ZENTRALEUROPÄISCHE DIABETESGESELLSCHAFT
Zentraleuropäische Diabetesgesellschaft
Central European Diabetes Association
Föderation der Internationalen Donau-Symposia über Diabetes mellitus
Federation of International Danube-Symposia on Diabetes mellitus

Nachruf

Professor Sotirios Raptis verstorben

Im Mai 2017 verstarb unser Gründungsmitglied der FID, FID-Präsident und FID-Ehrenmitglied Professor Sotirios A. Raptis, M.D., Ph.D., M.D. (hon), HMGSIM, HFEFIM, nach längerer Krankheit in seiner Heimatstadt.

Er wurde 1938 in Athen als Sohn eines Arztes geboren und besuchte dort die Schulen einschließlich der Hochschule.

1962 wurde er an der Universität Athen im Fach Medizin graduiert. Anschließend ging er mit einem Stipendium, das ihm Professor Malamos, ein Kollege und Freund des österreichischen Internisten Professor Karl Fellinger vermittelte, an dessen 2. Medizinische Universitätsklinik in Wien. Dort arbeitete er bis 1967 auf dem Gesamtgebiet der inneren Medizin und erwarb sich ein breites allgemeininternistisches Wissen. Der Referent (H.S.) lernte ihn an der Wiener Klinik während seiner eigenen dortigen Ausbildungszeit gut kennen. Er schätzte bereits damals an seinem griechischen Kollegen Sotos, wie er genannt wurde, dessen rasche Auffassungsgabe, Kombinationsfähigkeit und sein originelles, unkonventionelles Denken, das immer auch die praktische Durchsetzbarkeit im Auge hatte.

Diese Eigenschaften zeichneten ihn während seines gesamten Berufslebens aus und führten zu vielen hohen und höchsten Ämtern, Funktionen und Auszeichnungen, die alle aufzuführen hier der Platz fehlt. Die beeindruckende Liste kann in seinem Lebenslauf im Internet auf sechs Seiten nachgelesen werden, gefolgt von 375 Literaturstellen über seine Arbeiten auf vielfältigem Gebiet, erschienen in herausragenden Zeitschriften (http://www.hndc.gr/sa_raptis_cv.htm).

1967 bis 1978 arbeitete Professor Raptis bei Professor Ernst Friedrich Pfeiffer an der neu gegründeten Universität in Ulm, wo auch der Referent von 1969 bis 1976 tätig war. Das Bild aus diesen Tagen zeigt

Von links: Raptis, Mayer, Schatz, Pfeiffer senior.

den 34-jährigen Sotos Raptis bei der Feier zum 50. Geburtstag von Professor Pfeiffer am 10. April 1972 in Ulm.

In Ulm lernte Sotos seine aparte Ehefrau Ilse kennen, Tochter des Inhabers des Ulmer Geschäfts der Württembergischen Metallwarenfabrik WMF, deren Bestecke auch heute nach wie vor erhältlich sind und in vielen Haushalten verwendet wer-

Ilse und Sotos Raptis 2008 in München.

den, so auch dem des Referenten. Das Ehepaar bekam vier Kinder, die Töchter Marina, Dominique und Isabell sowie Sohn Agis.

Im Jahre 1978 übernahm Professor Raptis die Leitung des Diabeteszentrums des Departments of Clinical Therapeutics an der Athener Universität und war von 1982 bis 2005 Ordinarius für Innere Medizin und Chairman des 2. Departments für Innere Medizin – Propädeutik der Universität Athen.

1993 gründete er das „Hellenic National Center for Research, Prevention and Treatment of Diabetes Mellitus and its Complications". Von der Gründung bis zu seinem Tode war er dessen Präsident.

Während des 32. Internationalen Donausymposiums über Diabetes mellitus in Prag 2017, initiiert im Jahre 1969 in Wien von Alois Beringer mit Sotos als Mitbegründer, wurde am 22. Juni 2017 bekannt, dass Professor Raptis im Mai 2017 verstorben ist. Professor Werner Waldhäusl aus Wien als Kollege und jahrzehntelanger Weggefährte gedachte seiner bei der Eröffnungsveranstaltung.

Unser aller tiefes Mitgefühl gilt der Familie von Sotos, seiner Ehefrau Ilse und den Kindern. Wir werden ihm ein ganz besonderes, herzliches Andenken bewahren.

Helmut Schatz

Bochum, 29. Juni 2017

32nd Congress of the Federation of the International Danube Symposia on Diabetes mellitus/12th Congress of the Central European Diabetes Association

Jan Škrha

The 32nd Congress of the Federation of the International Danube Symposia (FID) and 12th Congress of the Central European Diabetes Association (CEDA) were organized in June 22–24, 2017 in Prague, Czech Republic. It was just twenty years later, when the 14th FID Donau Symposium was held in Prague as well.

This year the meeting was smaller with around 100 participants and a total of 55 presentations introducing actual topics in different fields in diabetes. The program contained 32 lectures of invited speakers and 23 posters.

Antidiabetic drugs and their effects

In the first session entitled „Antidiabetic drugs – Decisions for modern treatment" Ivan Tkáč (Slovakia) showed the possible application of pharmacogenomics into treatment of type 2 diabetes mellitus. Christoph Wanner (Germany) analyzed the benefits of empagliflozin on the progression of albuminuria and renal failure in the recent clinical trial EMPA-REG OUTCOME. This study could demonstrate renoprotection besides cardioprotective effects described earlier. Ilse Konrade (Latvia) summarized the positive effects of metformin not only in association with diabetes but in other clinical situations.

Diagnostic problems in diabetes

The second session was entitled „The way to proper diagnosis". Nanette Schloot (Germany) described actual problems with classification of diabetes and its significance for proper diabetes treatment. Štěpánka Průhová (Czech Republic) introduced the present status with diagnosis of maturity onset diabetes of the young (MODY) in the Czech Republic. Ondřej Cinek (Czech Republic) analyzed experience and his own data with viruses and bacteria as a compound of intestinal microbioma in the relationship to development of type 1 diabetes. Finally, Jan Škrha presented data of his 37 years experience with diagnosis and treatment of non-diabetic hypoglycaemia, including organic hyperinsulinism.

The program of the first day was closed by the symposium sponsored by Boehringer Ingelheim. Martin Prázný (Czech Republic) summarized cardiovascular effects of empagliflozin and Heinz Drexel (Austria) presented actual recommendations based on the new findings with gliflozins.

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Inter-organ relationships

The next day started with physiological regulation and inter-organ relationships entitled „The main players in metabolic regulations". Michael Roden (Germany) introduced actual findings in metabolic relationships between the muscle, liver and adipose tissue which have an important influence on insulin sensitivity. Martin Haluzík reported regulations originating from gastrointestinal hormones and their clinical utility in the treatment of diabetes. Erifili Hatziagelaki (Greece) analyzed the role of liver diseases, especially of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), and their influence on the diabetes control. Markolf Hanefeld (Germany) mentioned the clinical significance of the frailty in older patients as an important factor for individualization of the treatment.

Details of atherosclerosis

Complications in diabetes entitled „Pavement to vascular disease" were opened by Peter Nawroth (Germany) who discussed the role of fibrosis in the connective tissue as an important morphology in development of chronic vascular disease. Jan Škrha jr. (Czech Republic) mentioned biomarkers, especially microRNA, which could be used as early markers of vascular changes in diabetes. Kateřina Kaňková (Czech Republic) elucidated some indicators of diabetic kidney disease and demonstrated changes in the thiamin metabolism and the role of transketolase in renal pathology. Helmut Schatz (Germany) highlighted the news in dyslipidaemia in the development of atherosclerosis.

Diabetes control during physical activity

In the lunch symposium sponsored by Medtronic Tomasz Klupa (Poland) showed the important role of physical

activity in diabetes control maintained by insulin pumps and its monitoring in extreme conditions. He also invited participants to the next 33rd FID congress which will be held in Krakow, June 14–16, 2018.

Limb complications

In the afternoon the first session was entitled „Neural tissue and wounds – targets for treatment". Péter Kempler (Hungary) elucidated pathophysiology in close relationship of neuropathy and vascular changes in diabetes and its clinical consequences. In the next lecture Dan Ziegler (Germany) mentioned the actual possibilities in the drug treatment of diabetic neuropathy. Robert Bém and Michal Dubský (Czech Republic) introduced the stem cells as possible way in the treatment of diabetic wounds and critical ischaemia of the lower limbs.

Fig. 2: Congress president Jan Škrha (left) and Ivan Tkáč by chairing the first session.

Glucose variability and continuous glucose monitoring

New technologies entitled „Technologies – promising dreams and reality" were introduced by Roman Hovorka (United Kingdom) who demonstrated the actual development in the closed loop systems covering insulin pumps and continuous glucose monitoring including the use of bihormonal infusion (insulin and glucagon). Martin Prázný (Czech Republic) spoke about glucose variability as an important factor which should be monitored in insulin treated diabetic patients. In the following lecture Zdeněk Šumník (Czech Republic) described the care for diabetic children in the Czech Republic including the register „Čenda". Jan Šoupal reviewed own results with the continuous glucose monitoring in type 1 diabetic patients on insulin pumps and pens.

In the evening symposium sponsored by Eli Lilly Kateřina Štechová (Czech Republic) discussed innovations in insulin treatment, and Martin Haluzík (Czech Republic) spoke about the necessity of properly selected patients on GLP-1 receptor agonists.

