BAND 31

Diabetes Metabolism and the Heart

Diabetes, Stoffwechsel und Herz

CVOT Summit 2022

FINAL PROGRAMME AND ABSTRACTS

Virtual CVOT Summit 2022, 10–11 November 2022

10 European CME credits (EACCME)

The Virtual CVOT Summit 2022, Munich, Germany, 10/11/2022–11/11/2022 has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME®) with **10** European CME credits (ECMEC®s). Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity.

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KIRCHHEIM

Oliver Schnell
(Munich, Germany)

Welcome

Dear Colleagues,

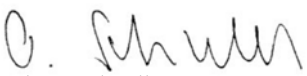
On behalf of the Local Organizing Committee, we would like to invite you to the Cardiovascular Outcome Trial (CVOT) Summit 2022 on Cardiovascular, Renal, Glycemic, and Metabolic Outcomes, which will take place as a virtual congress on 10 – 11 November. We are committed to creating an outstanding meeting with a highly interesting programme and an excellent international faculty.

We invite you to be part of the CVOT Summit 2022, bringing together general practitioners, diabetologists, nephrologists, and cardiologists. Over the past decade, CVOTs have tremendously impacted knowledge on diabetes mellitus and its cardiovascular and renal comorbidities. This year, also new treatment approaches and glycemic markers will be of particular interest. The CVOT Summit has become a well-established platform to discuss developments and opinions linked to CVOTs and aims at building a high-level framework for future scientific exchange.

Presentations and discussions will be given by highly distinguished professionals in the field and will include topics such as new CVOT outcomes, their impact on diabetes care and new guidelines, treatment options, and many more.

The CVOT Summit 2022 promises to be an outstanding event once more.

We look forward to meeting you on 10 – 11 November.



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General information

The CVOT Summit 2022 is run as virtual event. It can be visited on **www.virtual.cvot.org**.

CME accreditation

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THURSDAY, 10 NOVEMBER 2022 VIRTUAL

16:00–16:10 CET **Welcome and introduction**
Schnell O (Munich, Germany)

16:10–17:10 CET **Clinical guidelines on CVD, HF and diabetes: facilitating their development and implementation**
Chair: Mathieu C (Leuven, Belgium), Rydén L (Stockholm, Sweden)

16:10–16:25 **Update on CVD, HF, and CKD Treatment: The ADA-EASD Consensus Report 2022**
Mathieu C (Leuven, Belgium)

16:25–16:40 **New pharmacotherapies for Type 2 Diabetes: a systematic review and network meta-analysis of randomised controlled trials**
Mustafa R (Kansas City, US)

16:40–16:55 **Diabetes and CVD: achieving guideline-recommended management at 12 months**
Green J (Durham, US)

16:55–17:10 **Discussion**

17:10–18:40 CET **Keynote symposium: From early developments to improved daily clinical care**
Chair: Škrha J (Prague, Czech Republic), Forst T (Mannheim, Germany)

17:10–17:30 **Early Clinical Studies: Paving the road for outcomes trials in diabetes**
Hompesch M (San Diego, US)

17:30–17:40 **Discussion**

17:40–18:00 **Subtypes of Type 2 Diabetes – Shaping cardiovascular risk**
Birkenfeld A (Tuebingen, Germany)

18:00–18:10 **Discussion**

18:10–18:30 **CGM for changing Type 2 Diabetes medication**
Bergenstal R (Minneapolis, US)

18:30–18:40 **Discussion**

18:40–19:00 CET **Break**

19:00–20:00 CET **From evidence to practice in Type 2 Diabetes: How can we actually implement state-of-the-art care?**
Chair: Kanumilli N (Manchester, UK), Cheng A (Mississauga, Canada)
In cooperation with Guardians for Health

19:00–19:10 **Why should we mind the intention-action gap in guideline implementation?**
Kanumilli N (Manchester, UK)

19:10–19:25 **Deciphering guidelines – One voice on cardiorenal protection**
Cheng A (Mississauga, Canada)

19:25–19:40 **Screening for CKD in PCP clinic**
Rossing P (Copenhagen, Denmark)

19:40–19:50 **Never walk alone – Become a Guardian**
Kanumilli N (Manchester, UK)

19:50–20:00 **Q&A, summary and closing**
Cheng A (Mississauga, Canada)

FRIDAY, 11 NOVEMBER 2022 VIRTUAL

08:30 – 9:45 CET **Innovation and Implementation: Insulins, CGM and more**
Chair: Schumm-Draeger P (Munich, Germany), Mankovsky B (Kyiv, Ukraine)

08:30 – 08:45 **Further merging new glycemic markers with outcomes in diabetes**
Battelino T (Ljubljana, Slovenia)

08:45 – 09:00 **Combination therapy: When is the right time for insulin?**
Giorgino F (Bari, Italy)

09:00 – 09:25 **Inhaled Insulin: Initiation and titration to improve time in range**
Pettus J (San Diego, US), Edelman S (San Diego, US)

09:25 – 09:45 **Discussion**

09:45 – 10:30 CET **Real World Evidence (RWE): Shedding more light on the path to better clinical care**
Chair: Topsever P (Istanbul, Turkey), Kanumilli N (Manchester, UK)

09:45 – 10:00 **CKD: The importance of Real World Evidence (RWE) in clinical decision making**
Pecoits-Filho R (Curitiba, Brasil)

10:00 – 10:15 **Real world evidence in CVD: strengths and weaknesses**
Kanumilli N (Manchester, UK)

10:15 – 10:25 **OP 1: Risk of stroke in patients with Type 2 Diabetes receiving semaglutide or a dipeptidyl peptidase-4 inhibitor: A real-world US claims database analysis**
Evans M (Cardiff, UK)

10:25 – 10:30 **Discussion**

10:30 – 11:00 CET **Break**

11:00 – 12:30 CET **Recent advances in the management of CKD**
Chair: Heerspink H (Groningen, Netherlands), Ji L (Beijing, China)

11:00 – 11:15 **Treatment of CKD: SGLT-2-inhibitors and future developments**
Heerspink H (Groningen, Netherlands)

11:15 – 11:30 **GLP-1 RAs moving towards CKD: An update**
Nauck M (Bochum, Germany)

CKD in diabetes: clinical and practical considerations for nonsteroidal MRAs
Chair: Heerspink H (Groningen, Netherlands), Rydén L (Stockholm, Sweden)

11:30 – 11:45 **Management of CKD in diabetes - targeting unmet needs**
Groop PH (Helsinki, Finland)

11:45 – 12:00 **New treatment options for CKD in diabetes: Learnings from recent studies**
Hadjadj S (Poitiers, France)

12:00 – 12:30 **Panel Discussion**

12:30 – 13:00 CET **Break**

13:00 – 14:30 CET **Update on the management of heart failure**
Chair: Izthak B (Tel Aviv, Israel), Standl E (Munich, Germany)

13:00 – 13:20 **Monitoring and screening of heart failure in diabetes: The increasing role of biomarkers**
Ceriello A (Milan, Italy)

13:20 – 13:40 **Managing HFpEF with SGLT-2-inhibitors**
Solomon S (Boston, US)

13:40 – 13:50 **OP 2: Effectiveness and safety of empagliflozin in routine care: Results from the EMPagliflozin compaRative effectIveness and SafEty (EMPRISE) study**
Htoo PH (Boston, US)

13:50 – 14:00 **OP 3: Plasma mannose as a novel marker of myocardial infarction across different glycaemic states**
Fortin E (Stockholm, Sweden)

14:00 – 14:30 **Panel Discussion**

14:30 – 15:00 CET Break

15:00 – 16:30 CET Obesity and diabetes – In the midst of new treatment eras

Chair: Vilsbøll T (Copenhagen, Denmark), Rodbard H (Rockville, US)

15:00 – 15:20 **Present and future of weight management in obesity and diabetes**
Wilding JPH (Liverpool, UK)

15:20– 15:40 **Dual GIP/GLP Agonists: Guidelines and practical considerations in diabetes**
Davies M (Leicester, UK)

15:40 – 16:00 **Targeting obesity: High-dose GLP1-RAs and dual GIP/GLP Agonists**
Vilsbøll T (Copenhagen, Denmark)

16:00 – 16:10 **OP 4: Systolic blood pressure reduction with tirzepatide across SURPASS program: A mediation analysis using weight loss as a factor**
Ranta K (Indianapolis, US)

16:10 – 16:30 **Discussion**

16:30 – 17:30 CET Industry's perspective – panel discussion

17:30 – 18:30 CET Oral Presentations

Chair: Kanumilli N (Manchester, UK)

17:30 – 18:30 **OP 5: Effects of empagliflozin on markers of calcium and phosphate homeostasis in patients with Type 2 Diabetes**
Rau M (Aachen, Germany)

OP 6: Influence of continuous glucose monitoring on the glycemic control and quality of life in patients with Type 2 Diabetes mellitus and coronary heart disease
Saienko Y (Kyiv, Ukraine)

OP 7: Estimated glomerular filtration rate, mortality and MACE in men with hypogonadism and Type 2 Diabetes under long-term testosterone therapy
Saad F (Berlin, Germany)

OP 8: Investigating the role of small nucleolar RNAs (snoRNAs) as an early genetic marker of future adverse cardiovascular events
Kumar U (Cambridge, UK)

OP 9: SOdium-glucose CO-transporter inhibition in patients with newly detected Glucose Abnormalities and a recent Myocardial Infarction (SOCOGAMI)
Ferrannini G (Stockholm, Sweden)

18:30 – 18:45 CET Abstract Awards and Closing

Schnell O (Munich, Germany)

Oral Presentatins (OP)

OP 1

Risk of Stroke in Patients with Type 2 Diabetes Receiving Semaglutide or a Dipeptidyl Peptidase-4 Inhibitor: a Real-World US Claims Database Analysis

Marc Evans, Mansoor Husain, Ofir Frenkel, Kamal Kant Mangla, Ayush Srivastava, Ildiko Lingvay
Cardiff, United Kingdom

Background and Aims: People with Type 2 Diabetes (T2D) have a higher risk of stroke and worse outcomes than those without T2D. A meta-analysis of RCT data has shown that glucagon-like peptide-1 receptor agonists are associated with a significant reduction in the risk of stroke, but there remains a specific evidence gap for the real-world effectiveness of semaglutide on stroke risk. We compared risk of incident stroke in patients with T2D or with T2D and atherosclerotic CVD (ASCVD) initiating either semaglutide or a dipeptidyl peptidase-4 inhibitor (DPP-4i).

Methods: Adults (≥18 years) in a US claims database with a claim indicating initiation of semaglutide or a DPP-4i (index date) during the index period (1/1/18–30/9/20), a diagnosis code for T2D on or before index date, and 12 months' continuous enrolment pre-index were included. Exclusion criteria were a claim for semaglutide, DPP-4i or injectable glucose-lowering medication, or a diagnosis code for type 1 or secondary diabetes in the 12 months pre-index; or a claim associated with pregnancy or gestational diabetes at any time during the study period. Patients were propensity score matched 1:1 on baseline demographic and clinical characteristics (27 variables for T2D; 26 for T2D + ASCVD). The primary outcome was time to stroke event during follow-up (medical claim with stroke as primary diagnosis during inpatient or emergency room visit). Patients with no stroke event during follow-up were censored at end of enrolment or end of study period (30/9/20), whichever was earliest. Hazard ratios (HRs) for stroke were calculated using a Cox proportional hazard model, with DPP-4i as the reference group.

Results: In total, 18,856 patients initiating semaglutide and 45,442 patients initiating a DPP-4i were included in matching. Post-matching, there were 17,920 pairs with T2D and 4234 pairs with T2D + ASCVD. The groups were well matched on baseline characteristics, indicated by a standardized mean difference of ≤10 %. Median follow-up ranged between 237 and 258 days. Patients with T2D initiating semaglutide had a lower risk of stroke than those initiating a DPP-4i (HR 0.63 [95 % CI 0.41, 0.95]; p = 0.029). This result appeared more pronounced for T2D + ASCVD (HR 0.45 [0.24, 0.86]; p = 0.015). Overall, 34 patients with T2D receiving semaglutide (0.2 %) experienced a stroke event (incidence rate [IR] per 100 person-years 0.25), compared with 60 patients receiving a DPP-4i (0.3 %; IR 0.40; IR ratio [IRR] 0.62 [95 % CI 0.40, 0.95]). For T2D + ASCVD, 13 patients receiving semaglutide (0.3 %; IR 0.40) and 32 receiving a DPP-4i (0.8 %; IR 0.90) experienced a stroke event (IRR 0.44 [0.23–0.85]).

Conclusions: Our results provide preliminary information regarding the potential of semaglutide to reduce stroke in patients with T2D in a real-world setting. Analyses with additional comparison groups and longer follow-up are needed to determine the broader clinical and economic implications.

OP 2

Effectiveness and safety of empagliflozin in routine care: Results from the EMPagliflozin compaRative effectIveness and SafEty (EMPRISE) study

Phyo Than Htoo, Lisette Koeneman, Helen Tesfaye, Julie M. Paik, Deborah J. Wexler, Mehdi Najafzadeh, Robert J. Glynn, Anouk Déruaz-Luyet, Soulmaz Fazeli Farsani, Sebastian Schneeweiss, Elisabetta Patorno
Boston, MA, USA

Background and Aims: EMPRISE is a 5-year monitoring program that evaluates the effectiveness and safety of empagliflozin (EMPA) using Medicare and 2 U.S. commercial claims (2014–2019 [2018 for Medicare]).

