14:00–14:30 **SGLT2-inhibitors, MRAs and GLP1-RAs: The next decade**

Discussants:
Boehm M (Homburg/Saar, Germany)
Ceriello A (Milano, Italy)
Heerspink H (Groningen, Netherlands)
Lehrke M (Aachen, Germany)
Rosano G (Padova, Italy)
Rossing P (Copenhagen, Denmark)
Wanner C (Wuerzburg, Germany)

14:30–15:00 CET Break

15:00–16:15 CET Obesity and NASH: Where are we moving with GLP1-RAs and dual GIP/GLP1-RAs?

Chair: Wysham C (Rockwood, US),
Blueher M (Leipzig, Germany)

15:00–15:20 **CVOTs in GLP1-RA: The power of individual endpoints**
Nauck M (Bochum, Germany)

15:20–15:40 **Dual GIP/GLP1-RAs – outcomes and future perspectives**
Wysham C (Rockwood, US)

15:40–16:00 **Obesity and NASH: Novel treatment options**
Blueher M (Leipzig, Germany)

16:00–16:15 **Discussion**

16:15–17:15 CET Industry´s perspective – panel discussion

17:15–18:15 CET Oral presentations

Chair: Standl E (Munich, Germany)

17:15–18:15 **Healthy China Program – Early diabetic kidney disease screening**
Gu WJ et al. (Beijing, China)

Impact on diagnosis and management of diabetic kidney disease in real life clinical practice
Schultes B et al. (St. Gallen, Switzerland)

Cardiovascular pathology in patients with non-alcoholic fatty liver disease with overweight and obesity
Pivtorak K (Vinnytsia, Ukraine)

Autonomic neuropathy: impact on carbohydrate metabolism and therapeutical challenges
Kempler P et al. (Budapest, Hungary)

Effects of empagliflozin on lipoprotein subfractions in patients with type 2 diabetes – data from a randomized, placebo-controlled study
Rau M et al. (Aachen, Germany)

Updated meta-analysis of cardiovascular outcome trials evaluating cardiovascular efficacy of glucagon-like peptide-1 receptor agonists
Patoulias D et al. (Thessaloniki, Greece)

18:15–18:45 CET Abstract awards and closing

Schnell O (Munich, Germany)

OP 1

Healthy China program – early diabetic kidney disease screening

Gu WJ, Ma JH, Hong TP, Li XY, Shi LX, Wang YG, Xue YM, Yu XF, Zhu DL, Mu YM; Beijing, China

Background: To improve the prevention and treatment of diabetic kidney disease (DKD) in China, the Beijing Great Physician Commonweal Foundation launched the "Healthy China Program – Early Diabetic Kidney Disease Screening" in 2019. This project aims to evaluate the prevalence, awareness, and screening rate of albuminuria in adult type 2 diabetes mellitus (T2DM) patients in China.

Methods: Patients were eligible for inclusion in the study if they 1) had T2DM, 2) were 18 years old or older, and 3) received antidiabetic medication. Pregnant women with T2DM were excluded. A total of 50 general hospitals in 8 provinces were selected. 10 000 T2DM patients will be included in the database in 2021–2022. This database of T2DM patients includes basic information and biochemical blood results. The cohort will be followed up for 6 months.

The database includes two parts: demographic characteristics and laboratory measurements. A standard questionnaire was used in part one. In part two, routine blood and urine tests, HbA_{1c}, fasting blood glucose, fasting C-peptide, fasting insulin, blood electrolytes, high sensitivity CRP (hsCRP), blood lipids, liver, kidney, and thyroid function were measured. All data were recorded at baseline and at 6-month follow-up.

Descriptive statistics are used to describe the weighted sample characteristics and the prevalence of albuminuria. The association between the prevalence of albuminuria and risk factors is performed using the chi square test. The statistical significance of differences is estimated by Student's t-test and one-way ANOVA.

Results: This database will provide the following information: First, the changes in albuminuria and renal outcome in patients with T2DM; second, the relationship between albuminuria and other variables. The aim of this analysis is to identify clinical risk factors associated with the development of albuminuria and renal impairment in patients with T2DM. The change of HbA_{1c}, fasting insulin, blood pressure, blood lipids, uric acid, and the development of albuminuria will be investigated. The use of different hypoglycaemic drugs and the status of standardised diagnosis and treatment will be also evaluated in this project. Third, the effects of different oral hypoglycaemic drugs on albuminuria will be studied. The effects of SGLT-2 inhibitors on the change in urine albumin-to-creatinine ratio (UACR) and in the estimated glomerular filtration rate (eGFR) from baseline to the end of follow-up will be evaluated. The safety of SGLT-2 inhibitors will also be evaluated in this project.