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In the last congress day, the FID president Roger Lehmann (Switzerland) introduced the session „How to substitute disturbed function in diabetes" with the B-cell replacement therapy in diabetes with detailed description of different types of transplantation. Peter Girman (Czech Republic) reported the results with transplantations in the Czech Republic. Ivan Rychlík (Czech Republic) reviewed the care for diabetic patients in dialysis centres in the Czech Republic. This session was closed by Jan Polák (Czech Republic) with a report of a sleep apnea syndrome and the needs of its early detection and treatment.

Protecting B-cells

The last session entitled „Perspectives for diabetic patients" was introduced by Eberhard Standl (Germany) who summarized firstly the view of cardiologist Anselm Gitt (Germany) who acutely could not come and sent his lecture concerning the role of new antidiabetic drugs on cardiovascular system. Eberhard Standl than continued and demonstrated that the glucocentric view in the treatment of diabetes needs to be changed and longterm cardiovascular effects of antidiabetic drugs have to be evaluated in the light of recent studies with gliflozins and GLP-1 receptor agonists. Michael Nauck (Germany) remembered in excellent review the history of incretins and their introduction in clinical practice. Possible prevention of B-cell failure summarized Michal Anděl (Czech Republic) in the final lecture.

Dynamic development of diabetology

The posters from different fields of diabetes brought additional views into the program of the symposium which confirmed dynamic development of diabetology with new changes and considerations in classification, early diagnosis of complications and proper treatment. Participants from 11 countries created very active discussions during the entire symposium. The cordial athmosphere was filled by the get-together dinner in the modern „Dancing house" (called Ginger and Fred) built in the early nineties of the last century.

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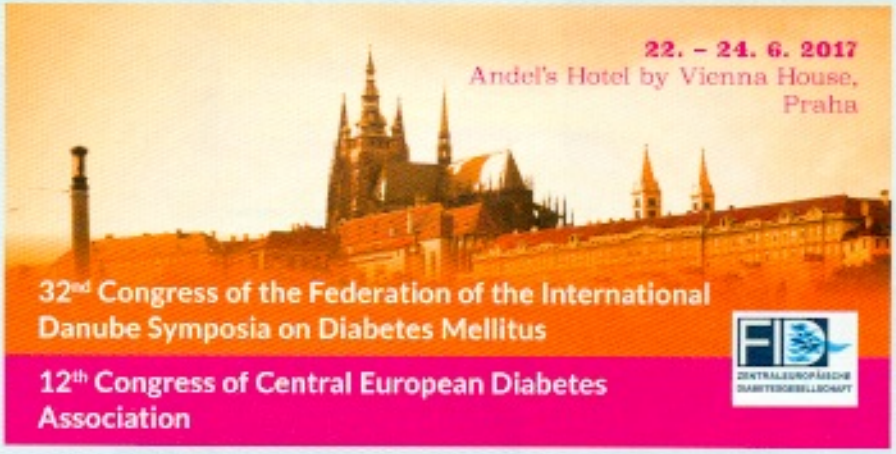

Abb. 1: The 32nd FID congress and the 12th CEDA congress were held in Prague.

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– 22–24 June 2017, Prague, Czech Republic –

P01

Abnormalities of thiamine metabolism induced by diabetes and kidney dysfunction in micro- and macrovascular cells

K. Chalásová[1], L. Pácal[1], K. Kaňková[1]

1) Department of Pathophysiology, Masaryk University, Brno, Czech Republic

Introduction: Pentose phosphate pathway (PPP) represents potentially protective pathway against hyperglycaemia-driven pathology in diabetes. Transketolase (TKT) is the key rate-limiting enzyme of non-oxidative branch of PPP whose activity depends on thiamine diphosphate (TDP) – an active form of thiamine (vitamin B_1) – as a cofactor. Thiamine (or benfotiamine) supplementation was shown to prevent development and progression of diabetic nephropathy (DN) in animal model of diabetes. Diabetic kidney disease (DKD), a common complication of both type 1 and type 2 diabetes associated with significant morbidity and mortality, represents the most common cause of chronic kidney disease (CKD). We hypothesized that protective PPP action in diabetes and eventually even more severely in concomitant DKD might be compromised by limited intracellular availability of an active TKT cofactor thiamine diphosphate (TDP).
Methods: Effect of hyperglycaemia and kidney disease on gene expression and protein levels of parameters related to PPP was studied in vitro using human cell lines relevant to diabetes (macrovascular HUVEC and microvascular HRGEC). Cells were cultured for 24 hours in normo- or hyperglycaemic conditions with 5 % pooled uraemic or control serum. Serum was obtained from blood samples provided by patients with ESRD prior to haemodialysis (HD, n = 20) or healthy volunteers without any sign or history of kidney disease (n = 10).
Results: Hyperglycaemia significantly decreased protein expression of RFC-1, THTR2 and TKT ($P < 0.01$) in HUVEC in vitro. Hyperglycaemia and uraemic serum mimicking CKD in diabetes did not affect TKT activity in HRGEC in vitro ($P < 0.05$).
Conclusion: Our in vitro experiments showed decrease of thiamine transport to the cells and of TKT protein expression induced by hyperglycaemia.

Acknowledgement: Study was supported by the grant 16-28040A from the Ministry of Health of the Czech Republic.

P02

Association between acylcarnitine concentration and muscle insulin resistance

I. Konrade[1], E. Makarova[1,2], G. Dambrova[1], I. Kalere[1], K. Vilks[2], K. Voļska[1,2], M. Dambrova[1,2]

1) Riga Stradins University, Riga, Latvia

2) Latvian Institute of Organic Synthesis, Laboratory of Pharmaceutical Pharmacology, Riga, Latvia

Introduction: Type 2 diabetes is characterized by impaired glucose metabolism and insulin resistance and significantly increases cardiovascular morbidity and mortality. Acylcarnitines provide long-chain fatty acid transport in mitochondria. In insulin resistant states insulin- stimulated glucose disposal in skeletal muscle is markedly impaired and increased fatty acid oxidation (FAO) rates are not followed by increased tricarboxylic acid cycle activity. We hypothesized that FAO intermediates, e.g. postprandial plasma acylcarnitines, would correlate with insulin sensitivity after fasting.
Material and methods: We enrolled 21 volunteers with BMI > 25 km/m². Blood samples were collected at four time points – baseline fasting and postprandially and following 36 h fasting and 2 h after a subsequent carbohydrate meal. Short-chain (C2 – C4), medium-chain (C5 – C12) and long-chain (C14 – C18:2) acylcarnitine concentration was measured by HPLC-MS-MS. C-peptide, free fatty acid, glucose and β-OH-butyrate concentrations were measured with commercially available kits. Insulin resistance index (HOMA-IR) was calculated with calculator from Oxford University website.
Results: Despite the increased BMI, the traditional insulin resistance tool HOMA-IR reflected a mild insulin resistance: 3.34 (1.18, 5.12), which was corrected already after 36 h fasting: 1.68 (0.98, 3.54), $p = 0.004$. After 36 h fasting acylcarnitine plasma concentration increased statistically significant 1.5 to 2 times. By contrast, two hours after meal short- and long-chain acylcarnitine concentrations decreased by about 30 %. The concentration of free fatty acids after the first meal decreased statistically significant by 45 %, but after the second meal by 93 % compared with the free fatty acid levels after 36 h fasting. The higher insulin resistance was, the lower was the postprandial decrease of C16 (Spearman's ρ 0.56, $p = 0.020$), C18:0 (ρ 0.69, $p = 0.002$),

C18:1 (ρ 0.55, p = 0.022), and C18:2 (ρ 0.60, p = 0.012), but higher was the increase of C18:0 (ρ 0.49, p = 0.047), C18:1 (ρ 0.64, p = 0.006), and C18:2 (ρ 0.59, p = 0.013) after fasting. After 36 h fasting the long-chain acylcarnitine concentration correlated with β-OH-butyrate: r = 0.44, but did not reach statistical significance (p = 0.07).
Conclusion: Our results provide evidence that the smaller changes in circulating postprandial long-chain acylcarnitine concentrations are characteristic for insulin resistance. Future studies are necessary to standardize assessment of postprandial change in long-chain acylcarnitine concentration to diagnose muscle-specific insulin resistance.

Funding: State Research Programme BIOMEDICINE.