Methods: We identified 190,226 patients ≥18 years with Type 2 Diabetes initiating EMPA or a dipeptidyl peptidase-4 inhibitors (DPP-4i) and followed them up for heart failure hospitalization in primary (HHF-Specific) or any discharge positions (HHF-Broad), a composite of myocardial infarction (MI) and stroke, and all-cause mortality (ACM) (Medicare only). Safety outcomes were lower-limb amputations (LLA), non-vertebral fractures, diabetic ketoacidosis (DKA), acute kidney injury (AKI), renal and bladder cancers. We estimated pooled HR (95 % CI) after propensity score matching, adjusting for 143 baseline covariates.

Results: Patient characteristics were generally balanced between EMPA and DPP4i groups. Mean age was ~60 years and ~44 % of patients were female. At baseline, overall, ~29 % of patients had baseline cardiovascular disease, ~9 % had chronic kidney disease and mean (SD) eGFR was 81.2 (13.0) in the EMPA group and 80.0 (22.2) in the DPP4i group. Compared to DPP4i, EMPA was associated with a reduced risk of HHF (HHF-Specific: 0.47 [0.41, 0.55]; HHF-Broad: 0.67 [0.62, 0.72]), a similar risk of the composite of MI or stroke (0.92 [0.84, 1.02]), and a reduced risk of ACM (0.56 [0.46, 0.68]). Compared to DPP4i, EMPA was associated with a reduced risk of AKI (0.73 [0.68, 0.78]), an increased risk of DKA (1.88 [1.51, 2.34]), and a similar risk of LLA (1.05 [0.86, 1.29]), fractures (1.02 [0.85, 1.22]), renal cancer (0.78 [0.54, 1.12]) and bladder cancer (1.20 [0.82, 1.75]).

Conclusions: Our findings support the cardiovascular effectiveness of EMPA in routine care with a safety profile in line with documented information.

OP 3

Plasma Mannose as a Novel Marker of Myocardial Infarction Across Different Glycaemic States

Elena Fortin, Giulia Ferrannini, Beatrice Campi, Linda Mellbin, Anna Norhammar, Per Näsman, Alessandro Saba, Ele Ferrannini, Lars Rydén
Stockholm, Sweden

Background and Aims: High mannose is associated with diabetes (DM), insulin resistance and coronary atherosclerosis. The relation between mannose concen-

trations and a first myocardial infarction (MI) in relation to the glycaemic state has not been explored. The aim of this study was to investigate the independent association between mannose and a first MI in a population with and without dysglycaemia.

Methods: Fasting plasma mannose concentrations were assayed in 777 patients 6–10 weeks after a first MI and in 770 sex- age- and area-matched controls from the Swedish PAROKRANK study, using high-performance liquid chromatography coupled to tandem mass spectrometry (HPLC-MS-MS). All participants without known DM were categorized as having normal glucose tolerance (NGT; n = 1045), impaired glucose tolerance (IGT; n = 246) or newly detected DM (n = 112) by means of an oral glucose tolerance test (OGTT). Mannose levels were compared by Mann-Whitney or Kruskal-Wallis test. The relationships between mannose concentrations and the glycaemic state, Body Mass Index (BMI), waist circumference and smoking habits were assessed by Spearman's correlation coefficient. The association between log-transformed plasma mannose and MI was investigated across different glycaemic states (NGT, IGT, newly detected DM and known DM) by logistic regression models, adjusting for significant covariates (including age, sex, smoking, family history of cardiovascular disease, and education level).

Results: Mannose levels gradually increased with increasing levels of dysglycaemia ($p < 0.0001$). Patients with a first MI had higher mannose levels than controls (median 74.5 vs 68.8 µmol/L; $p < 0.0001$). The correlation between mannose and insulin resistance, glycated hemoglobin, fasting plasma glucose and two-hour post-load glucose was low as it was for BMI, waist circumference, and smoking. Mannose levels were significantly associated with MI in participants with NGT (adjusted Odds Ratio [OR] patients vs controls: 2.0, 95 % CI 1.2–3.6), but not in dysglycaemic participants i.e. with IGT, newly detected or known DM (adjusted OR patients vs controls: 1.8, 95 % CI 0.8–3.7).

Conclusions: Mannose increased across worsening levels of dysglycaemia. Overall, the concentrations were significantly higher in patients with a first MI than in controls, but independently associated with MI only in NGT patients. These results reinforce previous findings that mannose is related to coronary atherosclerosis and glucose perturbations, adding that it may be possibly targeted for the early management of previously unidentified patients at high cardiovascular risk. Thus, the prognostic value of mannose in patients at high cardiovascular risk deserves further evaluation.

OP 4

Systolic Blood Pressure Reduction with Tirzepatide Across SURPASS Program: A Mediation Analysis using Weight Loss as a Factor

Kari Ranta, Ildiko Lingvay, Ofri Mosenzon, Katelyn Brown, Xuewei Cui, Laura Fernández Landó, Hiren Patel;
Indianapolis, IN, USA

Background and Aims: Tirzepatide (TZP) is a novel GIP/GLP-1 receptor agonist in development for the treatment of Type 2 Diabetes. Across the SURPASS 1–5 clinical studies, TZP 5, 10 and 15 mg demonstrated significant improvements in HbA_{1c} (–20.77 to –28.42 mmol/mol) (–1.9 to –2.6 %), body weight (–6.6 to –13.9 %) and systolic blood pressure (SBP) (–2.8 to –12.6 mmHg) at primary endpoint.

Methods: Patients were randomised 1:1:1:1 to TZP 5 mg, 10 mg, 15 mg or comparator, except in the SURPASS-4 study where patients were randomised 1:1:1:3. Primary endpoint was 40-weeks for (SURPASS-1, 2 and 5) and 52-weeks for (SURPASS-3 and 4). Post-hoc mediation analyses were conducted to evaluate weight loss dependent (WL-D) and independent (WL-IND) effects of TZP on SBP reductions across 5 SURPASS studies. Weight loss was considered an indirect effect (mediator), the effect not mediated by weight loss was considered a direct effect of tirzepatide on SBP. Correlation between SBP change and weight change was also conducted with pooled data of SURPASS 1 to 5.

Results: Concomitant antihypertensive medications were allowed during the SURPASS studies and 47 % (SURPASS-1) to 93 % (SURPASS-4) of patients were using anti-hypertensive medications at baseline. The difference in mean SBP change from baseline at 40-weeks (Total effect) between TZP and comparator group was –1.3 to –5.1 mmHg (TZP 5 mg), –1.7 to –6.5 mmHg (TZP 10 mg) and –3.1 to –11.5 mmHg (TZP 15 mg). In SURPASS-4 study which enrolled patients with established cardiovascular disease, WL-IND effects explained 33 % to 57 % of difference in SBP change between TZP and insulin glargine groups, with the remainder of 67 % to 43 % of the effect being WL-D. In a pooled analysis of SURPASS 1–5 studies, there was a significant ($p < 0.001$) but weak correlation ($r = 0.18$ to 0.22) between change in body weight and SBP.

Conclusions: In conclusion, TZP induced SBP reduction was largely mediated through weight loss, with different degrees of contributions from weight loss independent effects across the different trials.

OP 5

Effects of Empagliflozin on Markers of Calcium and Phosphate Homeostasis in Patients with Type 2 Diabetes

Matthias Rau, Kirsten Thiele, Niels-Ulrik Korbinian Hartmann, Julia Möllmann, Stephanie Wied, Mathias Hohl, Nikolaus Marx, Michael Lehrke;
Aachen, Germany

Background and Aims: Sodium-glucose cotransporter-2 (SGLT2) inhibitors, glucose-lowering drugs that increase urinary glucose excretion, have been shown to reduce CV events in patients with Type 2 Diabetes (T2D). Furthermore, several studies have demonstrated that treatment with SGLT2 inhibitors affect calcium and phosphate homeostasis, but the effect of empagliflozin on these biomarkers is hitherto not investigated in detail. This post-hoc analysis of the EMPA hemodynamics study examined effects of empagliflozin on calcium and phosphate homeostasis.

Methods: In this placebo-controlled, randomized, double-blind study patients with T2D were randomized to empagliflozin 10 mg (n = 20) or placebo (n = 22). Biomarkers of calcium and phosphate homeostasis were assessed

before, and after 3 days and 3 months of treatment.

Results: After 3 days of treatment empagliflozin significantly increased serum levels of phosphate (baseline: 1.10 ± 0.21 mmol/L; day 3: 1.25 ± 0.23 mmol/L; p = 0.036), parathyroid hormone (PTH) (baseline: 57.40 ± 30.49 pg/mL; day 3: 70.23 ± 9.25 pg/mL; p = 0.025) and fibroblast growth factor 23 (FGF23) (baseline: 77.92 ± 24.31 pg/mL; day 3: 109.18 ± 58.20 pg/mL; p = 0.001), and decreased 1,25-dihydroxyvitamin D (baseline: 35.01 ± 14.01 ng/L; day 3: 22.09 ± 10.02 mg/L; p < 0.001). No difference of these parameters was recorded after 3 months of treatment. Empagliflozin had no significant effects on serum calcium and markers of bone resorption (collagen type 1 β-carboxytelopeptide [β-CTX]) or formation (osteocalcin) after 3 days and 3 months of treatment.

Conclusions: Empagliflozin treatment of patients with T2D transiently increases serum phosphate, PTH and FGF23, and decreases 1,25-dihydroxyvitamin D. This might reflect a temporal increase of sodium driven phosphate reabsorption in the proximal tubule of the kidney caused by increased sodium availability in response to SGLT2 inhibition.

OP 6

Influence of Continuous Glucose Monitoring on the Glycemic Control and Quality of Life in Patients with Type 2 Diabetes Mellitus and Coronary Heart Disease

Ya. A. Saienko, G. B. Mankovsky, Ya. Yu. Dzhun, Ye. Yu. Marushko, N. M. Rudenko, B. M. Mankovsky
Kyiv, Ukraine

Background and Aims: There is strong evidence for the benefit of continuous glucose monitoring (CGM) for diabetes management. However, data regarding the influence of CGM on glycemic control and quality of life in one particular patient population, namely patients with Type 2 Diabetes mellitus and coronary heart disease, are lacking. Avoiding hypoglycemia in this patient group seems to be especially important. The aim of the study was to assess the influence of CGM on the quality of life, physical endurance, and glycemic control in these patients.

Methods: We examined 68 patients with Type 2 Diabetes and coronary heart disease (38 males, average age 58.1 ± 3.52 years and 30 females, average age 56.2 ± 3.12 years). Depending on the method of glycemic control, patients were divided into two groups. In group I, glycemic control was performed using CGM, while in group II, self blood glucose monitoring (SBGM) was performed 4 times a day. Patients in both groups were matched by gender, age, anthropometric characteristics, duration of diabetes, blood pressure, kidney function, use of antihyperglycemic medications. Quality of life was assessed by The Medical Outcomes Study 36-Item Short Form Health Survey (SF-36). The patients were followed for 3 months.

Results: The use of CGM for 3 months led to a statistically significant decrease in HbA_{1c} levels – from 8.4 ± 1.3 % to 7.3 ± 1.2 % (p < 0.05). In the SBGM group, the HbA_{1c} decrease was not significant – from 8.3 ± 1.2 % to 7.7 ± 1.2 % (p > 0.05). Physical activity significantly increased from 105 ± 18 to 134 ± 17 min/day in group I (p < 0.05) while in group II, there was no significant increase in physical activity – from 107 ± 18 to 114 ± 20 min/day (p > 0.05). Patients in group I noted improvement of their physical condition and quality of life with physical functioning increased from 58.5 ± 22.3 to 77.4 ± 13.9 (p < 0.01), while in group II, the increase was not significant – from 63.7 ± 19.4 to 66.4 ± 13.8 (p > 0.05). The scores of general health increased in group I (from 55.3 ± 19.2 to 67.4 ± 17.6, p < 0.05), and did not change in group II (59.7 ± 21.3 and 62.4 ± 18.9, p > 0.05). In addition, social functioning scores increased in group I from 60.2 ± 17.6 to 73.6 ± 17.2 (p < 0.05) but did not change significantly on group II – 61.7 ± 20.3 and 62.4 ± 20.3 (p > 0.05).

Conclusions: Control of glycemia using CGM in patients with Type 2 Diabetes and coronary heart disease led to an improved glycemic control, quality of life and increased physical endurance.

OP 7

Estimated Glomerular Filtration Rate, Mortality and MACE in Men with Hypogonadism and Type 2 Diabetes Under Long-Term Testosterone Therapy

Farid Saad, Karim Sultan Haider, Ahmad Haider, Gheorghe Doros, Abdulmaged Traish
Berlin, Germany

Background and Aims: Reduced estimated glomerular filtration rate (eGFR) is associated with cardiovascular risk and mortality. We aimed to assess eGFR, mortality, and major adverse cardiovascular events (MACE), defined as myocardial infarction (MI) or stroke, in men with hypogonadism and Type 2 Diabetes (T2D), with and without long-term testosterone therapy.

Methods: In an ongoing observational registry study in a urological office, 370 men with hypogonadism, defined as total testosterone levels ≤ 12 nmol/L and at least moderate symptoms on the Aging Males' Symptoms scale (AMS) had T2D. 190 received testosterone undecanoate 1000 mg/12 weeks (T-group), 180 opted against treatment (CTRL). Means and standard deviations of absolute measures over 13 years were reported. All men received standard diabetes treatment in the local diabetes center including mandatory education on lifestyle changes. eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formulae.

