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

Report on the Virtual CEDA Congress 2021, 10–12 June, Budapest, Hungary

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The annual congress of the Central European Diabetes Association (CEDA)/Federation of International Danube Symposia on Diabetes Mellitus (FID) was organized between 10–12 June 2021 in Budapest, Hungary. Due to the extension of pandemic regulations, the congress was finally arranged as an entirely virtual meeting broadcasted from the Hotel Aquincum on the Danube bank. Nonetheless, around 30 participants could follow the lectures projected in three separate rooms simultaneously. The congress program covered many aspects of clinical diabetology from diabetes technology to complications, treatment and some interesting borderline areas of diabetology like oral health and diabetes and COVID-19-related issues.

Technologies in diabetes treatment

The congress started with an opening ceremony comprising welcome addresses of Béla Merkely, rector of Semmelweis University (Budapest, Hungary), Thomas Stulnig (Austria), president of CEDA, and Péter Kempler (Hungary), the president of the local organizing committee, president of the Hungarian Diabetes Association and president-elect of CEDA. The first session on "New technologies in diabetes", chaired by Michael Roden (Germany) and Nebojsa Lalic (Serbia), involved three up-to-date lectures on technological innovations and their clinical use in diabetes: "Precision diabetology" by Michael Roden, "Role of technology in diabetes treatment: glucose sensing in focus" by Nebojsa Lalic and "Do it yourself-hybrid closed loop systems: challenges, risks and opportunities" by Tomasz Klupa (Poland). It was followed by a state-of-the-art lecture by Ferenc Oberfrank (Hungary) titled "The dilemmas of medicine in the 21th century".

Special aspects in diabetes treatment

The next session was related to the clinical aspects of diabetes. Dániel Végh (Hungary) reported on the associations between oral health and diabetes, while Jan Škrha held his lecture on their forty-years' experience with insulinoma patients. Dénes Páll (Hungary) discussed the treatment of hypertension in diabetic patients, Maciej Malecki (Poland) held his talk on special aspects of treating diabetes in the elderly. The last session of the first day was an industry symposium of Sanofi-Aventis chaired by Maciej Malecki on modern insulin-based treatment including lectures on simplification of complex insulin regimen to fix-rate combinations (Martin Haluzík, Czech Republic), "Simplification from premix to BOT treatments – a clinical and patient's perspective" (Florian Kiefer, Austria) and "Simplification in patients with chronic kidney disease" (Cristian Serafinceanu, Romania).

Aspects of diabetic neuropathy

On the second day of the congress, the first session involved a variety of topics in respect of (pre)diabetic neuropathy. Nikolaos Papanas (Greece) summarised recent knowledge about prediabetic neuropathy, followed by the excellent presentation of Christian Herder (Germany) on "The role of inflammation in the pathogenesis of diabetic neuropathy". Tamás Várkonyi (Hungary), who co-chaired the session with Péter Kempler, held his lecture on the border between gastroenterology and diabetology titled "Gastrointestinal motility in diabetes – any connection between symptoms and findings?". Anna Körei (Hungary) reviewed recent data on the five standard cardiovascular reflex tests and diagnostic limitations of the isometric handgrip test as well as associations with hypertension among diabetic patients. The last presentation of this session titled "Pathogenetic oriented therapy of diabetic neuropathy" was given by Péter Kempler, providing insights in the mechanism of action of the agents used and emphasised the eligibility of combination treatment options.

Cardiovascular risk in diabetes

The title of the Novo Nordisk symposium chaired by Péter Kempler was "Mapping the journey across cardiometabolic risk and complications exposure" and included the following lectures: "Management of T2DM: the role of semaglutide on glycaemic control" (Nebojsa Lalic), "Cardiometabolic health in the time of pandemic: why is so important?" (Anastasios Koutsovasilis, Greece), "Diabetes and cardiometabolic risk: the mechanisms of ASCVD and the lessons of the CAPTURE study" (Dániel Aradi, Hungary), "Residual inflammatory cardiovascular risk in T2DM? Semaglutide efficacy beyond glucose regulation" (Nóra Hosszúfalusi, Hungary), "The central role of GLP-1 RAs in weight and appetite regulation" (Martin Haluzík) and "Translating scientific evidence into clinical practice" (Cristian Guja, Romania).