P 0 3

Increased oxidative stress and endothelial activation in diabetic neuropathy in patients with type 1 diabetes mellitus

J. Škrha, jr.[1,2], T. Pelcl[1], J. Šoupal[1], M. Kalousová[2], M. Prázný[1], J. Škrha[1]

1) 3rd Dept. of Internal Medicine and Laboratory for Endocrinology and Metabolism, First Faculty of Medicine, Charles University in Prague and General University Hospital, Czech Republic

2) Institute of Medical Biochemistry and Laboratory Diagnostics, First Faculty of Medicine, Charles University in Prague and General University Hospital, Czech Republic

Oxidative stress (OxS) is believed to be an important factor in the development of vascular damage in diabetes. The aim of this study was to evaluate the relationship between the severity of diabetic neuropathy and markers of OxS and endothelial activation.
Our study involved 53 patients with type 1 diabetes (aged 37 ± 15 yrs). Neuropathy was evaluated by vibration perception threshold (VPT) measured repeatedly by Biothesiometer on both feet, and mean results > 15 V were considered as impaired VPT. OxS was evaluated by malondialdehyde (MDA) and antioxidative ascorbic acid (AA) plasma concentration. Markers of endothelial activation (ICAM-1, VCAM-1, vWF, soluble receptor for advanced glycation endproducts [sRAGE]), routine biochemical parameters and anthropometric data were measured in all patients.
Impaired VPT (iVPT) was present in 10 patients (VPT 28.3 ± 11.1 V). Significantly higher ICAM-1 and VCAM-1 were observed in iVPT group as compared with normal VPT patients (ICAM-1: 266 ± 75 vs. 214 ± 48 pg/l, p < 0.01; VCAM-1: 858 ± 200 vs. 686 ± 186 pg/l, p < 0.02). Similarly, significantly higher MDA was observed in iVPT group (0.83 ± 0.41 vs. 0.63 ± 0.16 µmol/l, p < 0.05), whereas AA was strongly reduced in these patients in comparison to normal VPT patients (46 ± 22 vs. 98 ± 37 µmol/l, p < 0.0005). Both sRAGE and vWF did not differ between groups (sRAGE: 1 115 ± 398 vs. 1 074 ± 388 ng/l, NS; vWF: 151 ± 114 vs. 138 ± 109 %, NS). Significant inverse relationship was found between VPT and AA (r = -0.48, p < 0.0001), while VPT was positively associated with MDA (r = 0.37, p < 0.01). Inverse relationship between MDA and sRAGE was observed (r = -0.35, p < 0.01). Higher markers of endothelial activation and OxS and lower antioxidative capacity in patients with impaired VPT supports the idea of their involvement in the pathogenesis of diabetes complications. For future treatment, it should be therefore useful to target antioxidative systems in order to delay the onset of diabetic neuropathy.

The study was supported by Research Project P25/LF1/2 and Grant 15-26705A of the Agency for Healthcare Research (AZV) of the Czech Republic.

P 0 4

MicroRNA-196 and -423 have different expressions in pancreatic cancer patients compared to those with chronic pancreatitis

P. Škrha[1], A. Hořínek[2], P. Frič[3], J. Hajer[1], M. Anděl[1], J. Škrha[2]

1) Dept. of Internal Medicine 2, 3rd Faculty of Medicine, Charles University, Prague, Czech Republic

2) Dept. of Internal Medicine 3, 1st Faculty of Medicine, Charles University, Prague, Czech Republic 3) Dept. of Internal Medicine, Military University Hospital, Charles University, Prague, Czech Republic

Introduction: The aim of this study was to distinguish chronic pancreatitis (CHP) from pancreatic cancer (PAC) which is often difficult. Diabetes mellitus (DM) may be the first symptom of PAC, but it is frequently associated with CHP. In this study the microRNAs were tested as potential markers in patients with PAC and CHP.
Methods: Seventy five patients with PAC (58/17 with/without DM), 26 with CHP (15/11 with/without DM), 39 diabetic patients without PAC or CHP and 30 healthy persons were examined in our study. DM diagnosis was made according to ADA criteria. Expressions of 8 miRNAs (miR-21, -30, -191, -192, -196, -200, -423 and -454) were determined in serum by the real-time PCR, carbohydrate antigen CA 19-9 as usually used tumor marker was measured in serum as well. Kruskal-Wallis ANOVA test was performed to evaluate the results.
Results: Expressions of miR-21, -30, -192, -196 and -200 and CA 19-9 were significantly elevated in PAC patients compared to the other groups (p < 0.01 to p < 0.0001). Micro-RNA 423 was significantly lower in CHP patients compared to DM patients with or without PAC and control persons (p < 0.0001). Performing the test of subgroups according to the presence/absence of DM, CA 19-9 failed to distinguish CHP patients from PAC patients without DM. However, the expressions of miR-196 and -423 were 5 to 6 times higher in DM patients with PAC compared to patients with CHP (p < 0.0001) as well as in non-DM patients with PAC compared to CHP (p < 0.0001). No difference in miRNA expressions was found between the subgroups of patients with and without diabetes within PAC and CHP groups.
Conclusions: Our study compares for the first time expressions of selected miRNAs in patients with CHP and with PAC associated with diabetes. We suggest miRNA-196 and -423 as new biomarkers for distinguishing the pancreatic cancer in DM from those with CHP.

P05

Severe diabetic ketoacidosis and phosphate deficiency

P. Tesinsky[1], A. Haken[2]

1) ICU, Dept. of Medicine 2, Charles University Hospital Kralovske Vinohrady, Prague, Czech Republic

2) 3rd Faculty of Medicine, Charles University, Prague, Czech Republic

Rationale: Severe diabetic ketoacidosis (DKA) is frequently accompanied by serum phosphate deficiency. Clinical manifestations may remain unestimated and include weakness, changes of state of consciousness, and muscle fatigue. The aim of this prospective study was to identify the presence of hypophosphataemia in severe diabetic ketoacidosis and to compare patients' metabolic state with specific clinical manifestation.
Methods: Patients with evidence of hypophosphataemia during treatment of DKA were monitored within a period of 48 hours after admission. Following parameters were evaluated at times 0, 12, 24, and 48 hours: pH, bicarbonate, glycaemia, potassium (K), phosphate (P), CRP, and urinary ketones. Simultaneously, cumulative doses of insulin, energy, fluids, K, and P during treatment were calculated.
Results: Out of 3 595 patients admitted to the medical ICU between January 1, 2012, and December 31, 2016, 113 patients had a diagnosis of DKA (3.14 %). 62 patients (49 %) had severe hypophosphataemia (less than 0.35 mmol/l), 41 patients (43 %) had mild hypophosphataemia(0.36 – 0.65 mmol/l), and 10 patients (8 %) were normophosphataemic during the treatment. 10 patients required temporary ventilatory support. The total dose of insulin was 223 U on average in the "severe" group in comparison to the mean value of the whole group (189 U). Fluid delivery was equal in both groups (4 750 ml vs. 4 719 ml). The cumulative phosphate substitution was 127 mmol vs. 103 mmol). The clinical symptomatology resumed completely in all patients within the next 24 hours after suplementation of fluid, energy, K, and P.
Conclusion: Although phosphate supplementation is not routinely recommended during treatment of diabetic ketoacidosis in the current guidelines, we should be aware of danger of hypophosphataemia. Therefore, monitoring of serum phosphate level and its repletion if necessary should be considered.

P06

The level of metabolic control (HbA_{1c}) in patients with type 1 diabetes mellitus in the Czech Republic and Slovak Republic: results of an international, multicenter, observational study (DIAINFORM)

J. Broz[1], D. Janickova Zdarska[1], J. Urbanova[2], M. Brabec[3], B. Krivska[4], V. Donicova[5], R. Stepanova[6], E. Martinka[7], M. Kvapil[1]

1) Department of Internal Medicine, 2nd Faculty of Medicine, Charles University, Prague, Czech Republic

2) Center for Research in Diabetes, Metabolism and Nutrition, 2nd Department of Internal Medicine, Third Faculty of Medicine, Charles University, Prague, Czech Republic

3) Institute of Computer Science of the ASCR, v. v. i., Czech Republic

4) Sanofi, Prague, Czech Republic

5) Private Department of Diabetology Internal Medicine and Metabolism, Kosice, Slovakia

6) ADDS s.r.o., Brno, Czech Republic

7) National Institute of Endocrinology and Diabetology, Slovakia

Introduction: Achieving targets for metabolic control of diabetes minimizes the risk of specific complications, and other comorbidities. Despite the ever-expanding therapeutic treatment options for type 1 diabetes (T1D), the percentage of patients achieving the recommended HbA_{1c} target is not high. The aim of the study was to determine the level of metabolic control in T1D patients in the Czech Republic and Slovak Republic.
Methods: A non-interventional (observational) project, which was conducted from January 2015 until April 2016 in the routine clinical practice setting at 141 centers in the Czech Republic and Slovak Republic. Data were analyzed from a total of 425 patients with T1D, proportionally corresponding to the number of patients in both countries. The inclusion criteria were patients with a minimum duration of one year on insulin therapy, strictly adhering to the schedule of follow-up visits and willing to fill in the study questionnaire. Patients treated with an insulin pump were excluded from the study. The primary objective of the study was to determine the percentage of patients with HbA_{1c} < 53 mmol/mol.
Results: In the entire group of patients (55.8 % men, mean age: 45.9 ± 14.83 years, BMI: 25.8 ± 4.21 kg/m^2, diabetes duration: 12.1 ± 9.44 years), the percentage of those who achieved HbA_{1c} levels below 53 mmol/mol was 29.9 %. The percentage rates in the Czech and Slovak Republics were 26.7 % and 36.4 %, respectively.
Conclusion: The overall percentage of patients with HbA_{1c} < 53 mmol/mol in the entire group was 29.9 %. Despite an increasing number of treatment options, a large majority of patients still fail to reach recommended HbA_{1c} targets.

The study was supported by Sanofi.