Results: Mean baseline age in the T-group was 61.0 ± 5.3 and 63.0 ± 4.9 years in CTRL (p < 0.0001). Mean (median) follow-up in T-group and CTRL was 9.0 (9) and 9.7 (11) years, respectively. Mean baseline testosterone was 9.2 ± 1.7 in the T-group and 9.8 ± 1.1 in CTRL (p < 0.0005). Creatinine (mg/dL) decreased from 0.95 ± 0.15 to 0.81 ± 0.07 in the T-group and increased from 1.00 ± 0.14 to 1.27 ± 0.22 in CTRL (p < 0.0001 for both). Systolic blood pressure (mmHg) decreased in the T-group from 163.0 ± 13.3 to 129.8 ± 6.5 and increased in CTRL from 145.5 ± 14.5 to 162.9 ± 13.1 (p < 0.0001 for both). Diastolic blood pressure (mmHg) decreased in the T-group from 97.3 ± 10.7

to 74.8 ± 3.1 and increased in CTRL from 84.7 ± 10.2 to 96.8 ± 7.5 ($p < 0.0001$ for both). T-group: eGFR (MDRD) (mL/min/1.73 m²) increased from 82.5 ± 12.8 to 94.4 ± 9.1. CTRL: eGFR decreased from 77.2 ± 12.1 to 56.9 ± 10.6) ($p < 0.0001$ for both). T-group: eGFR (CKD-EPI) (mL/min/1.73 m²) increased from 84.0 ± 15.4 to 87.5 ± 4.7. CTRL: eGFR decreased from 77.0 ± 13.9 to 49.8 ± 12.3) ($p < 0.0001$ for both). No MACE and 21 deaths (11.1 %) occurred in the T-group while in CTRL, 62 MIs (34.4 %), 51 strokes (28.3 %), and 62 deaths (34.4 %) were recorded ($p < 0.0001$ for all). All testosterone injections were administered in the urological office resulting in very high adherence.

Conclusions: Long-term testosterone therapy in men with hypogonadism and T2D prevents age-related deterioration in eGFR. Mortality and MACE were markedly reduced in the testosterone-treated group in comparison to the untreated hypogonadal control group.

OP 8

Investigating the Role of Small Nucleolar RNAs (snoRNAs) as an Early Genetic Marker of Future Adverse Cardiovascular Events

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Background and Aims: The PROSPER (PROspective Study of Pravastatin in the Elderly at Risk) study identified single nucleotide polymorphisms (SNPs) associated with cardiovascular deaths. SNPs at the 14q32 locus were found to specifically increase the risk of future adverse cardiovascular events. This locus also contains clusters of small nucleolar RNAs, which are non-coding but known to be involved in RNA remodelling and post-translational modification. We aimed to characterise the SNPs at the 14q32 locus, as well as investigate their effects on these snoRNAs and their suitability as a genetic marker to identify and screen the individuals at risk of future cardiovascular events. This approach would identify individuals at high risk of cardiovascular events and enable consideration of prophylactic preventative treatments.

Methods: Published SNPs (in our locus of interest) were filtered, by identifying and mapping the SNPs associated with more than one cardiovascular event (e.g., TIA, stroke, myocardial infarction). The strandedness of the wild-type gene and the SNP was compared using computational tools from the ViennaRNA suite. Using the SimRNA computational package and RNA contact prediction techniques, three-dimensional snoRNA structures with/without SNPs were predicted and compared, and potential RNA-protein complexes were investigated.

Results: We found that these snoRNAs bind to the methyltransferase fibrillarin, which is integral to nucleolar remodelling and is a component of the cellular response to stresses such as chronic hypertension. The 14q32 SNPs identified by PROSPER overlap significantly with the snoRNAs, suggesting effects on snoRNA structure. Significant differences in strandedness in the presence of the SNP compared to the wild-type gene were identified. We found that this resulted in significant changes in 3D snoRNA structure with significant changes in fibrillarin binding, snoRNA-fibrillarin complex formation, and function.

Conclusions: We, therefore, conclude that SNPs at the 14q32 locus led to significant snoRNA structural changes and aberrant fibrillarin complex function. We further suggest that this may result in pathological intracellular responses to cellular stresses. Genetic screening offers the ability to identify the individuals at high risk of future cardiovascular adverse events and therefore those who have the most to gain from early therapies to prevent disease occurrence and/or progression. These individuals are also potential targets for specific genetic therapies in the future.

OP 9

SOdium-glucose CO-transporter inhibition in patients with newly detected Glucose Abnormalities and a recent Myocardial Infarction (SOCOGAMI)

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Background and Aims: Established dysglycaemia (impaired glucose tolerance [IGT] or Type 2 Diabetes [T2DM]) is a risk factor for further cardiovascular events in patients with coronary artery disease. Sodium-glucose cotransporter 2 inhibitors reduce this risk. The aim of the present investigation was to test the hypothesis that empagliflozin exerts beneficial effects on myocardial function in patients with a recent acute coronary syndrome and newly detected dysglycaemia.

Methods: Forty-two patients (mean age 67.5 years, 81 % male) with recent myocardial infarction (n = 36) or unstable angina (n = 6) and newly detected IGT (n = 27) or T2DM (n = 15) were randomised to 25 mg of empagliflozin daily (n = 20) or placebo (n = 22) on top of ongoing therapy. They were investigated with oral glucose tolerance tests, stress-perfusion cardiac magnetic resonance imaging (CMR) and echocardiography at three occasions: before randomisation, after seven months on study drug and three months following cessation of such drug. Primary outcome was a change in left ventricular (LV) end-diastolic volume (LVEDV) and secondary outcomes were a change in a) systolic and diastolic LV function; b) coronary flow reserve; c) myocardial extracellular volume (ECV) in non-infarcted myocardium; d) aortic pulse wave velocity.

Results: Empagliflozin induced a significant decrease in fasting and post load glucose ($p < 0.05$) and body weight ($p < 0.01$). Empagliflozin did not influence LVEDV, LV systolic or mass indexes, coronary flow reserve, ECV or aortic pulse wave velocity. Echocardiographic indices of LV diastolic function (E/e' and mitral E/A ratio) were not influenced. No safety concerns were identified.

Conclusions: Empagliflozin had predicted effects on the dysglycaemia but did not influence variables expressing LV function, coronary flow reserve and ECV. An explanation may be that the LV function of the patients was within the normal range.

Novel Therapies

P 01

Tirzepatide Reduces Serum Triglyceride Concentrations Irrespective of Concomitant Fibrate Use in SURPASS-4 Participants with T2D at High Cardiovascular Risk

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Background and Aims: In the SURPASS-4 trial, participants with Type 2 Diabetes (T2D) inadequately controlled with 1–3 oral glucose-lowering medications and high cardiovascular (CV) risk (coronary heart disease, peripheral arterial disease, cerebrovascular disease, chronic kidney disease, or congestive heart failure) received the once-weekly GIP/GLP-1 receptor agonist tirzepatide (TZP) or titrated insulin glargine (iGlar). In the study, TZP reduced serum triglycerides and low-density lipoproteins cholesterol (LDL-C) levels significantly more than iGlar. In this analysis we evaluated the effect of concomitant use of fibrates or statins on reductions in these lipid parameters.

Methods: Participants (N = 2,002) were randomized 1:1:1:3 to once-weekly TZP (5, 10, 15 mg) or once daily iGlar. Lipoproteins were measured at baseline, 42, 52 (primary endpoint), 78 weeks and study end (median 85 weeks). This post-hoc analysis assessed percent change from baseline in lipids across subgroup categories in participants while on assigned treatment without rescue medication (efficacy estimand) using mixed-model repeated measures. Participants with baseline and at least 1 post-baseline measurement were included in the analysis.

Results: Overall, 12.4 % and 77.8 % of the participants were receiving fibrates and statins at baseline, respectively. Baseline triglyceride concentrations of participants receiving fibrates or not receiving fibrates were 2.59 mmol/L and 2.03 mmol/L, respectively, and for those receiving statins or not, they were 2.05 mmol/L and 2.26 mmol/L, respectively. Baseline LDL-C concentrations in participants receiving fibrates or not receiving fibrates were 2.13 mmol/L and 2.15 mmol/L, respectively and for participants receiving statins or not, they were 2.02 mmol/L and 2.59 mmol/L, respectively. At week 52, serum triglycerides and LDL-C were reduced by all 3 TZP doses, whether or not participants were receiving fibrates or statins at baseline. These reductions were maintained until 78 weeks (N = 574 for TZP). TZP dose-dependently reduced serum triglycerides, with the reductions being similar in those on fibrates/statins or not. The marked reduction in triglycerides (14–24 %) for TZP in the presence of fibrate therapy and no change for iGlar was clinically meaningful as the participants receiving fibrates still had elevated triglycerides at baseline. In general, TZP also reduced LDL-C more than iGlar. No differential treatment effects (TZP vs iGlar) on the reduction of triglycerides or LDL-C were observed for either fibrate or statin use.

Conclusions: In participants with T2D and high CV risk, TZP lowered triglycerides and LDL-C more effectively than iGlar, regardless of concomitant use of fibrates or statins.

P 02

Meta-Analysis Evaluating the Efficacy of Sodium-Glucose Co-transporter-2 Inhibitors in Patients with Acute or Recently Decompensated Heart Failure

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Background and Aims: Heart failure (HF) constitutes a major health problem worldwide, associated with significant morbidity and mortality. In addition, long-term outcomes of acute decompensated HF remain poor, with one-year mortality reaching up to 40 %. Sodium-glucose co-transporter-2 (SGLT-2) inhibitors have been recently approved for the treatment of HF with reduced left ventricular ejection fraction (HFrEF), while empagliflozin is also recommended for patients with HF with preserved left ventricular ejection fraction (HFpEF), regardless of diabetes mellitus status at baseline. We performed a meta-analysis seeking to determine the cardiovascular efficacy of SGLT-2 inhibitors in the setting of acute HF.

Methods: We searched PubMed and Cochrane Library databases, from their inception to 1st March 2022 for randomized controlled trials enrolling adult patients regardless of diabetes mellitus status at baseline, assigned either to SGLT-2 inhibitor or placebo/active comparator in the setting of acute HF. The primary safety endpoint was the effect of SGLT-2 inhibitors on the endpoint of recurrent worsening HF. We set as secondary efficacy outcomes the following: all-cause mortality, the composite endpoint of cardiovascular death or recurrent hospitalization for HF decompensation and the observed diuretic response.

Results: We pooled data from 3 relevant randomized controlled trials in a total of 1 831 patients. SGLT-2 inhibitors compared to placebo resulted in a significant decrease in the risk for recurrent worsening HF by 34 % (RR = 0.66, 95 % CI; 0.58–0.76, I2 = 0 %, p < 0.00001). In addition, SGLT-2 inhibitors led to a significant decrease in the risk for the composite of cardiovascular death or re-hospitalization for HF decompensation by 30 % (RR = 0.70, 95 % CI; 0.62–0.78, I2 = 0 %, p < 0.00001). There was no significant effect on all-cause mortality (RR = 0.72, 95 % CI; 0.48–1.09, I2 = 22 %, p = 0.12). Finally, a non-significant effect on diuretic response, defined as weight change per standard loop diuretic dose, was shown (MD = –1.15, 95 % CI; –3.18–0.17, I2 = 86 %, p = 0.26).

Conclusions: Overall, the present meta-analysis provides new insights into the potential role of SGLT-2 inhibitors on acute HF, demonstrating a significant risk reduction for recurrent worsening HF event, leading to a new hospitalization.

P 03

GLP-1 RA Treatment and the Risk of Pancreatic Cancer in a Cohort of 209,529 Type 2 Diabetes Israeli Patients: Cox Regression Analysis with Time-Dependent Covariates

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Background and Aims: Randomized controlled trials on GLP-1 receptor ag-

onists (GLP-1 RA) efficacy exclude patients with a history of pancreatitis or elevated amylase, as these drugs are possibly associated with risk for pancreatitis and pancreatic cancer (PC). We investigated the association of GLP-1 RA treatment as a time dependent exposure, with PC incidence, in a population-based cohort of Type 2 Diabetes (T2D) patients, while accounting for major confounding factors and time related biases, and adjusting for the history of other glucose-lowering medications (GLMs).

Methods: A historical cohort of all "Clalit" HMO adult members with T2D (N = 558,383) was followed from 2009, when GLP-1 RAs first became available in Israel, until PC diagnosis, death, or end of follow-up in December 2017. We used a discrete form of the weighted cumulative quarterly exposure to GLP-1 RA to evaluate its association with PC incidence. This was implemented in a time-dependent covariate Cox model, with time origin at 2 years post diabetes diagnosis, adjusting for age, sex, ethnic background, sociodemographic status, baseline BMI, smoking history, and all other GLM history. The latter adjustment was implemented via time-dependent covariates based on quarterly GLM purchase data. In a sensitivity analysis, to reduce any bias due to avoidance of GLP-1 RA because of pancreatitis in patients as yet undiagnosed with pancreatic cancer, we omitted from the model the GLP-1 RA exposure in the previous year.