Conclusions: This project aims to evaluate the prevalence of albuminuria in adult patients with T2DM in China, improve the awareness rate of DKD and provide a data platform for future in-depth research.

OP 2

Impact on diagnosis and management of diabetic kidney disease in real life clinical practice

Schultes B, Emmerich S, Kistler AD, Mecheri B, Schnell O, Rudofsky G; St. Gallen, Switzerland

Background: Quantitative albuminuria measurement using the albumin-to-creatinine ratio (ACR) is recommended according to various guidelines for the diagnosis of diabetic kidney disease (DKD). Our observational study aims at evaluating the impact of point-of-care testing (POCT) of ACR on DKD diagnosis and treatment management for glycaemic control and blood pressure.

Methods: Data of 236 patients with type 1 diabetes, 463 with type 2 diabetes, and 18 with other types of diabetes deriving from 3 diabetes centers were analysed. The impact of ACR POCT on DKD diagnosis and treatment management was assessed by using a case report form. The ACR POCT utilisation purpose and relevance for physicians was assessed using a questionnaire that was filled in by 8 physicians.

Results: Of all included patients (n = 717), 39.1 % had a confirmed or suspected DKD diagnosis, of whom 8.6 % were newly diagnosed with DKD, and 9.9 % were suspected with DKD based on the actual ACR POCT measurement. In 46.1 % of the patients with confirmed/suspected DKD (n = 280) the treatment was modified during the same visit of the ACR assessment. Initiation of glucagon-like peptide-1 (GLP-1) receptor agonists or sodium/glucose cotransporter 2 (SGLT-2) inhibitors treatment were the most frequent intervention, i.e. in 11.1 % or 8.9 % of patients with confirmed/suspected DKD, respectively. All of the 8 participating physicians indicated that they used ACR POCT measurement to examine patients with diabetes regardless of the presence of arterial hypertension, and 6 considered the measurement very important for patients with diabetes.

Conclusions: Our real life clinical practice study indicates that the implementation of ACR POCT has a relevant impact on DKD diagnosis and therapeutic management of patients with diabetes.

OP 3

Cardiovascular pathology in patients with non-alcoholic fatty liver disease with overweight and obesity

Pivtorak K; Vinnytsia, Ukraine

Background: The most common type of lesion among all chronic liver diseases is the non-alcoholic fatty liver disease (NAFLD). It is closely linked to obesity, insulin resistance and cardiovascular pathology.

The aim of this study was to evaluate the relationship between markers of endothelial dysfunction, insulin resistance, adipokines, and cholesterol level in patients with both NAFLD and overweight/obesity.

Methods: 223 patients with NAFLD were examined. We determined the level of inflammatory mediators, endothelin (ET-1), the activity of the von Willebrand factor (vWF), the thickness of the intima-media complex, the

presence of atherosclerotic plaque and stenosis of the carotid arteries, and the index HOMA-IR. The ratio between the content of adiponectin and leptin was represented as log A/L. In addition, an anthropometric survey, measurement of levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), the degree of liver fibrosis using elastography (FibroScan), ECG and echocardiography were conducted.

Results: Correlation analysis revealed a direct correlation between HOMA-IR and leptin ($r = 0.8$; $p = 0.00166$) and an inverse correlation between HOMA-IR and adiponectin ($r = -0.66$; $p = 0.0033$) (index log A/L [$r = -0.71$; $p = 0.0000$]). A comparative analysis of the level of C-reactive protein (CRP) inflammation marker in obese patients showed a direct relationship with HOMA-IR ($r = 0.58$; $p = 0.05$), glucose ($r = 0.44$; $p = 0.0045$) and insulin ($r = 0.66$; $p = 0.0001$) in the blood. The patients with NAFLD and obesity showed a reduction in endothelium-dependent vasodilation, indicating the presence of endothelial dysfunction. The concentration of proinflammatory cytokines such as TNF-α and IL-6 in patients with NAFLD was 3–7 times higher than similar parameters in patients with a similar degree of obesity but without an evident NAFLD. The concentration of ET-1 in the blood plasma of patients with NAFLD had a strong direct correlation with the degree of cardiovascular risk and cognitive deficit in the surveyed patients. It was found that many inflammatory mediators (TNF-α, IL-1, IL-6) and markers (C-reactive protein, fibrinogen) highly correlated with the degree of obesity, the concentration of ET-1, vWF and markers of insulin resistance, a predictor for cardiovascular risk.