P07

The level of metabolic control (HbA_{1c}) in insulin-treated patients with type 2 diabetes mellitus in the Czech Republic and Slovak Republic: results of a multinational, multicenter, observational study (DIAINFORM)

J. Broz[1], D. Janickova Zdarska[1], J. Urbanova[2], M. Brabec[3], B. Krivska[4], V. Donicova[5], R. Stepanova[6], E. Martinka[7], M. Kvapil[1]

1) Department of Internal Medicine, 2nd Faculty of Medicine, Charles University, Prague, Czech Republic

2) Center for Research in Diabetes, Metabolism and Nutrition, 2nd Department of Internal Medicine, Third Faculty of Medicine, Charles University, Prague, Czech Republic

3) Institute of Computer Science of the ASCR, v. v. i., Czech Republic

4) Sanofi, Prague, Czech Republic

5) Private Department of Diabetology Internal Medicine and Metabolism, Kosice, Slovakia

6) ADDS s.r.o., Brno, Czech Republic

7) National Institute of Endocrinology and Diabetology, Slovakia

Introduction: Achieving targets for metabolic control of diabetes minimizes the risk of specific complications, and other comorbidities. Despite the ever-expanding therapeutic treatment options for type 2 diabetes (T2D), the percentage of patients achieving the recommended HbA_{1c} target is not high. The aim of the study was to determine the level of metabolic control in patients treated with insulin in the Czech Republic and Slovak Republic.

Methods: A non-interventional (observational) project, which was conducted from January 2015 until April 2016 in the routine clinical practice setting at 141 centers in the Czech Republic and Slovak Republic. Data were analyzed from a total of 1 034 patients with T2D, proportionally corresponding to the number of patients in both countries. The inclusion criteria were patients with a minimum duration of one year on insulin therapy, strictly adhering to the schedule of follow-up visits and willing to fill in the study questionnaire. In the final phase of the study, the patients were enrolled so as to obtain a representative sample for all basic insulin regimens. Patients treated with insulin pump were excluded from the study.
Results: In the entire group of patients (50.3 % men, mean age: 63.9 ± 9.65 years, BMI: 31.0 ± 5.19 kg/m^2, diabetes duration: 12.4 ± 7.47 years, duration of insulin therapy: 5.8 ± 4.71 years), the percentage of those who achieved HbA_{1c} levels below 53 mmol/mol was 33.4 %. The percentage rates in the Czech Republic and Slovak Republic were 35.8 % and 28.3 %, respectively.
Conclusion: The overall percentage of patients with HbA_{1c} < 53 mmol/mol in the entire group was 33,4 %. Despite an increasing number of treatment options, a large majority of patients still fail to reach recommended HbA_{1c} targets.

The study was supported by Sanofi, Czech Republic.

P 0 8

FINDRISK as a screening tool for diabetes in the community: first application in Cyprus

C. Chrysostomou[1], A. Ioannou[1], G. Lavranos[1]

1) Department of Health Sciences, European University Cyprus

Background: Diabetes mellitus remains a major cardiovascular risk factor with epidemic trends across western Europe. In Cyprus, approximately 12 % of the population are estimated to suffer from diabetes, although no nationwide epidemiologic study has been performed to date. Unfortunately, due to lack of an early detection system, most patients are diagnosed only after symptom onset, with major complications such as myocardial infraction, stroke, end stage renal disease, blindness or amputation often being unavoidable at this stage.
Aim: The aim of this study was to validate the Greek version of the FINDRISK questionnaire as a screening tool for diabetes in a rural community setting in Cyprus.
Materials and methods: The validated translation of the Greek version of the FINDRISK questionnaire was used after permission provided both by the Finnish creators and the Greek translators. The study population consisted of the first 100 adult patients presenting in a rural primary care center during the predetermined sampling date. 98 individuals agreed to complete the questionnaire. Whenever a high risk was determined by FINDRISK, patient files were cross-checked to determine if the patient was a known diabetic and, if not, the patient was referred for disease confirmation via OGTT.
Results: Response rate was 98 % with no difficulties in terms of interpretation/comprehension or implementation. A total of 25 individuals in this convenience sample scored high risk in FINDRISK. Of these, 22 were known diabetic/prediabetic and the other 3 were newly diagnosed as prediabetic via OGTT. No known diabetic patients scored less than high via FINDRISK.
Conclusion: FINDRISK was found to be a feasible option for diabetes screening in the community in Cyprus. Its very high positive and negative predictive value and reasonably high yield for new case identification make it potentially suitable for population wide application as a screening protocol.

P 0 9

Differences in approach to screening for gestational diabetes – national patient survey on screening for gestational diabetes in the Czech Republic

P. Šimjak[1], K. Anderlová[1,2], H. Krejčí[1,2], A. Pařízek[1], P. Pařízková[3], V. Krejči[1], M. Kršek[4], M. Mráz[6], M. Haluzík[5,6]

1) Department of Obstetrics and Gynecology, 1st Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic

2) 3rd Medical Department, 1st Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic

3) Czech Society of Midwives

4) 2nd Internal Department, 3rd Faculty of Medicine, Charles University and Royal Vinohrady Teaching Hospital in Prague, Czech Republic

5) Department of Medical Biochemistry and Laboratory Diagnostics, Charles University and General University Hospital in Prague, Czech Republic

6) Center for Experimental Medicine and Diabetes Center, Institute for Clinical and Experimental Medicine, Prague, Czech Republic

Background: GDM is associated with an increased risk of short- and long-term complications for both mother and foetus, including pregnancy complications such a caesarean delivery, shoulder dystocia, macrosomia, and neonatal hypoglycaemia. In the long term, epigenetic changes induced by in-utero exposure to maternal hyperglycaemia increase risk of obesity, T2DM, cardiovascular diseases and neuropsychiatric morbidity. The aim of our survey was to investigate the correctness of methodology of the screening for gestational diabetes mellitus (GDM) according to new recommendations issued by the International Association of Diabetes and Pregnancy Study Groups.
Methods: A questionnaire for pregnant women assessed whether the screening for GDM in the Czech Republic was done in all eligible patients and whether the correct methodology and appropriate cut-offs were applied. We used the printed version of the questionnaire among patients in our obstetrical center (group 1, n = 1 100) and its on-line version posted on the website for pregnant women (group 2, n = 1 041).
Results: 45.3 % of included patients reported having fasting glycaemia measured in the first trimester of pregnancy. In the second half of the pregnancy, 85.6 % (88.5 % in group 1 vs. 82.0 % in group 2, p = 0.001) underwent oral glucose tolerance test (oGTT). Methodological errors in oGTT were common in both groups with most frequent ones being not acquiring fasting glycaemia results prior glucose challenge and not performing 3 point test. In total, only 16.3 % of tests were performed completely according to standards.

Conclusion: The screening for GDM in the Czech Republic is frequently not performed in accordance with new guidelines. The pursuit for its improvement should be one of the priorities in obstetrics. Misdiagnosed and untreated GDM threatens the mother and her fetus with a number of complications.

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P 10

Hypoglycaemia frequency and glycaemic outcomes in type 2 diabetes (T2DM) using different fasting plasma glucose titration targets: an analysis of studies with insulin glargine 100 U/ml

D. R. Owens[1], B. M. Frier[2], J. Chao[3], R. Perfetti[3], W. Landgraf[4]

1) Swansea University, College of Medicine, Swansea, UK

2) The Queen's Medical Research Institute, University of Edinburgh, Edinburgh, UK

3) Sanofi US, Bridgewater, USA

4) Sanofi, Frankfurt, Germany

		FPG target (mmol/l)		
		3.9–5.0 IDeg	3.9–5.0 Gla-100	4.4–5.5 Gla-100
Insulin-naïve*, total number of patients		**745**	**884**	**2837**
Age	(years)	57.7 (9.5)	57.8 (9.3)	57.7 (9.8)
Duration of diabetes	(years)	10.2 (6.6)	10.3 (6.3)	9.0 (6.4)
BMI	(kg/m²)	28.7 (4.6)	30.0 (4.7)	30.6 (5.3)
HbA_{1c}	baseline (%)	8.4 (0.9)	8.3 (0.9)	8.8 (1.1)
	week 24 or 26 (%)	7.2 (0.9)	7.1 (0.9)	7.2 (1.0)
	change week 0–24/26 (%-units)	-1.2 (1.0)	-1.3 (1.0)	-1.6 (1.2)
HbA_{1c} <7 % at week 24 or 26 (% people)		45	49	45
Fasting PG (FPG)	baseline (mmol/l)	8.9 (2.6)	9.0 (2.7)	10.8 (3.1)
	week 24 or 26 (mmol/l)	5.7 (2.0)	6.1 (2.1)	6.6 (2.2)
	change week 0–24/26 (mmol/l)	-3.2 (2.8)	-3.0 (2.9)	-4.2 (3.4)
Insulin dose	week 24 or 26 (U/kg)	0.47 (0.27)	0.57 (0.28)	0.44 (0.26)
	change week 0–24/26 (U/kg)	0.29	0.37	0.28
Hypoglycaemia[a]	overall (% people)	40.5	45.3	29.5
	overall (events/person-yr)	2.37	3.11	1.95
	nocturnal (% people)	11.4	18.7	10.7
	nocturnal (events/person-yr)	0.43	0.76	0.49
Insulin-naïve*, no SU users (number of patients)		**228**	**508**	**634**
Hypoglycaemia[a]	overall (% people)	28.5	39.7	16.9
	overall (events/person-yr)	1.42	2.69	0.79
	nocturnal (% people)	6.1	15.2	4.9
	nocturnal (events/person-yr)	0.18	0.60	0.26
Insulin-naïve*, SU users (number of patients)		**517**	**376**	**2203**
Hypoglycaemia[a]	overall (% people)	47.3	50.9	34.0
	overall (events/person-yr)	3.28	3.57	2.20
	nocturnal (% people)	15.1	22.4	11.0
	nocturnal (events/person-yr)	0.67	0.96	0.36

Mean (SD) or percent people; group numbers may vary if missing values; [a]confirmed plasma glucose <3.1 mmol/l; SU: sulfonylurea; *11 % (Gla-100) and 13 % (IDeg) of patients were insulin pre-treated

Tab. P10: Comparison of clinical outcomes in people with T2DM on basal insulin treatment in clinical trials of 24–26 weeks aiming for different FPG titration targets.