Results: During the follow-up period 1,473 PC patients were diagnosed over 3,389,807 person-years. Estimated hazard ratios (HRs) for PC per 1 defined daily dose (DDD) of GLP-1 RA were 0.70 (95 % CI: 0.39–1.27) taken during the previous year, 1.06 (95 % CI: 0.39–2.84) taken during the second to fourth year previously, and 0.28 (95 % CI: 0.08–1.07) taken during the fifth to seventh year previously. When GLP-1 RAs during the previous year was omitted, the estimated HRs were 0.71 (95 % CI: 0.33–1.52) taken during the second to fourth year previously, and 0.31 (95 % CI: 0.08–1.16) taken during the fifth to seventh year previously.

Conclusions: Our results do not support a positive association of GLP-1 RA treatment with pancreatic cancer incidence. It should be noted that physicians may avoid prescribing these medications to patients with a history of pancreatitis or high amylase, introducing differential selection bias within the GLP-1 RA treated patient population. Nevertheless, since most pancreatic cancer that follows pancreatitis is diagnosed within one year of the pancreatitis, our sensitivity analysis reduces the risk of this bias.

P 04

Meta-Analysis Evaluating the Effect of Sodium-Glucose Co-transporter-2 Inhibitors on Pulmonary Artery Pressure Indices

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Background and Aims: Pulmonary artery (PA) pressure indices have been shown to be highly predictive of surrogate cardiovascular outcomes, including cardiovascular mortality, especially in patients with heart failure (HF) or chronic kidney disease (CKD). Sodium-glucose co-transporter-2 (SGLT-2) inhibitors have demonstrated outstanding cardiovascular and renal benefits in patients with Type 2 Diabetes mellitus (T2DM), while these effects are sustained in patients with HF or CKD, regardless of T2DM status. Even though it is already established that SGLT-2 inhibitors improve left ventricular remodeling, their effect on right ventricular function and pulmonary vasculature are not known. Therefore, we sought to assess whether SGLT-2 inhibitors affect PA pressure indices in patients at high cardiovascular risk or with established cardiovascular disease.

Methods: We searched PubMed and Cochrane Library databases, from their inception to 15th February 2022 for randomized controlled trials enrolling adult patients regardless of T2DM status at baseline, assigned either to SGLT-2 inhibitor or placebo/active comparator. The primary safety endpoint was the change in mean PA pressure (PAP). We set as secondary efficacy outcomes the change in PA systolic pressure (PASP) and PA diastolic pressure (PADP).

Results: We pooled data from 3 relevant randomized controlled trials in a total of 168 patients. Treatment with SGLT-2 inhibitors resulted in a non-significant decrease in mean PAP by 1.44 mmHg (MD = –1.44, 95 % CI –3.00 to 0.13, I2 = 0 %, p = 0.07). In addition, SGLT-2 inhibitors did not pose a significant effect on PADP (MD = –1.77, 95 % CI –3.71 to 0.17, I2 = 50 %, p = 0.07). Finally, SGLT-2 inhibitors did not affect PASP compared to placebo (MD = –2.21, 95 % CI –4.71 to 0.3, I2 = 0 %, p = 0.08).

Conclusions: This is the first relevant meta-analysis addressing the effect of SGLT-2 inhibitors on PAP indices in adult patients with or without T2DM at baseline. Despite the fact that our results showed a numeric reduction in mean PAP, PADP and PASP, none of these effects was statistically significant. The results of our meta-analysis, despite being interesting, require further validation in larger prospective trials.

P 05

Effect of Sodium-Glucose Co-transporter-2 Inhibitors on Arterial Stiffness: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Background and Aims: Arterial stiffness represents an established cardiovascular risk marker. Sodium-glucose co-transporter-2 (SGLT-2) inhibitors have significant cardio-protective effects. Herein, we sought to determine the effect of SGLT-2 inhibitors on pulse wave velocity (PWV).

Methods: We searched PubMed, Cochrane Library, and grey literature from inception to 7th February 2022 for randomized controlled trials (RCTs) enrolling adult subjects with or without type 2 diabetes mellitus (T2DM), assigned to a SGLT-2 inhibitor versus control, and addressing their effect on PWV. We set as primary efficacy outcome the change in PWV with SGLT-2 inhibitors versus placebo or control.

Results: We pooled data from six trials in a total of 452 enrolled participants assigned either to SGLT-2 inhibitor or control. Overall, SGLT-2 inhibitor treat-

ment compared to control resulted in a nonsignificant decrease in PWV. Exclusion of a trial utilizing cardiac magnetic resonance imaging for the assessment of PWV demonstrated that SGLT-2 inhibitors induce a significant reduction in PWV by 0.21 m/s. When we restricted our analysis to RCTs enrolling subjects with T2DM, we observed that SGLT-2 inhibitor compared to control resulted in a significant decrease in PWV by 0.17 m/s.

Conclusions: SGLT-2 inhibitors do not decrease PWV in patients with established cardiovascular disease or cardiovascular risk factors. However, we have shown that SGLT-2 inhibitors lead to a slight, but significant decrease in PWV in patients with T2DM. The latter finding is of great value, based on the significant correlation between PWV and micro- and macrovascular complications of T2DM.

Cardio-vascular perspectives

P 06

Effect of SGLT-2 Inhibitors on Cardiac Autonomic Function in Type 2 Diabetes Mellitus: A Meta-Analysis of Randomized Controlled Trials

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Background and Aims: Cardiac autonomic neuropathy (CAN) is a common complication of Type 2 Diabetes mellitus (T2DM). We sought to determine whether sodium-glucose co-transporter-2 (SGLT-2) inhibitors affect indices of CAN in patients with T2DM.

Methods: We searched for parallel group or cross-over randomized controlled trials (RCTs) enrolling adult subjects with T2DM, assigned to a SGLT-2 inhibitor versus placebo or active comparator, and addressing their effect on CAN. PubMed, Cochrane Library and grey literature sources were searched. The primary efficacy outcome was the change in the low-frequency/high-frequency (LF/HF) ratio. We set as secondary efficacy outcomes the change in the standard deviation of all 5 min mean normal RR intervals (SDANN) as well as the change in the square root of the mean of the sum of the squares of differences between adjacent RR intervals (r-MSSD). The protocol has not been registered at a publicly available repository.

Results: We pooled data from four RCTs in a total of 247 subjects with T2DM. SGLT-2 inhibitor treatment did not have a significant effect on LF/HF ratio (MD = –0.11, 95 % CI; –0.35 to 0.12, I2 = 0 %, p = 0.36). SGLT-2 inhibitor treatment did not have a significant impact either on SDNN (MD = –2.83, 95 % CI; –7.41 to 1.75, I2 = 31 %, p = 0.23), or on r-MSSD (MD = –0.14, 95 % CI; –3.52 to 3.25, I2 = 46 %, p = 0.94). Overall risk of bias was graded as low across the selected RCTs.

Conclusions: SGLT-2 inhibitor treatment in patients with T2DM does not seem to provide any significant beneficial effect on CAN indices.

P 07

NT-proBNP Point-of-Care Testing as a Screening Tool for Heart Failure Risk and CVD Risk in Type 2 Diabetes

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Background and Aims: Heart failure (HF) is a common chronic and serious complication of Type 2 Diabetes (T2D) and should be detected as early as possible. Recent international practice guidelines recommend measuring the blood concentration of the natriuretic peptide NT-proBNP in patients with suspected HF for confirming or ruling out the diagnosis. Therefore, the measurement of NT-proBNP in patients with T2D, using a point-of-care testing (POCT) system may be helpful for HF detection and for identifying high-risk patients for preventative interventions. The primary objective of this observational study was to identify the number of T2D patients with a NT-proBNP concentration equal or above 125 pg/ml using a POCT system. The secondary objective was to determine the prevalence of HF in this subset of patients.

Methods: Overall 259 participants with T2D and hypertension, aged 50 years or older, with diabetes for more than 10 years, and absence of overt cardiovascular disease were recruited at two study centers. Demographic information on the patients was acquired by their attending physician during the visit. Additionally, circulating levels of NT-proBNP were measured by POCT using the CARDIAC proBNP+ assay (Roche) and the cobas h232 instrument (Roche). Patients were clustered according to their NT-proBNP concentration value in two groups: with NT-proBNP < 125 pg/ml and with NT-proBNP ≥ 125 pg/ml. Descriptive statistics was used for analysis of the clinical characteristics and laboratory values of both groups of patients. The differences between non-normally distributed baseline characteristics were analysed by Mann-Whitney U test. Chi-square test was employed for the comparison of categorical variables and testing the null hypothesis.

Results: Mean age was 66.1 ± 9.2 years, 55.2 % were female, 44.8 % were male, 60.6 % (n = 157) had a NT-proBNP < 125 pg/ml and 39.4 % (n = 102) had a NT-proBNP ≥ 125 pg/ml. Differences were observed among those with low and high NT-proBNP in mean age (63.4 ± 8.8 years vs. 70.1 ± 8.2 years, p < 0.001), diabetes duration (15.4 ± 5.9 years vs. 17.9 ± 7.3 years, p = 0.003), estimated glomerular filtration rate (eGFR) (86 ± 16 ml/min/1.73 m^2 vs. 76 ± 20 ml/min/1.73 m^2, p < 0.001), and prevalence of other comorbidities (45.9 % vs. 64.7 %, p < 0.00001).

Conclusions: Our results suggests that in diabetes NT-proBNP ≥ 125 pg/ml is associated with older age, a longer diabetes duration, a lower eGFR and a higher prevalence of comorbidities. These data may help stratify targeted screening for people with T2D at high risk of HF.

P 08

LV Remodeling Following Acute Myocardial Infarction: Differences Between ST-Elevation Myocardial Infarction and non-ST-Elevation Myocardial Infarction

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Background and Aims: The aim was to study the differences in left ventricular (LV) remodeling patterns in both ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) patients and outcomes at 12 months.

Methods: 103 patients presented with acute myocardial infarction (STEMI or NSTEMI) were retrospectively enrolled in the study. The LV remodeling was studied by 2D Echocardiography. At 12 months, information was collected by telephone for a clinical update (death and/or hospitalizations) or hospital out-patient visit for all patients.

Results: Of the 103 patients studied, 34 were female, 95 were hypertensives and 64 had diabetes. The mean age was 59.4 ± 14.6 years (median age: 60 years). A majority had experienced a STEMI (n = 54), while 49 patients experienced an NSTEMI. The patients with NSTEMI were older (p = 0.07) and had significantly greater number of hypertensives (p = 0.007). 98 patients were followed-up after 1 year. At 1 year, there were 4 deaths and 7 re-admissions for heart failure. The time to readmission for heart failure in patients with STEMI was 6.2 ± 0.89 months and 5.9 ± 1.1 months in patients with NSTEMI (p = 0.19). At baseline, NSTEMI patients had greater LV remodeling, which did not regress after 1 year. On the other hand, STEMI patients had lesser LV remodeling than NSTEMI patients at baseline, which regressed significantly at 1 year.

Conclusions: In patients with NSTEMI, the incidence of adverse LV remodeling was greater than in patients with STEMI. The patients with greater adverse LV remodeling at baseline, did not undergo negative remodeling at 1 year. This did not affect the clinical outcomes of death and re-admission for heart failure.

P 09

Arterial Stiffening, Blood Pressure Profiles and Melatonin Levels in Patients with Type 2 Diabetes Mellitus and Cardiac Autonomic Neuropathy

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Background and Aims: Diabetes-associated cardiac autonomic neuropathy (CAN) is often underdiagnosed serious complication of diabetes mellitus (DM) with approximately five-fold risk of mortality. Increased arterial stiffness (AS) and violated daily blood pressure (BP) profile are considered as the strongest predictors of cardiovascular morbidity and mortality. Melatonin has a role in the circadian rhythms, quality of sleep and has been additionally identified as one of the important regulators of glucose metabolism. The present study was designed to determine the relationship between AS, BP profiles, insulin resistance (IR) and melatonin levels among patients with type 2 DM (T2DM) and CAN.

Methods: The study involved 92 patients with T2DM, among them 46 patients with definite CAN and 46 without CAN. Patients were aged 50 – 59 yrs, had BMI of 26.8 ± 0.32 kg/m^2, a mean duration of diabetes of 7.4 ± 0.5 yrs and HbA_{1c} level of 7.3 ± 0.18 %. The diagnosis of CAN was based on the results of 5 standard cardiovascular tests. 24-hrs heart rate variability was evaluated using ECG "EC-3H" ("Labtech"), AS monitoring and BP daily patterns were assessed via TensioMedTM Arteriograph 24 (Hungary). Homeostasis model assessment IR (HOMA-IR) was calculated as follows: fasting glucose (mmol/l) × fasting immunoreactive insulin (mcIU/ml)/22.5. Melatonin in saline and immunoreactive insulin in blood were determined by enzyme-linked immunosorbent assay (ELISA) using kits by DRG (USA). Statistics: ANOVA.

Results: We found out that development of CAN was associated with an increase in HOMA-IR (6.03 ± 0.9 vs 4.12 ± 0.7, p < 0.001) and pulse wave velocity (PWV) (10.95 ± 0.23 vs 8.7 ± 0.43 m/sec, p < 0.001), as well as with a decrease in melatonin levels (9.3 ± 0.9 vs 19.7 ± 1.2 pg/ml, p < 0.001). Arterial stiffness parameters among patients with CAN exceeded physiological values and were considered high. The daily value of PWV was normal in 19.6 %, elevated in 47.6 % and pathological in 32.6 % of cases. No statistically significant changes in systolic and diastolic diurnal index of BP among the two groups of patients (p > 0.05) were found. However, 60.9 % of patients with CAN had violations of diurnal BP profile, namely the daily profile of "non-dipper" was found in 45.7 %, and the "night-peaker" profile in 19.6 % of cases. Multiple regression analysis, after controlling for age, gender, diabetes duration, BP, HbA_{1c} and left ventricular mass index, showed an independent inverse association of melatonin levels with HOMA-IR and PWV (p < 0.001).