Conclusions: The development of NAFLD is associated with the development of endothelial dysfunction, increased levels of leptin, and decreased levels of adiponectin in patients with NAFLD, overweight and obesity.

OP 4

Autonomic neuropathy: impact on carbohydrate metabolism and therapeutical challenges

Kempler P; Budapest, Hungary

Cardiac autonomic neuropathy (CAN) represents a serious complication as it carries a fivefold risk of mortality in patients with diabetes. The high mortality rate may be related to silent myocardial infarction, cardiac arrhythmias, cardiovascular and cardiorespiratory instability and to other causes not explained yet. Usually, we consider autonomic neuropathy as a complication of diabetes. However, it is worth to evaluate this problem from the other side as well: Could autonomic neuropathy have an impact on carbohydrate metabolism? The answer is yes. On the one hand, autonomic neuropathy among patients with newly diagnosed type 2 diabetes mellitus is associated with postprandial hyperglycaemia. On the other hand, it is well known that autonomic neuropathy is associated with hypoglycaemia unawareness and a higher frequency of severe hypoglycaemia. If sympathetic autonomic failure is present, signs of adrenergic activation (tachycardia, hunger, sweating) are frequently absent. As a consequence, hypoglycaemia may occur as a sudden loss of consciousness. Postprandial hyperglycaemia, as well as hypoglycaemia may lead to increased glucose variability, being associated with poor prognosis.

The above mentioned aspects imply various therapeutical implications as well. On the one hand, especially among diabetic patients with autonomic neuropathy, the use of antidiabetic agents not being associated with hypoglycaemia should be preferred. Moreover, agents decreasing postprandial hyperglycaemia (DPP-4 inhibitors, GLP-1 receptor agonists, short acting insulin analogues) are suggested for use. Another important place for therapeutical intervention is neuropathy. In this respect, the use of pathogenetic-based, disease-modifying causal therapy should be used. Pathogenetic oriented treatment with benfotiamine and/or alpha-lipoic acid has an impact on neuropathic damage/deficit and disability, while, on the other hand, it has a documented effect on the improvement of neuropathic pain and quality of life as well. Benfotiamine is a transketolase activator and inhibits harmful alternative metabolic pathways such as the polyol pathway, the exosamin pathway, advanced glycation end product formation, as well as the protein kinase C pathway. Alpha-lipoic acid is considered nowadays the most potent antioxidant agent. Combination therapy with benfotiamine and alpha-lipoic acid is suggested for use more commonly.

OP 5

Effects of empagliflozin on lipoprotein subfractions in patients with type 2 diabetes – data from a randomized, placebo-controlled study

Rau M, Thiele K, Hartmann NUK, Möllmann J, Wied S, Böhm M, Scharnagl H, März W, Marx N, Lehrke M; Aachen, Germany

Background: Sodium-glucose cotransporter 2 inhibitors, as glucose-lowering drugs that increase urinary glucose excretion, have been shown to reduce cardiovascular (CV) events in patients with type 2 diabetes (T2D), although these agents increase blood levels of the proatherogenic low density lipoprotein cholesterol (LDL-C). It has been hypothesized that haemoconcentration due to osmotic diuresis, effects on calculated LDL particle size, or a modulation of lipoprotein subfractions may play a role in this context, but to date the underlying mechanisms remain largely unexplored. Therefore, the present study examined effects of empagliflozin on LDL-C and lipoprotein subfractions including calculated LDL particle size and composition.

Methods: In this placebo-controlled, randomized, double blind study, patients with T2D were randomized to empagliflozin 10 mg ($n = 20$) or placebo ($n = 22$). Composition of lipoprotein subfractions was assessed before and after 3 months of treatment. Lipoproteins were separated using a combined ultracentrifugation-precipitation method (β-quantification).

Results: Empagliflozin increased