Background and aims: To explore the impact of different fasting plasma glucose (FPG) titration targets on hypoglycaemia frequency and glycaemic outcomes in people with T2DM commencing insulin glargine 100 U/ml (Gla-100) in combination with oral agents.

Methods: Patient-level data from 15 studies involving Gla-100 (n = 2 837) targeting FPG < 5.5 mmol/l over a 24-week treatment period were pooled. Additionally, 4 studies (26 week duration) with a FPG target < 5.0 mmol/l were identified (published reports: NN-3586, NN-3668, NN3672, DUAL V), in which Gla-100 was the reference basal insulin vs. insulin degludec (IDeg) or vs. IDeg/liraglutide fixed ratio combination. Only results from those patients randomised to once daily Gla-100 (n = 884) or once daily IDeg (n = 745) were meta-analysed. Incidence and event rate of plasma glucose confirmed hypoglycaemia (PG < 3.1 mmol/l), glycaemic outcomes and insulin doses from these two study cohorts were compared descriptively.

Results: Baseline characteristics of Gla-100- and IDeg-treated patients were comparable across the two study pools although baseline HbA_{1c} and FPG were slightly lower in studies using a lower FPG target (Table). Endpoint FPG and HbA_{1c} in Gla-100-treated patients were slightly lower in studies with a lower FPG target. As anticipated a higher percentage of patients achieved study specific FPG target and HbA_{1c} < 7 % at endpoint in the lower FPG target studies (FPG: 37 vs. 34 %; HbA_{1c}: 49 vs. 45 %). The incidences and event rates of overall and nocturnal confirmed hypoglycaemia (PG < 3.1 mmol/l) were considerably higher in the study pool attempting the lower FPG target (Table). In this cohort patients received a higher mean final Gla-100 dose (0.57 vs. 0.44 U/kg) and had a greater dose increment (+0.37 vs. +0.28 U/kg). Patients receiving a sulfonylurea (SU) had a higher risk of hypoglycaemia (overall; nocturnal) vs. those not receiving a SU, irrespective of lower or higher FPG titration target (Table).

Conclusions: This post-hoc analysis suggests that a lower FPG titration target (< 5.0 mmol/l) leads to an increased hypoglycaemia risk with no or little improvement in overall glycaemic control in people with T2DM commencing Gla-100.

P 11

Software module for automatic detection of decrease in glycaemia associated with higher intensity of physical activity in data from activity trackers and CGM used by patients with type 1 diabetes

A. Holubová[1,2], J. Mužík[1,2], M. Poláček[2], J. Kašpar[1,2], K. Hána[1], P. Smrčka[1], J. Brož[3]

1) Department of Information and Communication Technologies in Medicine, CTU, Prague, Czech Republic

2) Spin-Off Application Centre of the 1st Faculty of Medicine, Charles University, Prague, Czech Republic

3) Department of Internal Medicine, 2nd Faculty of Medicine, Charles University, Prague, Czech Republic

Introduction: Increased physical activity (PA) in insulin-dependent patients with diabetes requires proper dosing of insulin and carbohydrate supplementation to keep blood glucose stable, which is not easy for patients to manage. Activity tracker together with continuous glucose monitor (CGM) allow them to track and learn from the data produced by these devices when planning similar activities. The aim was to build and test a software module capable of automatically searching for situations of decreased glycaemia associated with higher intensity of PA.

Methods: The telemonitoring system Diani enables to store data transferred from various devices, including CGM and activity tracker. The created software module uses these stored data to search for incidents of increased PA associated with decrease in blood glucose level, considering initial settings such as the range of the intensity of PA, the level of blood glucose decrease and its duration, and an option to select hypoglycaemia occurrence only. As a result, a table with a list of incidents is displayed with further information, i.e. the total number of steps, the level of blood glucose decrease and its duration, and a reference to display a daily graph with patient's records.

Results: The data from 75 patients with type 1 diabetes monitored with activity tracker and CGM for 7 ± 3.1 days were used to test the module. With the initial settings of the intensity of PA to 50 – 500 steps/5 min, the decrease in blood glucose to 2 – 5 mmol/l and the duration to > 10 min, the system detected 401 segments in total (5.3 ± 5.1 segment per patient) of which 63 were identified in the range of 4 – 5 mmol/l and 59 below 3.9 mmol/l. By extending the drop in blood glucose to 2 – 20 mmol/l, the number of identified glycaemia below 3.9 mmol/l increased up to 88 and those in the range of 4 – 5 mmol/l raised up to 166. The "manual" data analysis confirmed that the module had detected all sections according to the assignment.

Conclusion: The module enables to quickly identify situations of increased PA associated with decrease in blood glucose level after the initial settings of parameters are made. By referring to a selected incident in graph, patients and physicians can analyze given situation in details and in the context of other parameters, such as insulin doses and carbohydrate intake, if being recorded by the patients.

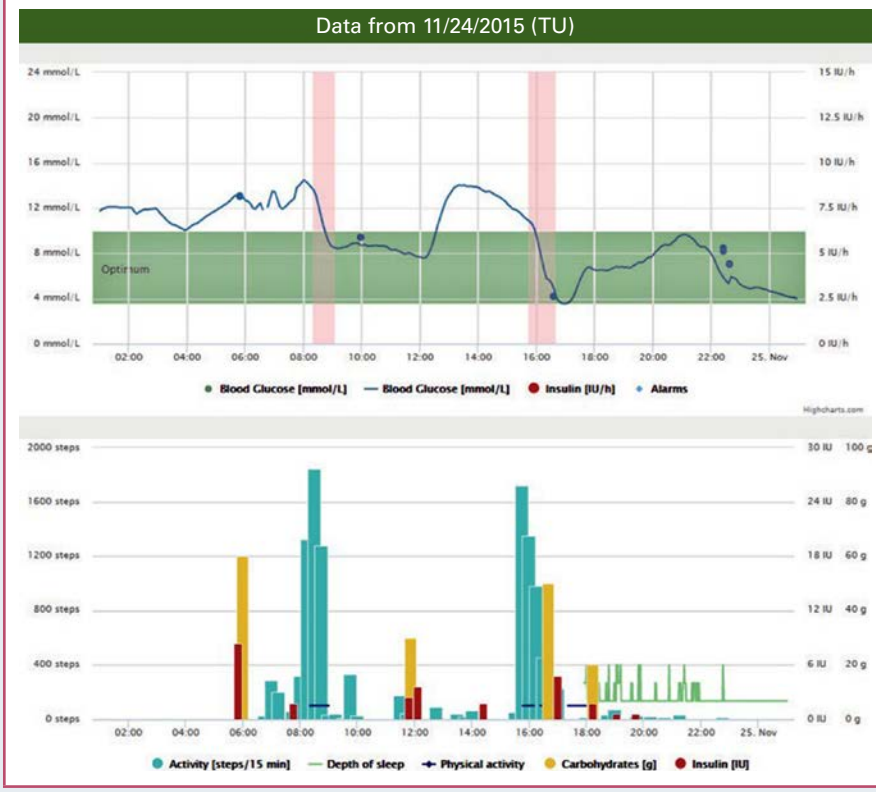

Fig. P11

P 12

TRPV4 modulates insulin mRNA expression and cell death in insulin producing INS-1E cells

M. Billert[1], M. Skrzypski[1], T. Wojciechowicz[1], M. Strowski[2,3], K.W. Nowak[1]

1) Department of Animal Physiology and Biochemistry, Poznań University of Life Sciences, Poznań, Poland

2) Department of Hepatology and Gastroenterology, Interdisciplinary Centre of Metabolism, Endocrinology, Diabetes and Metabolism, Charité-University Medicine Berlin, Berlin, Germany

3) Department of Internal Medicine-Gastroenterology, Park-Klinik Weissensee, Berlin, Germany

Introduction: Transient receptor potential channel vanilloid type 4 (TRPV4) is a Ca^{2+} permeable ion channel, activated by different chemical and physical stimuli. In pancreatic beta cells TRPV4 stimulates Ca^{2+} influx and insulin secretion and is involved in islet amyloid polypeptide-stimulated apoptosis. Although it was shown that TRPV4 enhanced insulin secretion by Ca^{2+}-dependent mechanism, the role of TRPV4 in controlling insulin genes expression in pancreatic beta cells remains unknown. The aim of this study was to investigate the effects of TRPV4 activation on insulin mRNA expression and cell death in insulin producing INS-1E cells and rat pancreatic islets. Furthermore, we studied the mechanism by which TRPV4 modulates pancreatic beta cell functions.