Conclusions: Nocturnal melatonin secretion is independently and inversely associated with IR, violation of BP profile and increase of AS. Further work is needed to fully elucidate the exact role of melatonin on the regulation of metabolic processes, BP patterns and arterial wall rigidity.

P 10

Is There Any Connection Between Plasma B12 Vitamin, Total Serum Homocysteine, and Increased Risk of Myocardial Infarction in NIDDM?

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Background and Aims: This study was undertaken to assess the association of vitamin B12 with homocysteine (Hcy) in people with diabetes on metformin (> 5 months), and to observe whether Hcy increased the risk of CVD, especially myocardial infarction (MI).

Methods: Case-control study was conducted to assess the effect of metformin treatment on Hcy, and Cbl in 53 Type 2 Diabetes (T2D) out-patients aged > 45 years without bariatric surgery or gastric bypass. The study was conducted during one-to-one visits with endocrinologists and cardiologists in Georgia. The participants visited 8 endocrinologist and 5 cardiologists in 5 primary care clinics in the city Batumi in the period between March 10 and April 20, 2022. The patients were categorized into a metformin (33) and non-metformin group (20). Fasting serum tHcy and Cbl plasma level were measured in 33 non-insulin dependent diabetes mellitus (NIDDM) patients who

had received treatment with metformin (500–2000 mg) for at least 5 months before the doctor's visit, and in NIDDM patients not treated with metformin and analyzed for Hcy using HPLC with fluorometric detection, and plasma vitamin B12 using RIA.

Results: The Hcy levels showed no significant difference (p = 0.530) among participants in the metformin group compared with those in the non-metformin group (10.5 +/– 5.2 mol/L vs. 10.2 +/– 4.3 mol/L). There was a significant difference (p = 0.011) in the levels of plasma vitamin B12 among patients in the metformin group and among those in the non-metformin group (318.0 +/– 192.2 pg/mL vs. 434.3 +/– 300.7 pg/mL). The serum total Hcy levels showed a significant correlation with the duration of metformin treatment (p = 0.013) and the amount of metformin received per day (p = 0.014). It should be noted that plasma cobalamin was particularly low in patients with CVD.

Conclusions: This study found that plasma vitamin B12 deficiency in NIDDM is unequivocal, but requires further, in-depth studying to establish an accurate correlation between plasma vitamin B12 levels and hyperhomocysteinemia.

P 11

Yoga: A Practice to De-escalate Inflammatory Factors to Overcome Hypertension in Prediabetic Patients

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Background and Aims: Prediabetes is associated with the simultaneous presence of insulin resistance and β-cell dysfunction. These abnormalities start well before glucose changes are detectable. Many complementary and alternative practices have been explored in both the prevention and treatment of diabetes. Yoga is one such Eastern practice. It has beneficial effects in terms of glycaemic control and scarce data is available regarding its effect on anti- and pro-inflammatory markers. The present study was designed to determine the effect of yoga on β-cell function, insulin resistance and inflammatory markers in patients with prediabetes in the age group between 18 and 60 years.

Methods: In this study from the Endocrinology and Medicine OPD, hundred diagnosed people with prediabetes were recruited and followed for 6 months to assess the effect of yoga therapy. Fasting and postprandial glucose (PPG), fasting insulin, IL-6, hsCRP and HbA_{1c} at baseline were assessed. 3 months and 6 months of yoga were performed under direct supervision of a trained yoga instructor. IL-6, hsCRP, insulin and adiponectin were based on ELISA principle were measured. Data was analyzed using SPSS and ANOVA. Pearson's correlation and multivariate linear regression were applied.

Results: After starting yoga therapy, the prevalence of impaired fasting glycaemia (IFG) and of impaired glucose tolerance (IGT) declined. Moreover, yoga therapy was found to have favorable effect on weight in form of significant average weight loss. Reduction in hip and waist circumference and BM, body fat content percentage and visceral adiposity index, blood pressure, parameters of hyperglycemia, inflammatory markers, i.e. IL-6, hsCRP, triglycerides and LDL cholesterol with improvement in HDL cholesterol levels, and adiponectin levels (anti-inflammatory marker) was observed. VAI (visceral adiposity index) was maximally positively correlated with fasting plasma glucose (FPG), PPG & HbA_{1c}. Out of a total 13 IFG patients at baseline, 1 patients converted to euglycemia at 3 months and 4 patients at 6 months, and among 15 IGT patients at baseline, 3 patients converted to euglycemia at 6 months. From 72 IFG and IGT patients at baseline 6 patients achieved euglycemic state.

Conclusions: It can be concluded that yoga has an undoubted role in decreasing insulin resistance and hence, has promising role in prevention of prediabetes to diabetes conversion. The ease of doing yoga and its feasibility for every age group can make it a lifestyle intervention of choice in the future. Larger studies with a variety of ethnic groups are need for further guidelines mandating yoga for prevention of this disease with huge public health burden.

Diabetes and Obesity Management

P 12

Insulin Resistance, Sarcopenic Obesity in Patients with Non-Alcoholic Fatty Liver Disease

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Background and Aims: Recent studies have shown that skeletal muscle acts as an endocrine organ. Sarcopenia is based on several pathological processes: reduction in the number of muscle fibers, reduction in their size, violation of the innervation of myofibrils, as well as fatty infiltration of muscles (myosteatosis). Several studies have shown that fatty infiltration of muscles not only leads to loss of muscle mass and strength, but also contributes to insulin resistance, non-alcoholic fatty liver disease (NAFLD) and Type 2 Diabetes. Insulin resistance often accompanies NAFLD. Sarcopenic obesity in combination with progressive loss of skeletal muscle mass adversely affects the metabolic status, leading to a decrease in quality of life and the development of cardiovascular disease. The aim of this study was to establish the relationship between markers of inflammation, insulin resistance and sarcopenia in NAFLD patients.

Methods: The study involved 256 patients with NAFLD and normal weight, overweight or obesity, and 108 patients without NAFLD. An anthropometric survey, MRI and ECG were conducted. Levels of AST, ALT, GGT, the degree of liver steatosis and fibrosis using elastography (FibroScan) were measured. The ratio between the content of adiponectin and leptin was represented as log Adiponectin/Leptin. The stratification of CV risk was evaluated by the SCORE scale version for countries with high risk. We determined the level of inflammatory mediators (TNF-α, IL-1, IL-6), markers (CRP, fibrinogen), endothelin-1, insulin resistance index HOMA-IR, the thickness of the intima-media complex, presence of atherosclerotic plaque and stenosis of the carotid arteries for all patients.

Results: The body weight of men with NAFLD was 1.3 times higher

and their BMI was 1.4 times higher than in the group of healthy men. The body weight of women with NAFLD was 1.5 times higher compared to the group of healthy women. Their BMI was also 1.4 times higher than in the group of healthy women. Muscle mass of men and women with NAFLD was significantly lower ($p < 0.05$) than that of the respective healthy group. Moreover, muscle mass in healthy men was significantly higher ($p < 0.05$) than in the corresponding groups of women – healthy men had a 20.5 % increase in muscle mass compared to healthy women. Higher levels of inflammation, HOMA index, and a decrease in adiponectin levels were found in patients with NAFLD and sarcopenia compared with patients with preserved muscle mass. The component composition of body weight in NAFLD changed. Compared to healthy men with NAFLD, body fat was 35.2 % higher, while muscle mass and bone mass were lower by 29.1 % and 32.0 %, respectively. Compared to healthy women, body fat in women with NAFLD was 30.2 % higher, while muscle mass and bone mass were decreased by 17.4 % and 22.7 %, respectively. In men and women with NAFLD, strong inverse correlations ($r = 0.71$, $p < 0.001$) were found between muscle mass and hsCRP levels.

Conclusions: The pathogenesis of sarcopenia and NAFLD have common mechanisms: insulin resistance, increased inflammation, skeletal muscle secretion of myokines, myostatin and decreased adiponectin levels.

P 13

Remission of Type 2 Diabetes (T2D) and Weight Loss in Men with Hypogonadism and T2D Receiving Long-Term Testosterone Therapy in a Real-World Registry Study

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Background and Aims: Hypogonadism is highly prevalent (up to 50 %) in men with Type 2 Diabetes (T2D) as well as in men with obesity. We aimed to assess long-term effects of testosterone therapy in hypogonadal men with T2D.

Methods: In a registry of 883 men with hypogonadism, 370 men (41.9 %) had T2D. 190 received testosterone undecanoate (TU) 1000 mg/12 weeks following an initial 6-week interval (T-group), 180 opted against treatment (CTRL). All patients received standard diabetes care including lifestyle courses at a diabetes center. Remission was defined as discontinuation of diabetes drugs and $HbA_{1c} < 6.5$ % for the remaining observation time of at least six months. Weight and waist circumference were measured at every visit. Means and standard deviations of absolute measures over 13 years of treatment are reported.

Results: Mean follow-up was 9.3 ± 3.2, baseline age was 61.0 ± 5.3 (T-group) and 63.0 ± 4.9 (CTRL) years ($p < 0.0001$). 302 men (81.6 %) were obese at baseline, 62 (16.8 %) overweight and 6 (1.6 %) had normal weight. HbA_{1c} decreased from 9.5 ± 1.4 % to 5.5 ± 1.2 % (79.8 ± 15.5 to 36.6 ± 1.9 mmol/mol) in the T-group and increased from 7.8 ± 0.7 % to 10.5 ± 1.2 % (61.8 ± 7.7 to 91.7 ± 13.3 mmol/mol) in CTRL ($p < 0.0001$ for both). Fasting glucose (mmol/L) decreased from 7.9 ± 1.3 to 5.4 ± 0.1 in the T-group and increased from 6.4 ± 0.8 to 8.2 ± 1.3 in CTRL ($p < 0.0001$ for both). HOMA-IR decreased from 10.2 ± 2.1 to 1.5 ± 0.3 in the T-group and increased from 7.3 ± 1.3 to 14.8 ± 2.5 in CTRL ($p < 0.0001$ for both). In the T-group, 89 men (46.8 %) received insulin at baseline at a mean dose of 38.0 ± 13.3 U/d. Dose requirement declined from 38.0 ± 13.3 to 4.1 ± 5.7 during the observation period. In CTRL, 71 men (39.4 %) received insulin at baseline at a mean dose of 31.2 ± 6.1 U/d. Dose requirement increased from 31.2 ± 6.1 to 44.5 ± 5.6 ($p < 0.0001$ for both). In the T-group, 108 patients (56.8 %) went into remission. The median time to remission was 87 months. No patient in CTRL achieved remission. Waist circumference (cm) decreased from 117.9 ± 14.8 to 98.2 ± 4.3 in the T-group and increased in CTRL from 116.9 ± 13.5 to 119.0 ± 8.4 ($p < 0.0001$ for both). Weight (kg) decreased from 114.4 ± 13.8 to 88.3 ± 7.6 in the T-group and increased in CTRL from 102.7 ± 14.1 to 104.5 ± 10.2 ($p < 0.0001$ for both). Weight change from baseline was –21.5 ± 5.2 % in the T-group and +9.3 ± 3.0 % in CTRL ($p < 0.0001$ for both).

Conclusions: Long-term testosterone therapy with TU in men with hypogonadism and T2D progressively improved glycemic control. More than half of men achieved remission while glycemic control deteriorated in untreated men. Men treated with testosterone had sustained and progressive reductions in waist circumference and weight. Weight loss as well as improved body composition (reduction of fat mass and increase of lean body mass), a well-established effect of testosterone therapy, may have contributed to the improvements in glycemic control. Testosterone therapy in men with hypogonadism and T2D is a lifelong treatment.

P 14

Analysis of the Relationship Between Physical Activity and the Severity of COVID-19 in Hospitalized Patients with Diabetes

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Background and Aims: Due to the impact of physical activity on the immune system it is expected that regular physical activity can modify the course of an infectious disease. International Physical Activity Questionnaire (IPAQ) is a tool to measure health-related physical activity. This study aimed to analyze whether prior to hospitalization the level of physical activity modified the severity of COVID-19 in patients with diabetes mellitus (DM).

Methods: Between November 2021 and March 2022, patients with COVID-19 were asked to complete the IPAQ. Information about comorbidities, basic parameters about patient status and the course of the disease were recorded in the hospital's source. The following were designated as the severity of the disease: death or a move to the Intensive Care Unit, the occurrence of complications, the length of hospitalization, the need for oxygen therapy, CRP (C reactive protein), procalcitonin (PCT). For this part of the study, only data from patients with

DM were analyzed. The approval of the bioethical commission of the Wroclaw Medical University was obtained.