Diabetes and COVID-19

The afternoon of 11th June was continued with a "COVID-related issues" session focusing on morbidity and mortality of COVID-19 and its associations with diabetes and obesity as comorbidities. The session was chaired by Manfredi Rizzo (Italy). In the first presentation, Anca Pantea Stojan (Romania) reported on the Romanian COVID-19 multi-centre comorbidity study in patients with diabetes as a comorbidity. It was followed by the lecture of Manfredi Rizzo referring to the associations of "COVID-19, diabetes and obesity". The last speaker of the session was Helmut Schatz (Germany) who summarised current treatment options for COVID-19 highlighting agents that are traditionally used for the therapy of diabetes or endocrinological disorders. The second day of the congress ended with a clinical science session chaired by Nanette Schloot (Germany) and Zdravko Kamenov (Bulgaria) and gave a wide-ranging spectrum on special problems of clinical diabetology such as "Diabetes and menopause" (Zdravko Kamenov), "Polycystic ovary syndrome, insulin resistance and metformin" (Gyula Petrányi, Cyprus). Nanette Schloot presented new insights in type 1 diabetes related to its pathogenesis and prevention trials. Angelo Avogaro (Italy) gave the last presentation of the session focusing on "Therapeutic approaches to target both micro- and macrovascular disease in patients with type 2 diabetes".

New therapeutics for type 2 diabetes

The third day of the congress started with the last industry symposium sponsored by Boehringer Ingelheim. The symposium was arranged as a pros and cons debate between Thomas Stulnig and Péter Kempler (Hungary) on the issue whether SGLT 2 inhibitors should be used for early diabetes patients and it was followed by a hot debate involving both live online and local participants. After the break, the last session of the congress reflected on the cardiovascular risk in diabetes. The first presentation hold by István Wittmann (Hungary), president-elect of the Hungarian Diabetes Association, was "Risk of morbidity and mortality in patients with type 2 diabetes treated with SGLTi and/or DPP4i: a nationwide study", followed by the lecture of Gyula Jermendy (Hungary) on "Changes in trends of epidemiological data (incidence, prevalence, mortality) among people with pharmacologically treated T2DM between 2001 and 2016 in Hungary". Thomas Stulnig and Erifili Hatziagelaki (Greece) gave their lectures on cardiovascular risk reduction in diabetes focusing on the efficacy of new antidiabetic agents beyond glucose regulation.

E-posters on the CEDA website

On the website of the congress, an e-poster session was also accessible throughout the three days covering topics from basic science and diabetes complications (e.g. neuropathy, chronic kidney disease and erectile dysfunction) to depression in diabetes and the associations between insulin resistance and 25OH-vitamin D levels as well. CEDA abstract prizes were awarded to Anna Vágvölgyi (Hungary) and Haifa Maalmi (Germany) for their excellent presentation. The CEDA abstract prize includes a travel fellowship (500 €) for the CEDA congress 2022 in Vienna, Austria.

With more than 710 registered participants, live online discussions and a vibrant scientific programme, the congress was very successful.


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CEDA diabetes

Abstracts of the Virtual CEDA Congress 2021, 10–12 June, Budapest, Hungary

1

Insulin resistance and 25 hydroxy vitamin D levels in women with thyroid diseases

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Insulin resistance has an increasing prevalence worldwide, thus pathogenic interconnections with other hormones are of interest. On one side, observational and randomised studies highlighted an improved insulin resistance (IR) after the vitamin D deficit is corrected. On the other side, a neutral relationship between them was observed. We designed a cross-sectional study that included all women presented in an endocrinology ambulatory clinic in Bucharest for routine examination. The study included 353 patients diagnosed with thyroid pathology, with a mean age of 58.5 ± 13.7 years, most of them overweight (mean body mass index of 27.36 ± 4.87 kg/m^2), and a mean level of 25 hydroxy vitamin D (25OHD) of 39.53 ± 15.73 ng/ml. The prevalence of IR was 30.31 %. In univariate analysis, homeostatic model assessement of insulin resistance variant 1 and 2 (HOMA-IR) and quantitative insulin sensitivity check index (QUICKI) levels were not different between women with vitamin D deficit versus those with normal values. Also, there was no significant association between 25OHD and the response variables considered by us – body mass index, age, low- and high-density lipoprotein cholesterol, triglycerides, magnesium, and thyroid function in the multivariate analysis. We observed a weak association between the high level of 25OHD and an increase in HbA_{1c} and insulin resistance, but with no clinical relevance. Other modifiable or non-modifiable factors override 25OHD influence on IR in adult overweight women with a normal serum level.