Methods: TRPV4 was downregulated using siRNA technique. TRPV4 was activated by its agonist GSK1016790A. Intracellular calcium level was studied using Fluo-3AM. Gene expression was evaluated by real time PCR. ERK1/2 phosphorylation was measured using Western blot. Nitric oxide production was evaluated by chemiluminescent reaction. Cell death was studied by evaluation of cytoplasmic histone-associated DNA fragments.
Results: GSK1016790A increased intracellular calcium levels in INS-1E cells. GSK1016790A increased insulin mRNA expression after 1 and 3 h incubation. By contrast, GSK1016790A supressed insulin mRNA expression in cells treated for 24 h. Furthermore, stimulation of INS-1E cells with GSK1016790A for 24 h induced cell death. Downregulation of TRPV4 by siRNA transfection attenuated the effects of GSK1016790A on insulin mRNA expression. Moreover, we found that GSK1016790A increased ERK1/2 phosphorylation and NO production in INS-1E cells. Blockade of ERK1/2 phosphorylation by U0126 attenuated GSK1016790A-stimulated insulin mRNA expression. GSK1016790A failed to supress insulin mRNA expression and induce cell death in the presence of L-NAME (the nitric oxide synthase inhibitor). In rat pancreatic islets GSK1016790A stimulated insulin mRNA expression, but had no effects on cell death.
Conclusion: TRPV4 modulates insulin mRNA expression and cell death via ERK1/2 and NO-dependent mechanisms.

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P 13

Associatons between biomarkers of subclinical inflammation and depressive symptoms in patients with type 1 and type 2 diabetes

C. Herder[1,2], A. Schmitt[2,3], F. Budden[1,2], A. Reimer[2,3], B. Kulzer[2,3,4], M. Roden[1,2,5], T. Haak[2,3,4], N. Hermanns[2,3,4]

1) Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany

2) German Center for Diabetes Research (DZD), München-Neuherberg, Germany

3) Research Institute of the Diabetes Academy Mergentheim (FIDAM), Bad Mergentheim, Germany

4) Department for Psychology, Otto Friedrich University of Bamberg, Bamberg, Germany

5) Department of Endocrinology and Diabetology, Medical Faculty, Heinrich Heine University Düsseldorf, Düsseldorf, Germany

Introduction: Subclinical inflammation has been implicated in the development of depression, a common comorbidity of type 1 diabetes (T1D) and type 2 diabetes (T2D). This study compared the relationships of pro- and anti-inflammatory immune mediators with depressive symptoms between patients with T1D and T2D.
Methods: Six biomarkers of inflammation were measured in serum samples of participants with elevated depressive symptoms and T1D (n = 389, diabetes duration 15 ± 11 years) or T2D (n = 204, diabetes duration 13 ± 8 years). Subclinical depression was examined using three questionnaires (Center for Epidemiologic Studies Depression [CES-D] score, Patient Health Questionnaire [PHQ9], 5-item World Health Organization Well-Being Index [WHO5]). Associations between biomarkers and depression scores were estimated using multiple linear regression with comprehensive adjustment for confounders.
Results: In T1D, serum levels of interleukin-1 receptor antagonist (IL-1RA) were positively associated with depression for two scores (CES-D, PHQ9), and high-sensitivity C-reactive protein (hsCRP) was positively associated with depression for one score (WHO5) after adjustment for age, sex, study, BMI, diabetes duration, metabolic variables, medication and comorbidities (p = 0.008 – 0.042). In T2D, IL-18 and IL-1RA were positively associated with depression for two scores (IL-18: PHQ9, WHO5; IL-1RA: CES-D, WHO5), hsCRP for one score (PHQ9), and adiponectin showed an inverse association with depression also for one score (PHQ9) after adjustment (p = 0.006 – 0.048). No associations were found for IL-6 and monocyte chemoattractant protein-1 (MCP-1/CCL2).
Conclusion: We observed associations between hsCRP, IL-1RA and depressive symptoms in patients with diabetes. In T2D, there was additional evidence for associations between IL-18 and (inversely) adiponectin with depressive symptoms. The strength of the associations appeared to depend on diabetes type and the method used to assess depressive symptoms.

P 14

Tumor necrosis factor induces syndecan 4 expression in adipocytes from subcutaneous adipose tissue during surgically-induced weight loss

A. Jürets[1,2], B.K. Itariu[1], M. Keindl[1], L. Leitner[1], G. Prager[3], F. Lange[3], V. Grablowitz[4], M. Zeyda[1,5], T.M. Stulnig[1]

1) Christian Doppler Laboratory for Cardio-Metabolic Immunotherapy, Clinical Division of Endocrinology and Metabolism, Department of Medicine III, Medical University of Vienna, Vienna, Austria

2) Department of Life Sciences, University of Applied Sciences Krems, Krems, Austria

3) Department of Surgery, Medical University of Vienna, Vienna, Austria

4) Department of Surgery, Göttlicher Heiland Hospital, Vienna, Austria

5) Department of Pediatrics and Adolescent Medicine, Clinical Division of Pediatric Pulmonology, Allergology and Endocrinology, Medical University of Vienna, Vienna, Austria

Introduction: Syndecan 4 (SDC4) is a ubiquitously expressed extracellular matrix protein, involved in focal adhesion during matrix remodeling, cell signaling, and LDL-uptake. We recently showed that tumor necrosis-factor (TNF) is highly upregulated in the subcutaneous adipose tissue one year after bariatric surgery, without aggravating inflammation. It seems to induce local insulin resistance and orchestrate adipose tissue catabolism. We hypothesized that TNF, which is described to induce SDC4 in an endothelial-like cell line, may also induce SDC4 upregulation in the catabolic subcutaneous adipose tissue during surgically-induced weight loss.
Methods: We performed gene expression analysis from subcutaneous needle-biopsies from 31 patients shortly before and one year after bariatric surgery. These were compared to the gene expression of adipose tissue sample from a lean/overweight control group, matched according to age and sex. Gene expression was analyzed by RT-qPCR using TaqMan Assays. Regression analysis was used to determine independent predictors for SDC4. Furthermore, we

performed in vitro stimulation experiments using cultured primary adipocytes and determined gene expression by RT-qPCR afterwards.
Results: SDC4 was highly upregulated by 1176 % ($p < 0.001$) one year after bariatric surgery and by 170 % ($p < 0.05$) in the obese compared to the lean control group. By analyzing gene expression profiles from the post-obese group using regression analysis, we saw that TNF expression is an independent positive predictor for SDC4 gene expression. Additionally, a 24-hour in vitro stimulation of primary adipocytes with TNF induced an upregulation of SDC4 expression by 250 % ($p < 0.01$).
Conclusion: The induction of SDC4 by TNF and the high upregulation in the subcutaneous adipose tissue one year after bariatric surgery points to an important role of SDC4 in adipose tissue catabolism during weight loss.

P 15

Decreased CCL2 (MCP-1) secretion of leucocytes in LADA compared to type 1 and type 2 diabetes

M. Ooms[1], A. Strom[1], K. Strassburger[1], B. Menart[1], N. C. Schloot[1]

1) Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich-Heine-University, Düsseldorf, Germany

Latent autoimmune diabetes in adults (LADA) is pathogenetically classified as a subtype of type 1 diabetes (T1D) and is diagnosed in clinical type 2 diabetes patients (T2D) who are positive for T1D associated autoantibodies. It is not much known about chemokine secretion of leucocytes in LADA versus T1D and T2D. We investigated the mitogen and antigen stimulated chemokine secretion in vitro to learn more about the immunological role of chemokines in the different diabetes forms.
We analysed supernatants of ELISPOT stimulated leucocytes of 32 T1D, 22 LADA, 49 T2D for CCL2 (MCP-1), CXCL10 (IP10), and CCL5 (RANTES) by a multiplex-bead-array-assay method. Cells were stimulated with phorbol-myristate-acetat/ionomycin (PI), HSP60, p277, pGAD and pIA-2 and chemokine content was analysed after 40 h upon stimulation in vitro. Stimulation indices (SI) were calculated as a ratio of chemokine concentration with and without stimulation. Data were analysed for differences between groups non adjusted with Kruskal-Wallis-Test and Mann-Whitney-Test and also adjusted for anthropometric or clinical-chemical parameters like gender, age, diabetes duration and BMI respective blood glucose, HbA_{1c}, triglycerides and C-peptide with multiple linear regression analysis.
Chemokine secretion of CXCL10 and CCL5 did not differ between diabetes groups. Upon stimulation with PI, CCL2 was decreased in LADA compared to T1D (unadjusted $p < 0.05$) and T2D (unadjusted $p < 0.01$, adjusted for clinical-chemical parameters $p < 0.05$). Median (interquartile range) for SI was 1.1 (3.9) for LADA and 6.5 (24.7) for T1D respective 7.6 (18.0) for T2D. Upon stimulation with pIA-2, CCL2 was decreased in LADA compared to T2D (adjusted for clinical-chemical parameters $p < 0.05$). Median (interquartile range) for SI was 1.2 (5.9) for LADA and 2.6 (14.5) for T2D. CCL2 secretion was similar in diabetes groups when stimulated with HSP60, p277 and pGAD.
These data from in vitro stimulation of fresh leucocytes suggest a decreased CCL2 response in LADA upon stimulation with PI and autoantigenic peptide pIA-2. The lower CCL2 response in LADA versus T1D with PI could reflect a decreased proinflammatory status in LADA, who have a slower rate of β-cell deterioration. Future studies need to be performed to verify these findings.