Results: During the mentioned period 640 patients were hospitalized, and 124 gave their written consent to participate in the study, including 31 patients with DM. The patients' characteristics (mean/range): age: 72.1/37–91 years; BMI: 29.4/25.4–36 kg/m²; HbA_{1c}: 8.4/5.4–14.6 %. 27 (87.1 %) patients recovered and 5 (16.1 %) developed complications. The mean length of hospitalization was 14.3 (range: 4–49) days. 10 (32.3 %) patients did not need any type of oxygen therapy. The mean CRP was 72.1 (range: 3.6–300.1) mg/l and mean PCT was 0.82 (range: 0.01–9.3) ng/ml. The analysis of physical activity showed that 18 (58.1 %) patients had low, 10 (32.3 %) had moderate, and 3 (9.7 %) had a high level of physical activity. The mean energy expenditure was 1198.1 (range: 0–9240) MET-min/week. For any of the parameters describing the severity of the disease, no significant correlation was found with the level of declared physical activity. However, there was a tendency for a negative correlation between the IPAQ expressed in METs and the length of hospitalization (the higher the METs, the shorter the hospitalization). There was also no correlation between BMI and the need for oxygen therapy, but also for this analysis, a tendency to negative correlation was shown (the lower the BMI the lower risk of any form of oxygen therapy).

Conclusions: Although no statistically significant correlations between the level of physical activity and the severity of COVID-19 have been confirmed, the observed trend of shorter hospitalization in more physically active patients encourages research on a larger group. The limited size of the group also resulted in a lack of significance of the relationship between BMI and COVID-19 severity, which was previously confirmed in other studies. Unfortunately, a barrier to further research in this field may be a lower number of COVID-19 cases and the reliability of the retrospective use of IPAQ. However, given the expected benefits of regular exercise for the immune system, similar studies can be conducted to assess its effect on other inflammatory respiratory disorders.

P 15

Effect of the Online Services on Diabetes Compensation and Decompensation, also Blood Pressure and Low-Density Lipoprotein Changes under Quarantine and Isolation Conditions in Adjara

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Background and Aims: The COVID-19 pandemic has been a global challenge for the entire world. Medical workers in particular have been forced to adopt new technologies in order to adequately manage chronic diseases under conditions of social isolation and distancing. Online services, social media and mobile communication have all become an important element of their contact with patients. The aim of the study was to determine the impact of online services on the compensation and decompensation of diabetes mellitus, as well as on the variation of blood pressure (BP) and low-density lipoproteins under conditions of quarantine and isolation.

Methods: A retrospective cohort study examined the histories of patients before and after the pandemic (years 2019–2021) who used online services. The following parameters were evaluated: initial HbA_{1c}, LDL and BP from December 2019 and 2021.

Results: The medical history of 52 patients with Type 2 Diabetes, 24 women and 28 men, aged 42 to 67 years, average age 47 years, was studied. The duration of diabetes was from 4 to 7 years. All of them used online services during the quarantine period to control their disease. Initial HbA_{1c} was 6.2 % ± 0.6 % (4.3–5.6 %), LDL was 80–150 mg/dl (100–129 mg/dl) and BP was 120/70. During the pre-lockdown period, all were on medical treatment with statin and ACE inhibitor. Around 2020–2021, all patients got COVID-19. 44 were vaccinated (12 with Astra Zeneca, 22 with Pfizer, 10 with Sinopharm). 27 (51.9 %) patients had increased BP and needed anti-hypertensive drug dose correction. Glycated hemoglobin improved in 32 (61 %) cases, but worsened in 4 (7 %) cases. Lipid profile worsened in 22 (42 %) cases. 6 (11 %) patients stopped the statin without consulting a doctor, 2 of them developed myocardial infarction.

Conclusions: Online services are very important when managing patients in social isolation. HbA_{1c} improved by 61 %. Patients participating in the study had emotional stress due to the COVID pandemic, which was mainly manifested by an increase in BP. Deterioration of diabetes control in the remaining patients was explained by lack of exercise and weight gain. Control of the lipid spectrum and appropriate drug therapy reduce the risk of cardiovascular diseases and mortality.

P 16

Exploring the Effect of Garlic Extract on Weight, Insulin Resistance and Gut Microbiota in Obese Non-Diabetic Women: A Double-Blind Randomized Controlled Trial

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Background and Aims: The prevalence of worldwide obesity and overweight has nearly tripled over the past three decades and obesity is considered the most common health problem, causing many chronic diseases. Nowadays, medicinal plants have become more popular due to their higher access and relatively fewer side effects. To assess the gut microbiota-mediated weight loss effects of garlic extract, this randomized double-blind clinical trial was conducted to investigate the effects of Allium (garlic extract) on anthropometric indices, insulin resistance and gut microbiota composition in obese non-diabetic women who were treated with a low-calorie diet.

Methods: 43 obese women were randomly divided into a garlic extract (400 mg Allium sativum powder containing 1 100 mcg allicin/tablet) (n = 21) or a placebo (n = 22) group by balanced block randomization. Women between 20 and 45 years of age, with body mass index (BMI) in the range of 30–40 kg/m², willing to comply with the study criteria, were included in this study. Sub-

jects in both groups took two pills per day for 2 months. To reduce the daily caloric intake by 500 kcal, both groups were given a low-calorie diet throughout the study. Anthropometric measurements and collection of blood and faecal samples were performed at the beginning and at the end of the clinical trial. The composition of gut microbiota was evaluated using quantitative real-time PCR, and short-chain fatty acids (SCFAs) in faecal were determined by gas chromatography.

Results: 16 people in each group completed the 2-month trial. The participant's mean age in the Allium and placebo groups was 38 and 34 years. Side effects reported by two participants in the Allium group included itchy skin and heartburn. In the placebo group, two people also complained of bloating and insomnia. The Allium and placebo caused a 1.7 % and 2.7 % decrease in body mass index (BMI) from the baseline values ($P < 0.01$). Fasting insulin concentration significantly decreased in both groups ($P < 0.01$). The level of homeostasis model assessment of insulin resistance (HOMA-IR) decreased significantly in the Allium group ($P = 0.007$). The frequency of Akkermansia had decreasing trend while the abundance of Faecalibacterium and Bifidobacterium increased in the Allium group. Although changes in the concentration of faecal SCFAs in the Allium group were not significant, the concentration of butyrate had a slightly increasing trend. Faecal SCFAs levels had no significant difference between the two groups ($P > 0.05$).

Conclusions: Despite weight loss and improvement of insulin resistance after taking Allium, slight changes were shown in the composition of gut microbiota in obese women.

P 17

Insulin Resistance as One of the Main Mechanisms in the Development of Metabolic Syndrome and Type 2 Diabetes

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Background and Aims: Metabolic syndrome (MS) is a contemporary problem in modern medicine, both due to its high prevalence and significant influence on the risk of developing Type 2 Diabetes mellitus (T2DM). This study aimed to analyze literature on the mechanisms of development of insulin resistance and T2DM as one of the constituent components of MS.

Methods: During the scientific search, 50 sources of modern foreign literature were analyzed.

Results: Increase in adipose tissue in the body, especially abdominal fat, leads not only to psychological and aesthetic problems, but it can also be a trigger factor for a high risk of MS, which in turn is a trigger for the development of T2DM. One of the main causes of MS is insulin resistance (IR). IR manifests as the resistance of the body's cells to the effect of insulin and occurs as a result of a disturbance of the insulin signaling in these cells. In MS, proliferation and hypertrophy of adipocytes occurs together with their infiltration by macrophages and the subsequent development of inflammatory reactions, as a result of which the metabolic activity of adipose tissue is changed.

Conclusions: The citated literature indicate that MS proceeds with significant deviations from the physiologic level concentrations of proinflammatory cytokines and adipokines.

Clinical Perspectives

P 18

Cushing's Disease and Secondary Hypertension – A Case Report

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Background and Aims: Hypercortisolemia associated with Cushing's disease is one of the rare causes for secondary hypertension.

Clinical Case: A case of a 48-year-old male patient with metabolic syndrome, insomnia and impotence is presented. The patient had a rounded and plethoric facial appearance. Initial Overnight 1 mg Dexamethasone Suppression Test demonstrated no cortisol suppression (Cortisol 547 nmol/L), and the patient was referred to the University Clinic of Endocrinology, Diabetes and Metabolic Disorders for further investigation. Baseline laboratory results were ACTH = 101.3 pg/ml, Triglycerides = 1.9 mmol/L, Total Cholesterol = 6.4 mmol/L, HDL = 1.2 mmol/L, LDL = 4.9 mmol/L, Na = 140 mmol/L, K = 4.3 mmol/L, Ca++ = 1.19 mmol/L, VMA = 28.9 µmol/dU, Metanephrines = 1.0 µmol/dU. Daily cortisol rhythm was impaired (1 200/808 nmol/L, 1 600/704.6 nmol/L, 2 000/680 nmol/L, 2 400/730.4 nmol/L, 0600/901 nmol/L), while High Dose Dexamethasone 8mg Suppression Test showed cortisol suppression (906 nmol/L, 255.1 nmol/L). Additional tests included OGTT, DXA and chest X-ray with normal findings, abdominal CT with normal findings of adrenal glands, whereas MRI of the pituitary gland demonstrated asymmetry of pituitary with a presence of focal lesion centrally and posteriorly, 3 x 4 mm. Also, a CRH Stimulation Test was performed (0': Cortisol = 89.6 nmol/L, ACTH = 86.2 pg/ml, 30': Cortisol = 932.0 nmol/L, ACTH = 175.0 pg/ml, 60': Cortisol = 1 100.0 nmol/L, ACTH = 190.5 pg/ml, 90': Cortisol = 1 369 nmol/L, ACTH = 345.9 pg/ml, 120' Cortisol = 1 550 nmol/L, ACTH = 436.9 pg/ml) in favour of pituitary Cushing's disease. Blood pressure was above the reference values and treated with an ACE inhibitor (Tbl. Enalapril 5 mg 2 x 1) at the beginning of the investigations, and gradually increased to 10 mg 2 x 1. After proving the diagnosis of pituitary Cushing's disease, a radiosurgery with gamma knife was applied to the patient. During the postoperative monitoring of the condition, withdrawal of symptoms occurred. Normalized blood pressure values were recorded and the treatment with ACE inhibitor was discontinued.

Conclusions: The patient was investigated for hypercortisolemia according to Sy Cushing diagnostic algorithm and was diagnosed with pituitary Cushing's disease (Morbus Cushing). Surgical intervention led to the normalization of cortisol values, thus eliminating the cause of secondary hypertension.

P 19

Late Diagnosis of Dilated Cardiomyophaty and Fatal Outcome

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Background and Aims: Dilated cardiomyopathy (DCM) is a common cause of heart failure (HF) and is the most common diagnosis in patients who undergo cardiac transplantation. DCM is characterized by dilatation and systolic dysfunction of one or both ventricles. Diagnosing cardiomyopathy in children in the acute care setting is essential, but frequently such patients present symptoms more commonly associated with other diseases.

Clinical Case: A 17-year-old male patient came to the emergency department with a complaint in the epigastric area and vomiting associated with eating pizza. It should be noted that 2 days before admission, the patient was hospitalized with the same complaint. Routine tests were performed. It was considered as food intoxication and the patient was discharged. In our clinic he had HR – 178', T/A – 107/70 mmHg, RR – 27', T – 36.7°C, SatO2 – 96 %, weight – 55 kg. Tachycardia was the reason of referral to a cardiologist. An echocardiogram demonstrated a severely dilated left ventricle, severely depressed left ventricular function, mitral and aortic regurgitation. The patient had a shortening fraction EF of 16 %, was diagnosed with DCM and referred to a specialized cardiological department. The patient died before implantation of cardiac pacemaker (after 2 months). Early and accurate diagnosis of a child with heart failure can be a difficult task. There are no definitive tests for myocarditis or cardiomyopathy. The clinician must be alert for the possibility of HF in any patient, and should start with a thorough physical examination, paying special attention to presenting vital signs. The patient's heart rate may be a clue of underlying cardiac disease. Tachycardia is commonly seen and usually relates to fever, fear, or a pulmonary problem. However, tachycardia may also be seen in a failing heart with arrhythmias or decrease in ventricular contractility, causing poor cardiac output. Bradycardia is rarely seen in an acutely ill patient and merits further evaluation for cardiac dysfunction. Patients with HF may present a normal cardiovascular examination, but a careful evaluation can reveal important markers of cardiac disease. Abdominal pain can be a presenting symptom in patients with HF.

Conclusions: Diagnosing HF in the pediatric population begins with maintaining a high level of suspicion. Vital signs should be reviewed, and potential diagnoses considered comprehensively. In addition, the physical examination should be thorough and directed. Only after a diagnosis is considered, additional testing can be performed and lead to the appropriate treatment. It is often difficult to make the diagnosis of HF if the disease is not consciously considered as a possibility. Armed with knowledge and clinical suspicion, the astute physician will make this diagnosis difficult to miss.

P 20

Cardiovascular Risk Reduction Following Bariatric Surgery in a Patient with Type 1 Diabetes

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Background and Aims: Type 1 Diabetes mellitus (T1DM) is traditionally considered a disease of lean people. However, obesity is becoming increasingly common in individuals with T1DM – about 30 % of T1DM patients are overweight or obese. The consequences of obesity in these patients are of particular concern, as they increase the risk of both diabetes-related and obesity-related complications, including CVD risks and various types of cancer. Important targets for risk reduction include hypertension, proteinuria, obesity, HbA_{1c}, lipid levels, and smoking cessation. The reduction in body weight after surgery is accompanied by a reduction in total daily insulin requirements in patients with obesity and T1DM. There is good evidence that lowering HbA_{1c} levels will decrease the risk of CVD, retinopathy, neuropathy, and nephropathy. While bariatric surgery has long been considered an effective treatment option for patients with Type 2 Diabetes, the evidence regarding its benefits on weight loss and the prevention of complications in T1DM patients is scarce.