P 16

Bone turnover markers in serum correlate with indices of glycaemic regulation in obesity

B. K. Itariu[1,2], R. Marculescu[3], P. Pietschman[4], G. Prager[5], T. M. Stulnig[1,2]

1) Department of Internal Medicine III, Clinical Division of Endocrinology and Metabolism, Medical University of Vienna, Vienna, Austria

2) Christian Doppler-Laboratory for Cardio-Metabolic Immunotherapy, Medical University of Vienna, Vienna, Austria

3) Department of Medical and Chemical Laboratory Diagnostics, Medical University of Vienna, Vienna, Austria

4) Department of Pathophysiology and Allergy Research, Center of Pathophysiology, Infectiology, and Immunology, Medical University of Vienna, Vienna, Austria

5) Department of Surgery, all Medical University of Vienna, Vienna, Austria

Alterations in glucose metabolism as detected in obesity are believed to influence bone turnover, although data are so far inconclusive. Moreover, the association between fat intake and bone metabolism is unclear. Here we aimed to investigate (i) the association between indices of insulin resistance (IR) and beta-cell function in a cohort of obese non-diabetic subjects and the serum concentration of established bone turnover markers (BTM), and (ii) the impact of n-3 polyunsaturated fatty acids (n-3 PUFA) supplementation on BTM.
We randomly treated 55 severely obese ($BMI > 40\ kg/m^2$), non-diabetic patients with either 4 g/d n-3 PUFA (Omacor®) or an equivalent amount of butterfat as a control for eight weeks. Serum concentration of bone alkaline phosphatase (BAP), procollagen type 1 N-terminal propeptide (P1NP), osteocalcin (OC), osteopontin (OPN), cross-linked C-telopeptide (CTX) and indices of IR and beta-cell function assessed by a 2 h oral glucose tolerance test (OGTT) were at baseline and at end of treatment. Data were analyzed by ANCOVA and Spearman's rank correlation.
Serum concentrations of BTM at baseline were in age and sex specific normal ranges. We detected a positive correlation between P1NP, BAP, CTX and OPN with fasting insulin concentration, HOMA-IR and HOMA-beta (all $P < 0.05$). At baseline, HbA_{1c} negatively correlated with OC serum concentration ($rho = -0.29$, $P = 0.03$). N-3 PUFA treatment had no significant impact on the serum concentration of the analyzed BTM at the end of the treatment.
Markers of insulin resistance and/or beta-cell function correlates positively with BTM concentration, which points to a crosstalk between bone metabolism and glucose homeostasis. Bone turnover seems unaffected following an eight week treatment with n-3 PUFA.

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P17

Osteopontin is overexpressed in NAFLD-induced hepatocellular carcinoma and might modulate liver inflammation and macrophage activation

A. D. Nardo[1], N. G. Grün[1], M. Zeyda[1], T. M. Stulnig[1]

1) Christian Doppler Laboratory for Cardio-Metabolic Immunotherapy and Clinical Division of Endocrinology and Metabolism, Department of Medicine III, Medical University of Vienna, Vienna, Austria

Background: Hepatocellular carcinoma (HCC) is the cause of approximately one million deaths yearly. In addition to chronic hepatitis B and C infections, nutrition-related diseases significantly contribute to the increasing prevalence of HCC. In obesity, osteopontin (OPN, gene Spp1) is upregulated in adipose tissue and liver and induces inflammatory and metabolic processes, which lead to insulin resistance, type 2 diabetes, fatty liver and NASH.
Methods: Using a recently established mouse model, which faithfully reproduces human NAFLD-induced HCC development by treating newborn mice with streptozotocin (STZ) and feeding them a high fat diet (HFD) (STAM mice), we investigated metabolic and immunological parameters throughout the entire disease evolution.
Results: Compared to HFD-fed-only (HFD-o) mice, STAM mice showed comparable increased hepatic expression levels of metabolic genes. The expression of pro-inflammatory markers was, however, significantly higher in the STAM animals, indicating the induction of inflammation to further develop fibrosis and HCC. Between 15 and 19 weeks of age, STAM mice, but not HFD-o and STZ-injected-only (STZ-o) mice developed liver tumors. In contrast to HFD, STZ alone recruited comparable levels of liver macrophages (LM) as observed in STAM mice, but the expression of M1-activation marker Cd11c and notably of Spp1 was significantly lower. Furthermore, Spp1 and other main immunological cytokines look like to be transiently modulated between the 15th and 19th week in order to elicit first a M2-like (implicated in tumor expansion and metastasis) and later a M1-like LM polarization.
Conclusion: Our preliminary data confirm the necessity of inflammation for the establishment of HCC and point for the first time to a potential role of Opn in NAFLD-induced liver cancer.

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Diabetes mellitus and hypothyreosis as potential drivers of colorectal cancer progression and mortality: view of the pathologist

M. Powell[1,2], P. Srna[2], P. Dundr[3], Z. Špůrková[4], P. Heneberg[1]

1) 3rd Faculty of Medicine, Charles University, Prague, Czech Republic

2) Department of Pathology, Hospital Jablonec nad Nisou, Jablonec nad Nisou, Czech Republic

3) Department of Pathology, First Faculty of Medicine, Charles University, Prague, Czech Republic

4) Department of Pathology, Na Bulovce Hospital, Prague, Czech Republic

Introduction: Colorectal carcinoma (CRC) is a highly prevalent malignant disease affecting both genders worldwide, with one of highest incidences known from the Czech Republic. It is associated with significant mortality and morbidity despite the implementation of modern treatment and preventive programs. In most patients, some comorbidities exist at time of the diagnosis. The aims of this study were to find out which endocrinology comorbidities might be associated with colorectal carcinoma and to evaluate to what extent it could mean risk factors for the disease progression.
Methods: We evaluated 246 cases (age 47–84) diagnosed at the Departments of Pathology of four Czech hospitals in 2002–2015. We correlated clinical and histopathological data, including grade and stage, with the occurrence of metabolic and endocrinology abnormalities, mainly with diabetes mellitus and with abnormal thyroid glands.
Results: Within the study cohort, the most frequent endocrinology comorbidities were diabetes mellitus (41 cases) and hypothyreosis (17 cases). 37 men and 8 women passed away, mostly from generalized CRC. However, histopathological analyses suggested that the mortality was not necessarily linked to the worst differentiation of the tumor. Clinically, there was a decreased incidence of diabetes in men, who survived 4–9 years since the resection, while the prolonged survival was associated with an increase in the incidence of hypothyreosis, the incidence of which increased from 7.2 % during the first year after resection to >20 % at ≥10 years after the resection. The same trends can be observed in women, but as the cohort of the women was smaller, we had sufficient data for only post-resection years 1–8.
Conclusions: Diabetes mellitus and hypothyreosis are differentially associated with the survival of CRC patients.

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Association of charcot osteoarthropathy complications with treatment modalities and early diagnosis

M. Flekac[1], P. Trachta[1], M. Prazny[1]

1) 3rd Department of Internal Medicine, 1st Faculty of Medicine, Charles University, Prague, Czech Republic

Introduction: The aim of this study was to document the importance of early-onset therapy of the Charcot neuroarthropathy (CN) in relation to the development of CN complications. The early stage of the Sella-Barrette classification (stage 0) CN involves the presence of clinical symptoms (swelling, elevated skin temperature) often following a provoking moment in a risk patient with neuropathy with no findings presented on X rays.
Methods: A retrospective data analysis from 88 patients investigated and subsequently treated in the outpatient clinic of the diabetes centre (3rd Department of Internal Medicine in Prague) was performed. Patients were referred from the outside of the diabetes centre. Two cohorts of patients were compared. The first group (A) were those in whom the early active phase (stage 0) did not

progress to the stage of deformity, the second group (B) patients who progressed this early active phase of the disease into the destructive phase. The presence of complications such as CN associated ulceration, diabetic foot infection, the presence of osteomyelitis, need for surgical therapy and the risk of foot amputation have been evaluated. In both groups, an analysis of the CN complications described above was performed in relation to the chosen off-loading method.

Results: Determination of the diagnosis of CN at stage 0 was delayed in group A by 3.9 ± 0.3 weeks compared to 8.7 ± 2.9 weeks in group B ($p < 0.05$). During follow-up (138 ± 22 weeks), at least one complication (mostly uninfected ulceration) was documented in 64 % of cases. Patients in group B developed more complications than in group A (65.3 % vs. 12.3 %, $p < 0.05$), in group B reactivation was more frequently observed (25.0 % vs. 3.5 %, $p < 0.001$), and switching to inactive phase of disease (duration of the off-loading treatment) lasted longer for group B (34.7 ± 8.4 vs. 12.7 ± 2.4, $p < 0.001$). The risk of the contralateral limb affection was not influenced by the early diagnosis. Interestingly, the risk of developing CN complications in relation to the chosen method of off-loading did not differ between groups.

Conclusion: This study shows that a key factor influencing CN treatment outcomes in preventing complications is not the therapeutic modality, but early diagnosis of CN based on the inclusion of this disease in differential diagnosis process in the risk population.

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The daily basal insulin requirement in insulin pump therapy and association with metabolic control, age and BMI in adult type 1 diabetes mellitus treated with personal insulin pumps

B. Matejko[1,2], A. Kukułka[3], T. Klupa[1,2]

1) Department of Metabolic Diseases, Jagiellonian University Medical College, Krakow, Poland

2) University Hospital, Krakow, Poland

3) Faculty of Electrical Engineering, Automatics, Computer Science and Biomedical Engineering, AGH University of Science and Technology, Krakow, Poland

Background: Basal rate (BR) profiles in continuous subcutaneous insulin infusion (CSII) therapy mimic physiological insulin requirement during the day. There is an agreement that BR usually comprises 30–50 % of the total daily insulin dose. However, whether profile settings are constant or differ depending on metabolic control (below and above 7 % HbA_{1c}) and age (below and above 25 yrs) in adult type 1 diabetic patients treated with CSII has not been assessed so far. This study analyzed the associations between variability of BR profiles/doses and glucose control, BMI and age in adult type 1 diabetes mellitus.