Clinical Case: A retrospective study was conducted on a 37-year-old male patient with T1DM who has been on insulin therapy since he was 14 years old. The patient underwent sleeve gastrectomy. Short-term outcomes of bariatric surgery were examined, including insulin doses, HbA_{1c} levels, lipid profile, blood pressure and body mass index (BMI), and were compared prior to the surgery to 6 months after the surgery. Bariatric surgery was associated with a significant reduction in insulin requirement. Daily doses of insulin glulisine decreased from 120 unit to 28 unit after 6 months. There was no significant decrease in insulin glargine daily doses. HbA_{1c} level decreased from 10.2 % to 7.1 %. A decrease in BMI was documented 6 months after the bariatric surgery from 39.5 kg/m^2 to 27.8 kg/m^2. The surgery was also associated with a statistically significant reduction in systolic and diastolic blood pressure and a significant beneficial rise in high-density lipoprotein (HDL), reduction in the levels of low-density lipoprotein (LDL) and triglycerides (TG) without antihypertensive and lipid-lowering therapy. Microalbuminuria was not present prior to the surgery. The weight loss after the surgery increased physical activity level of this patient. Smoking cessation is strongly recommended to all patients before bariatric surgery. The patient quit smoking after the surgery.

Conclusions: Bariatric surgery offered a significant reduction in BMI in a patient with T1DM and obesity. It provided a myriad of health benefits. It can be concluded that the normalization of metabolic parameters starting with lipid levels to blood glucose levels, following bariatric surgery in a timely manner, could reduce the incidence of adverse cardiovascular events. Smoking cessation is part of an overall strategy to lower CVD in T1DM patients. Studies show that performing more than 150 minutes of moderate physical activity, or 75 minutes of vigorous physical activity, every week can achieve a 30 % CVD risk reduction, and walking at least two hours a week reduced the incidence of premature death from CVD by about 50%. The patient is currently in follow up.

P 21

Diabetes and its Legacy Effects

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Background and Aims: Metabolic syndrome is the concurrence of the metabolic risk factors for both diabetes and cardiovascular disease, namely, hypertension, hyperglycemia, dyslipidemia and abdominal obesity.

Clinical Case: A case of 59 yrs old morbidly obese Saudi lady is described. She had Type 2 Diabetes for 34 yrs, hypertension, advanced proliferative diabetic retinopathy (S/P laser), ischemic heart disease, chronic kidney disease 5-A3, dyslipidemia, osteoarthritis knees and obstructive sleep apnea (on O_2 inhalation, 4 ltrs/m and BiPAP). The patient was non-compliant to medications, diet, exercise and follow-ups. No hypoglycemic episodes were evident at home. She had decreased hearing from both ears. There was a past history of left breast abscess (S/P incision & drainage twice), recurrent urinary tract infections, acute right hemispheric stroke following acute coronary syndrome (5yrs ago, S/P percutaneous coronary intervention and stenting), ischemic neuritis right ear and cataract extraction. There was a positive family history of Type 2 Diabetes and obesity. She was allergic to Ceftriaxone and Strawberries, and was on basal bolus insulin regime, Linagliptin, dual anti-platelets, statin, Hydralazine, calcium carbonate,1 alphacalcidol and a proton pump inhibitor. On evaluation last on 10.11.2020, the patient had moderate bilateral pedal edema (L>R) and absent vibration sensation at left ankle. Her available records indicated the following trends for her physical and biochemical values from 2015–2020: BMI (41.33–53.24 kg/m²), HbA_{1c} (14.1–6.5 %), eGFR (44–10 ml/min), Albumin/Creatinine ratio (643–1 119.58 mg/g). Subsequently, the patient was lost for follow-up.

Conclusions: The case depicts the legacy effect of uncontrolled diabetes (with microvascular and macrovascular sequelae), and the tendency for recurrent infections. It is also apparent that as the patient's renal function progressively deteriorated, her blood glucose started coming under control, due to reduced insulin clearance through the affected kidneys.

P 22

Indian Consensus for the Utilisation of Combination of Dual Antiplatelet and Statin Therapy for the Stratified Treatment of Acute Coronary Syndrome

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Background and Aims: The aim was to formulate a consensus statement for the utilization combination of dual antiplatelet (DAPT) and statin combination in the stratified treatment of acute coronary syndrome (ACS) based on the contemporary evidence and the real-world experiences of the Indian cardiologists.

Methods: A virtual collaborative educational initiative was convened from May 27, 2022, to June 18, 2022, through a series of 16 nationwide virtual interactive meetings by leading cardiologists (n=275) at the forefront of ACS management. The cumulative clinical experience was approximately 2,200-man-years. The participants rated their level of agreement on 6 questions with each item on a 5-point Likert scale. This was preceded by a contemporary evidence-based discussion on the contemporary updates for the combination of DAPT and statin. The consensus was pre-defined as >60 % of the panel agreeing/disagreeing on any item. There were 4 objective choice – best suited response-based questions. GraphPad 9.4.0 and ANOVA were used for statistical analysis.

Results: The highest agreement was for the concurrence on THE clinical relevance of the concept of stratified treatment of ACS (95.4 %). The agreement score (%) for that DAPT/statin combination is underutilized was 83.8 %, followed by the need for optimal management of ACS (75.5 %), the relevance of BATTLE AMI hypothesis (74.6 %), clopidogrel preferred for de-escalated DAPT approach (72.1 %), de-escalation therapy is part of the optimization approach (61.8 %) (p<0.0001). The participants opined that: ischemic risk is the most important factor to choose DAPT (67.6 %), other ongoing therapy is an important determinant of DAPT adherence (59.5 %), and patients with high CV risk are the best suited for prolonged DAPT therapy (46.5 %), DAPT should be continued for at least 1 year (50 %).

Conclusions: We observed a high preference for the combination of DAPT and statin for the stratified treatment of ACS, including patients with diabetes, who have high cardiovascular risk. We attribute this to a high level of perceived effectiveness based on the recent clinical trials. The combination of DAPT and high potent statin, like rosuvastatin, provides an additional choice in the therapeutic armamentarium for the optimal management of ACS.

P 23

Evaluation of Specialized State Program of Outpatient Care in Terms of Effective Monitoring of Diabetes Mellitus and Detection of its Complications in Tbilisi

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Background and Aims: The implementation of any state program is related to the provision of a full range of outpatient services to patients. Carrying out preventive measures necessary for diabetes mellitus and its complications prevents disease decompensation and impedes development of late complications. Family doctors are considered as the main link in the outpatient service. As for the management of diabetes mellitus, in this service endocrinologist, cardiologist, ophthalmologist, nephrologist and angiologist were involved. The awareness of doctors and patients and continuous medical education / professional development serve as the basis for ensuring effective control of diabetes mellitus and early diagnosis of its complications. The study was aimed at evaluating the state program outpatient services in terms of diagnosing diabetes mellitus and revealing its complications in Tbilisi population.

Methods: A cross-sectional study using a special structured questionnaire de-

veloped by us was conducted in 11 outpatient facilities of high referral index in Tbilisi. 25 family doctors, 25 ophthalmologists and 15 cardiologists took part in the study. Participation in an extra training course in diabetology and main diabetic complications were monitored.

Results: 70 % of family physicians and only 22 % of ophthalmologists have passed additional training in diabetes mellitus, with 96 % and 70 % of which, respectively, reported participation in continuous medical education and/or professional development programs at least twice a year. 40 % of cardiologists have passed additional training in diabetes mellitus, although every cardiologist reported participation in continuous medical education and/or professional development programs, and majority of them (67 %) do so at least once a year. For early detection of the complications of diabetes mellitus, family doctors most often suggested carrying out regular organized screening (glucose monitoring, glycated hemoglobin test) in different target groups (88 %), raising awareness in the population through mass media (85 %) and/or implementation of interdisciplinary approach (56 %). Arterial hypertension and cardiovascular diseases were most frequent complications (45 %). According to 96 % of ophthalmologists, retinopathy is the most common complication of Type 2 Diabetes mellitus (91 %). 92 % of them meet the patients requiring emergency treatment due to diabetic retinopathy. 96 % of ophthalmologists are aware of information about the geographical and financial availability of laser surgery for treatment of diabetic retinopathy (fully aware – 68 %, partially aware – 28 %). 96 % of cardiologists believe that cardiac ischemia is the most common complication of Type 2 Diabetes mellitus. According to the survey respondents (60 %), patients with Type 2 Diabetes mellitus should see a cardiologist at least once a year, and patients with complications – twice a year (60 %), respectively. 87 % of cardiologists provide patients with detailed information about complications.

Conclusions: It is necessary to boost additional training capacity in diabetes for auxiliary specialists, as well as early referral of the patients with developed complications to the relevant specialized clinics under the state program that will significantly increase the quality of services for diabetic patients, prevent disability at retinopathy and reduce the mortality rate caused by cardiovascular diseases.

P 24

Current Lessons and Perspectives from the 2022 Virtual International Heart Failure Summit for Angiotensin Receptor-Neprilysin Inhibition (ARNI) as Revolutionary Drug Among Guideline-Based Treatments in Heart Failure with Reduced Ejection Fraction (HFrEF)

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Background and Aims: Contemporary global evidence and practices for the management of heart failure (HF) with emphasis on HF with reduced ejection fraction (HFrEF), and the role of ARNI in the forefront were disseminated through live symposia.

Methods: A virtual learning collaborative educational initiative was convened on 14th May 2022 by Prof. Michael Bohm live from Germany with high expertise rank within 0.015 % of authors worldwide. The participants included 659 people from India at the forefront of HF management.

Results: The science of neuroendocrine modulation in HF has developed to be a cornerstone that supports the combination therapy to block the mediators of HF. PARADIGM-HF trial provides new insights into the role of reverse cardiac modeling as a marker of better prognosis in HF and supports the arguments for the early initiation of ARNI. Early use is likely to have a positive impact on patient outcomes, and postponing treatment might cause events. There is a reverse J-curve relationship between on-treatment blood pressure (BP) and all-cause mortality with a nadir of risk at a BP of 132/74 mmHg in patients with HF. PARADIGM-HF analysis reflects the dynamic changes in cardiovascular and systemic parameters prior to sudden cardiac death. ARNI may lead to a substantial reduction in diuretics. Patients with diabetes and HFrEF enrolled in PARADIGM-HF who received ARNI had a greater long-term reduction in HbA_{1c}.

Conclusions: Newer insights reveal ARNI are distinctive for the modulation of neuroendocrine pathways. The early treatment for maximal outcomes is now evidence-based and the contemporary 2021 ESC Heart Failure Guidelines recommend ARNI to be started early.

Experimental Cardiometabolic Outcomes

P 25

The Use of Novel Animal Models in silico to Identify Obesity-Associated Variants That May Influence Risk of Developing Cardiovascular Co-morbidities

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Background and Aims: Genetic loci associated with the development of obesity may overlap with regions exerting pleiotropic effects on risk factors for cardiovascular disease. However, existing work investigating the genetic basis of obesity in humans is restricted by limitations of sample size, and only explains a small proportion of the heritability of obesity-related traits. Species such as the domestic dog (Canis lupus familiaris) and the pig (Sus domesticus), in which selective breeding has created genetic bottlenecks which enable genotype-phenotype correlations to be identified with increased power, may provide novel insights. If translatable to humans, this may suggest new indirect candidates in the context of polygenic risk scoring for cardiovascular disease.

Methods: Single nucleotide polymorphisms (SNPs) that were significantly associated with body condition score in Labrador Retrievers (n = 241) were identified following a genome-wide association study. Positional candidate genes were identified and their role in the development of obesity was explored using the following lines of evidence: i)

the identification of statistically over-represented signalling pathways; ii) tissue-specific expression data; iii) in vivo modelling databases; iv) comparison with loci associated with adipose accumulation in pigs following analysis of publicly available quantitative trait locus data; and v) data from existing human studies.

Results: The Wnt signalling pathway was overrepresented amongst the 19 canine candidate genes when compared to the genome as a whole ((X2(1, N = 20 700) = 16.5881, p < 0.000001). Tissue-specific enrichment of cdh8 expression in the brain compared to peripheral tissues in Canis lupus familiaris may support a potential role of central Wnt signalling in determining obesity risk. In pigs, the Wnt signalling-associated gene lrp5 was found within the chromosomal region most strongly associated with adiposity.

Conclusions: This investigation suggests that genetic variants within the Wnt signalling pathway may influence obesity risk across several species, and hence be associated with increased incidence of cardiovascular disease. This in silico approach will be supplemented with work in vitro and in vivo to elucidate the mechanisms by which dysfunctional Wnt signalling can contribute to obesity development.

P 26

Hypoxic Preconditioning Effects under Insulin Resistance and Heart Hypertrophy in Rats

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Background and Aims: Cardioprotective mechanisms in the hypertrophied or insulin resistant heart is not fully elucidated. Insulin like growth factor IGF-1 is known to exert cardioprotective effects through downstream kinases PI3K/Akt/GSK-3beta, and to regulate myocardial remodeling, glucose metabolism, cell survival, apoptosis, oxidative stress etc. The aim of this study was to characterize IGF-1/PI3K/Akt-mediated cardioprotection in hypertrophied or insulin resistant hearts after hypoxic preconditioning in response to severe whole-body hypoxia or isolated heart ischemia/reperfusion.