Materials and methods: Data of 260 T1DM adult patients (159 women and 101 men) treated with CSII who met the inclusion and exclusion criteria and who signed an informed consent at the Department of Metabolic Diseases, University Hospital, Krakow, Poland, were analyzed. The mean age of the subjects was 26.6 ± 8.2 years, BMI 23.1 ± 3.0 kg/m^2 and duration of diabetes 13.3 ± 6.4 years. The mean HbA_{1c} level in the entire study group was 7.4 % (57 mmol/mol). All data as recorded during outpatient visits were retrospectively collected from patients' charts. Analyses were performed using Statistica software.

Results: Mean percentage of total basal insulin was 42.1. Circadian basal insulin requirement differed significantly between the two age and metabolic control groups. For each hour interval analyzed differs were statistically significant ($p < 0.001$). BMI was independent predictor of total daily basal insulin dose.

Conclusion: Age is one of the primary factors that influence circadian distribution of basal insulin also in adult T1DM CSII-treated patients. Low dose basal insulin infusion has a positive effect on metabolic control and BMI.

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Impact of incretins in people with type 2 diabetes on insulin pumps

R. Chlup[1,2,3], J. Zapletalova[4], T. S. Cheng[1], Z. Ramik[1], M. Slezakova[1], H. Zalesakova[3]

1) Department of Physiology, Faculty of Medicine, Palacký University, Olomouc, Czech Republic

2) 2nd Department of Medicine, University Hospital, Olomouc, Czech Republic

3) Department of Diabetes, Moravský Beroun, Institute Paseka, Czech Republic

4) Department of Medical Biophysics, Faculty of Medicine, Palacký University, Olomouc, Czech Republic

Introduction: Metabolic control improvements resulting from continuous subcutaneous insulin infusion (CSII) in insulin + metformin (M) treated people with type 2 diabetes (PWD2) are often not sufficient to achieve optimal state. The aim of this prospective pilot study was to assess the influence of incretins (liraglutide 1.2 mg/d or exenatide QW 2 mg) added to M (3 g/d) + CSII (insulin aspart) therapy on insulin requirements (INS/d), HbA_{1c}, mean plasma glucose of a daily 10-point glycaemic profile (MPG) and body mass (BM).

Methods: Fourteen PWD2 (8 men) on CSII + M, without serious complications, age 52.7 (34.3–68.8) y, diabetes duration 16.5 (5.0–20.3) y, BMI 36.6 (31.6–57.6) kg/m^2, were monitored at 4 visits: 1) before CSII, 2) on CSII + M, 3) on CSII + M before incretin start, 4) on CSII + M + incretin after 3.1 (2.5–7.1) months. Medians (minimum–maximum), Wilcoxon Signed-Rank test and Bonferroni cor-

Visit	1 before CSII	2 CSII + M	3 CSII + M	4 CSII + M + incretin	P 2 vs. 1	P 4 vs. 1	P 4 vs. 3
Insulin [U/d]	85 38–122	60 37–77	77 61–112	64 47–98	0.022	NS	NS
HbA_{1c}	80 65–91	78 52–118	79 66–117	63 51–109	NS	NS	0.008
MPG [mmol/l]	11.4 8.8–14.5	10.3 8–12.7	9.4 6.7–12.7	7.7 5.5–12.2	NS	0.008	0.004
Body mass [kg]	110.8 89–147.5	108.7 87.9–145.4	111.6 91.8–144.4	109.6 90.6–143.5	NS	NS	0.008
Correlation was revealed between the change of INS and change of BM at visit 4 vs. visit 1 ($r = 0.582$, $P = 0.029$) and also at visit 3 vs. visit 1 ($r = 0.574$, $P = 0.032$)							

Tab. P21: Diabetes control at visit 1–4. N = 14; Median, Min–Max; $P < 0.05$.

rection were applied to assess evolution of respective parameters. Correlation r (Spearman) between the change of respective parameter at visit 4, 3, 2 vs. visit 1 and at visit 4 vs. visit 3 was sought for. $P < 0.05$ was considered significant.
Results: see Table P21
Conclusion: CSII appeared to enable reduction of INS with no increase of HbA_{1c}/MPG. Incretins added to CSII + M resulted in significant reduction of both the HbA_{1c} and BM. So, incretins may be considered as an effective addition to PWD2 treated with CSII + M.

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Hyperglycaemic coma as a primo-manifestation of diabetes mellitus – case report

J. Křížová[1], P. Trachta[1], E. Kotrlíková[1]

1) 3rd Medical Department General Faculty Hospital and 1st Medical Faculty, Charles University, Prague

61 years old patient was admitted to the hospital because of disturbance of consciousness. She was obese (BMI 51 kg/m²), she had arterial hypertension, hypothyreosis, no other diseases were reported. Her problems started one week after respiratory infection, she had polyuria and polydipsia. In the hospital, the glycaemia was measured as 115 mmol/l, so she was immediately referred to intensive care unit. At the time of the admission she was somnolent, severe dehydration was present, hypotension, tachycardia. In laboratory results, very high osmolarity was found (411 mosm/l), decreased renal functions (urea 22,5 mmol/l, creatinine 362 µmol/l) and elevated CRP (152 mg/l), mild metabolic acidosis pH 7,247, base deficit 2,1 mmol/l. She was treated by intensive rehydration, insulin was administered continuously (rate 2–4 U/h). Arterial blood pressure invasively measured remained very low, therefore norepinephrine treatment was started. Antibiotics were given. During the first 12 hours of the stay in our ICU, the glycaemia decreased to 49 mmol/l, positive fluid balance was present, the patients clinical state improved. In the next days, intensified insulin regimen was set together with the reduction diet. Her glycated haemoglobin was 186 mmol/mol.
Conclusion: Hyperglycaemic hyperosmolar coma is not a very frequent complication of type 2 diabetes mellitus. Compared to ketoacidotic coma, it has a higher mortality. The inducing factors are severe infections. It was surprising that even nowadays in the time of the widespread education the obese patient with regular physicians examination can scape early detection of diabetes mellitus and the first manifestation is hyperglycaemic hyperosmolar coma and hypovolemic shock.

P 23

Structured group programme improves metabolic control and psychological status in people with diabetes

J. Stefankova[1], A. Jirkovska[2], T. Hrachovinova[2], A. Adamikova[3], J. Hradec[6], J. Jirkovska[4], K. Cechova[2], V. Havlova[2], R. Rihankova[5]

1) Diabetologie-HK, Hradec Kralove, Czech Republic

2) Institute for Clinical and Experimental Medicine, Prague, Czech Republic

3) Hospital of T. Bata, Zlin, Czech Republic

4) Medical Department of the First Faculty of Medicine and Military University Hospital, Charles University, Prague, Czech Republic

5) University Hospital Pilsen, Pilsen, Czech Republic

6) IDE CR, Chrudim, Czech Republic

Background: Group education is one of the most effective forms of education in patients with diabetes mellitus. It has several benefits, including developing interpersonal relationships, reducing feelings of loneliness and reassuring people that other patients also have to deal with similar problems as them.
Aims: To assess the effect of group education onto metabolic control of diabetes and psychological status of patients with diabetes.
Material and methods: The project of structured group programme was implemented in 9 diabetes outpatient clinics in the Czech Republic during 2016. It had a form of four 2-hour sessions, 8 hours in total. 62 patients (age 63.3 ± 8.2 years, 53 % men, initial BMI 32.9 ± 6,7 kg/m²) with diabetes mellitus type 2 treated with insulin worked in groups of 6–12 people. Interactive form of education was preferred. Selected metabolic parameters and psychological status were evaluated before, as well as after the course and within an interval of 3 and 6 months. Psychological status was evaluated by the method SUPSO.
Results: The outcomes showed statistically significant improvement in following metabolic parameters: fasting plasma glucose decreased from 8.8 ± 2.8 mmol/l initially to 7.9 ± 2.5 mmol/l ($p = 0.008$) after 3 months and 7.7 ± 2.1 mmol/l ($p = 0.0002$) after 6 months, respectively. HbA_{1c} decreased from 70.0 ± 16.2 mmol/mol (8.6 ± 3.6 %) initially to 63.7 ± 12.6 mmol/mol (8.0 ± 3.3 %) ($p = 0.0001$) after 3 months and 63.1 ± 12.6 mmol/mol (7.9 ± 3.3 %) ($p = 0.0001$) after 6 months, respectively. Percentage of patients with relative good diabetes control ($HbA_{1c} < 60$ mmol/mol, 7.6 %) improved significantly from 26 % to 42 % ($p < 0.01$) after 3 months and 45 % ($p < 0.01$) after 6 months. Reduction of body weight on average was 0.8 kg ($p = 0.004$) after 3 months and 0.9 kg ($p = 0.005$) after 6 months. Systolic blood pressure decreased from 140 ± 18 mmHg to 135 ± 14 mmHg ($p = 0.047$) after 6 months. No significant changes were observed in diastolic blood pressure and serum lipids. During the programme there was a significant increase in mental activity of patients ($p < 0.05$), decrease in depression ($p < 0.05$) and reduction of feelings of loneliness ($p < 0.05$).
Conclusions: Structured group education is an effective form of education of patients with diabetes mellitus in outpatient clinics. The results showed a significant improvement of metabolic and psychologic status after the course and during 6-month follow-up period. The extension of this programme in the Czech Republic is a priority task of the Working Group for the Education of the Czech Diabetes Society. We thank all participants of this programme for active cooperation.