Methods: Experiments were performed in male adult Wistar rats, and spontaneously hypertensive rats (SHR) with pressure overload-induced heart hypertrophy. Insulin resistance was induced by high fat diet (58 % kcal from fat). The animals were exposed to hypoxic preconditioning using mild hypobaric hypoxia séances in barochamber (5 600 m, 3 h). In 24 h, hearts were isolated with urethane narcosis and subjected to ischemia/reperfusion in a Langendorff mode, infarct size was detected with TTC staining. The other group of rats after preconditioning were subjected to severe hypoxia (9 000 m, 3 h). PI3K inhibitor wortmannin or IGF-1 receptor blocker picropodophyllin were used for testing of cytoprotective signaling. Protein expression was assayed by Western blotting. Proapoptotic response was evaluated using caspase-3 activity assay. Myocardial injury was examined by electron microscopy.

Results: In SHR, the left ventricular expression of IGF-1 and Akt was lower by 42 % or 63 %, respectively, compared to Wistar rats. Insulin resistance increased GSK-3beta expression and phosphorylation. Hypoxic preconditioning intensified IGF-1/PI3K/Akt-mediated cardioprotective effects preventing myocardial injury and mortality in severe hypoxia, limiting infarct size and improving postischemic functional recovery of isolated hearts. These effects were less pronounced in hypertrophied or insulin resistant hearts. PI3K inhibitor or IGF-1 receptor blocker decreased Akt phosphorylation, and diminished cytoprotective effects of preconditioning. In SHR, influences of the blockers were significantly reduced.

Conclusions: The pressure overload-induced left ventricular hypertrophy is accompanied with reduction of IGF-1/PI3K/Akt-dependent prohypertrophic and cardioprotective signaling. Insulin resistance stimulated GSK-3beta-mediated proapoptotic signaling. Hypoxic preconditioning mediated by IGF-1/PI3K/Akt-signaling loses its effectiveness during prolonged cardiac hypertrophy, as well as insulin resistance development.

P 27

snoRNAs as a Novel Genetic Marker to Facilitate Patient-Specific Conduit Choice for Coronary Artery Bypass Grafting

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Background and Aims: Specific snoRNAs (small nucleolar RNAs) are associated with failed venous grafts after coronary artery bypass grafting (CABG). It is hypothesised that snoRNAs have a structural similarity to the spliceosome (a cellular assembly involved in splicing of the pre-mRNA transcript to produce mature mRNA). We further investigated this hypothesised structural similarity of snoRNAs to the spliceosome, with the aim of proposing a mechanism for their role in CABG failure and other cardiovascular diseases in general.

Methods: snoRNA and spliceosomal RNA sequences from the human reference genome (GRCh38) were obtained from Rfam (a repository of non-coding RNAs). 2D and 3D structural modelling of the snoRNAs were undertaken using the ViennaRNA suite of computational tools and SimRNA, respectively. Utilising multiple tools within ViennaRNA, sequential and structural similarities between individual snoRNAs and the spliceosome were investigated to identify the snoRNAs with the greatest similarity, which were our candidate snoRNAs for in-depth pairwise comparison.

Results: The initial results suggested that the vast majority of the forty snoRNAs of interest showed some form of structural similarity to the spliceosome. Subsequently, 3D structural prediction and comparison (using SimRNA) was undertaken (selected as described above) to identify the snoRNAs with high degrees of structural 3D similarity. Mapping of the regions of similarity subsequently confirmed these sites to be located within the catalytically active site of the spliceosome. These mapped sites are thus functionally important for the spliceosome's role in splicing, meaning that this structural similarity has functional significance.

Conclusions: We therefore propose that these snoRNAs mimic spliceosomal structure and interfere with spli-

ceosomal function. Variation in the snoRNAs could therefore lead to mis-splicing of pre-mRNA and subsequently pathological tissue remodelling. Tissue remodelling is a key part of vascular tissue response in venous grafts after CABG and relies on physiological as well as appropriate pre-mRNA splicing. Mis-splicing due to variation in these snoRNAs could explain the significantly increased graft failure rates for venous grafts after CABG. On the contrary, arterial conduits for CABG are used less frequently in cardiovascular surgery but have much lower long term graft failure rates. Therefore, it is proposed that arterial conduits should be the preferred conduit for an individual with the snoRNA variants associated with increasing risk of venous graft failure. Thus, genetic screening for snoRNAs of interest, as identified in this study, could inform the choice of conduits for CABG and therefore provide a novel approach for surgical workup, improving patient outcomes by reducing likelihood of graft failure and need for re-intervention.

P 28

The Cardioprotective Effect of Hypoxic Preconditioning and its Mechanisms in Rats Exposed to Severe Hypoxia

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Background and Aims: With the COVID-19 pandemic, the issue of increasing the protection of body tissues against severe hypoxic damage has become urgent. Hypoxic preconditioning (HP) is known for its protective effect in ischemic heart damage, but its possible protective effects in severe hypoxia (SH) have not yet been investigated. The aim of this work was to determine the protective effect of HP and its mechanisms under conditions of exposure to SH.

Methods: The experiment was performed on adult male Wistar rats. HP was carried out by "lifting" in a pressure chamber at 5 600 m for 3 h. After 24 h, SH was reproduced according to our own method, "lifting" the animals to 9000 m for 3 h in a pressure chamber. To study the mechanisms, a phosphoinositide-3-kinase (PI3K) blocker, wortmannin, was used, which was administered intravenously 30 minutes before SH at a dose of 2 µmol/L of circulating blood volume. The ultrastructure of the myocardium was assessed using electron microscopy.

Results: HP contributed to 100 % survival of rats in SH, including using wortmannin, which significantly increased lethality under conditions of SH. SH increased the number of structurally altered mitochondria, led to their pathological swelling, which indicated their dysfunction. SH also caused an increase in the thickness of the endothelium of the myocardial capillaries, which led to disturbances in metabolism and gas diffusion. SH contributed to swelling and destruction of myofibrils. The use of wortmannin significantly increased the destructive changes of both myofibrils and mitochondria, which were subjected to irreversible necrotic processes. Also, wortmannin significantly increased the thickness of the histohematal barrier and reduced the number of polysomes. As a result, the synthetic function of cell proteins decreased. Instead, HP contributed to an increase in the total number of mitochondria and polysomes, which is a sign of the activation of their morphogenesis, caused a slight swelling of mitochondria, which may indicate the optimization of the work of organelles while preserving the integrity of membranes. HP reduced the thickness of the endothelium of capillaries, significantly reduced the violation of the ultrastructure of myofibrils and mitochondria, and prevented further development pathological injuries from exposure to SH. With the administration of wortmannin, the protective effects of HP were slightly reduced.

Conclusions: Our results indicate a protective effect of HP in rats under conditions of SH, which is manifested by an increase in animal survival, a decrease in morpho-functional disorders of the myocardiocytes ultrastructure, and activation of compensatory and adaptive reactions of cells. One of the mechanisms involved in the protective effects of hypoxic preconditioning is the signaling pathway involving PI3K.

P 29

Oral Insulin Delivery Improves Blood Viscosity Alterations in Type 1 Diabetes

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Background and Aims: Elevated blood viscosity is a pathogenic factor of diabetic cardiovascular complications. Hyperglycemia provokes diuresis which leads to decreased plasma volume, increased hematocrit and subsequently the blood viscosity. In a previous study, we demonstrated that insulin administrated orally allows a better control of glycemia than subcutaneous insulin. In this study, we aimed to evaluate the impact of insulin in its two forms on the rheological properties of blood.

Methods: Our study was carried out in 3 groups of Wistar rats with induced diabetes. Group 1 received oral insulin-loaded nanoparticle, group 2 – subcutaneous insulin, and group 3 of untreated diabetic rats was set as negative control. Glycemia was measured and whole blood viscosity was estimated by using a validated formula based on hematocrit and total plasma proteins. A correlative study was carried out.

Results: Whole blood viscosity was significantly higher in group 2 compared to group 1 and group 3 ($P < 0.001$). Indeed, the difference between whole blood viscosities of diabetic rats treated with oral insulin with non-diabetic rats was not significant. Hyperglycemia was positively correlated with whole blood viscosity and hematocrit concentration ($r2 = 0.8228$ and $r2 = 0.7528$; $P < 0.05$).

Conclusions: Our results show that insulin delivered orally can improve alterations in blood viscosity, since it allows good glycemic control, and could prevent cardiovascular complications.

P 30

Type 2 Diabetes Aggravates Metabolic and Regulatory Disturbances under Comorbid LPS-Induced Acute Lung Injury

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Background and Aims: Patients with Type 2 Diabetes demonstrate marked vulnerability to respiratory diseases, including COVID-19. This requires the study of changes in metabolic regulation in the comorbid course of inflammatory lung disease and metabolic disorders. The aim of this study were to characterize the changes in metabolic regulation in the acute lung injury on the background of Type 2 Diabetes.

Methods: In male Wistar rats, Type 2 Diabetes was simulated using a high-fat diet and streptozotocin administration (25 mg/kg). The inflammatory process was induced by administration of lipopolysaccharide (LPS). Lung tissue injury was evaluated by electron microscopy. The function of mitochondria was investigated by Chance polarographic method. Protein expression was assayed with immunoblotting.

Results: In contrast to control animals, in diabetic rats the introduction of LPS caused increased mortality and was accompanied by significant ultrastructural injury in the lungs, manifestations of mitochondrial dysfunction, suppression of mitochondrial respiration with the use of various metabolic substrates, excluding lipid substrate (palmitoyl). In diabetic rats with comorbid lung injury, the mitochondrial SOD induction, SREBP-2 protein expression and cleavage, and Akt phosphorylation were changed, and leptin-dependent regulation was disturbed.

Conclusions: Type 2 Diabetes aggravates metabolic, regulatory and mitochondrial dysfunction caused by endotoxin-induced lung injury.

P 31

Hypoxic Preconditioning Changes the Function of Myocardial Mitochondria in Rats with Insulin Resistance and Arterial Hypertension

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Background and Aims: Maintaining energy metabolism protects the heart from ischemic and hypoxic damage. However, the effect of cardiac preconditioning on myocardial energy metabolism, especially in pathological conditions, is insufficiently studied. This study aimed to investigate the function of myocardial mitochondria in rats with insulin resistance and arterial hypertension after exposure to hypoxic preconditioning (HP).

Methods: The experiment was performed on adult male Wistar and spontaneously hypertensive (SHR) rats. Insulin resistance was induced by a high fat diet (HFD) for 2 weeks (58 % kcal from fat) and confirmed by an insulin-resistant test. HP was modeled by "lifting" the animals in a barochamber to a height 5 600 m for 3 hours. In 24 hours, the hearts were removed under urethane anesthesia. The functional activity of mitochondria was studied by the method of Chance using different oxidation substrates.

Results: In Wistar rats with HFD, we observed a tendency to decrease the parameters of mitochondrial respiration with oxidation of FAD- or NAD-dependent substrates. HP in these animals increased the rate of ADP-stimulated respiration and respiratory control (RC). At the same time, the rate of RC in metabolic state 4 (V3/V4 ATP) decreased under conditions of oxidation of the NAD-dependent substrate sodium palmitoyl. It should be noted that a more significant increase in the coupling of respiration with phosphorylation (V3/V4 ATP) occurred during palmitoyl oxidation. RC under the conditions of oxidation of sodium succinate increased by 5.6 %, sodium glutamate – by 3 %, and sodium palmitoyl – by 8 %. In SHR, RC and phosphorylation efficiency (ADP/0) were significantly lower compared to Wistar, but the rate of active respiration (V3) did not differ. HFD caused a tendency to decrease energy metabolism. After the HP there was a tendency to increase RC with oxidation of both FAD- and NAD-dependent substrates.

Conclusions: In Wistar and SHR rats with insulin resistance, hypoxic preconditioning caused the favorable changes in the functional activity of mitochondria associated with the restructuring of complexes I and II of the electron transport chain.

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The Impact of HypoxamiRs in Rat Diabetic Cardiomyopathy

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Background and Aims: Heart function is severely compromised in diabetes mellitus and results in a cardiac remodeling process. On molecular level, this may cause microRNAs alterations. However, little is known about hypoxia's effect on the microRNA system in the heart. Our work aimed to discover microRNA shifts in the diabetic myocardium and during hypoxia.

Methods: Type 2 Diabetes mellitus was induced in adult male Wistar rats with high-fat diet and low dose of streptozotocin. Part of the animals were subjected to 5 interval hypoxia trainings (1 training per 3 days) by "lifting" in barochamber on 3500 meters. MicroRNAs expression in the heart was measured using a PCR technique. All results were analyzed statistically via the SPSS program.

Results: Expression of microRNA-1 and microRNA-320 were reduced in diabetic myocardium. While hypoxia lowered the microRNA-1 expression in the control group, hypoxia demonstrated multidirectional effect on microRNAs expression in diabetic rats. Namely, microRNA-320 expression was reduced by 28% and microRNA-1 was elevated by 60% in diabetic rats exposed to hypoxia. We found a direct correlation of this variations with the animal's glycose level.

Conclusions: Reduction of microRNA-1 and microRNA-320 expression could stimulate its target gene expression (e. g. IGF) in diabetic cardiomyopathy. The microRNA-dependent mechanisms differ in hypoxic conditions. We assume that microRNA-1 is involved in the restriction of the heart remodeling process. On the other hand, hypoxia has the tendency of lowering microRNA-320 expression in both the control group and diabetic myocardium. Thus, microRNAs could be an important regulating link in pathological mechanisms of diabetic cardiomyopathy and could be modulated by hypoxia.

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