2

Factors influencing survival in diabetic patients with end-stage chronic kidney disease undergoing haemodialysis during COVID-19 pandemic: focus on malnutrition

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Introduction: Since January 2019, an RNA viral infection with a pathogen from the family Coronaviridae, called coronavirus 2019, has spread rapidly around the globe. Patients with chronic diseases suffered either by direct exposure to infection, or indirectly through difficult doctor-patient interaction. Epidemiological studies have shown that patients with diabetes and COVID-19 infection had twice the mortality rate and risk of disease severity. Mortality was greatly increased among haemodialysis patients.
Materials and methods: We conducted an observational, prospective cohort study lasting 6 months. The study included all patients with diabetes and chronic end-stage renal disease coming for weekly haemodialysis in the National Institute of Diabetes, Nutrition and Metabolic Diseases NC Paulescu.
Results: Our study included 21 patients, of whom 7 were female and 14 were male, with a median age of 56 ± 16 years. The mean duration of diabetes was 20 ± 16.5 years, and the mean period of haemodialysis was 3 ± 2 years. During the 6 months of follow-up, there were 2 deaths caused by SARS-CoV-2. No other deaths were reported. In the survival analysis, there were no differences between patients diagnosed with malnutrition by both bioimpedance, and hand grip test (HGT).
Discussion: Previous studies have shown that the diagnosis of chronic kidney disease (CKD) since hospitalisation for COVID-19, respectively the development of acute renal injury, are associated with increased mortality. Our study did not show a relationship between SARS-CoV-2 mortality and malnutrition, as other authors have suggested. The result is influenced by the short follow-up period, the small number of patients included, a single determination of biological values, a single bioimpedance assessment, and also the optimal dialysis parameters.
Conclusions: In our clinic there was a low mortality rate caused by SARS-CoV-2 infection. Protein malnutrition assessed by bioimpedance does not appear to influence the mortality rate.

3

Evaluation of the cardiovascular autonomic and peripheral sensory nervous systems' function in top athletes at conditioned and deconditioned states

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Objectives: The aim of our work was to identify the cardiovascular autonomic and peripheral sensory nervous systems' changings in top athletes to the conditioned and the deconditioned state.
Patients and methods: Autonomic function was characterized by the five standard cardiovascular reflex tests while peripheral sensory system was studied by neurometer assessing the current perception thresholds (CPT) at the median and peroneal nerves. 22 male soccer players, 12 female handball players, 13 female water polo players, and as

controls 21 healthy women and 20 men were involved.
Results: The Valsalva ratio in conditioned soccer players (mean ± SD, athletes vs. controls: 1.71 ± 0.32 vs. 2.15 ± 0.48; p = 0.0018) and in conditioned handball players (1.63 ± 0.26 vs. 1.87 ± 0.51; p = 0.0019) was lower than in controls. During the deconditioning period, the Valsalva ratio for soccer (1.7 ± 0.34 vs. 1.94 ± 0.43; p = 0.025) and water polo players (1.71 ± 0.54 vs. 2.66 ± 0.27; p = 0.007) was higher than their conditioned values. In the conditioned state, neurometer showed higher CPT at the index at 2000 Hz and at 5 Hz in water polo players and in football players at 250 Hz compared to controls. At the hallux at 2000 Hz football players had higher CPT compared to controls. During the deconditioning period, a decrease in the CPT on the index was found in football players at 5 Hz (73.2 ± 20.25 vs. 57.1 ± 29.06 mA; p = 0.023), and in water polo players at 2000 Hz (229.6 ± 44.43 vs. 169.38 ± 70.33 mA; p = 0.033) compared to their conditioned state.
Conclusions: The conditioned seasonal reduction in Valsalva ratio for handball and football players indicates sympathetic predominance. For football and water polo players, the higher Valsalva ratio during the deconditioning period indicates a decreased sympathetic tone. The decreased sensory threshold during the deconditioning period in football and water polo players may reflect an increased peripheral sensitivity.
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4

Are there ECG parameters representing cardiac repolarisation influenced by the presence cardiovascular autonomic neuropathy in type 1 diabetes during exercise?

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Introduction: Alterations of repolarisation markers in resting ECG (QT, QTc, T_{peak}-to-T_{end}; T_pT_e) correlate significantly with ventricular arrhythmias. Among diabetic patients autonomic neuropathy is also a risk factor of malignant arrhythmias. In this case report we compared changes of ECG repolarisation markers during ergometry among a healthy and an otherwise healthy type 1 diabetic (DM1) patient, as well as a type 1 diabetic patient with autonomic neuropathy (AN).
Methods: Age of the participants was similar (33–43 years) and so the diabetes duration among diabetic individuals (18 and 20 years). Diabetics underwent standard neuropathy tests not earlier than six month prior to ergometry. The indication of the ergometry was undefined chest pain, the study was completed by using MDE Heidelberg ergometry system with modified Bruce protocol. During the test we measured changes in heart rate (HR) QRS, QT, QTc and T_pT_e time.
Results: Compared to the controll and otherwise healthy type 1 diabetic individual, patient with autonomic neuropathy produced a moderate increase in heart rate (ΔHR: controll = 54/min; DM1 = 71/min, AN = 36/min). Also, QT and T_pT_e times shortened moderately (ΔQT: controll = –63 msec; DM1 = –99 msec; AN = –9 msec; ΔT_pT_e: controll = –44 msec, DM1 = –42 msec, AN = –7 msec), but QTc time lenghtened (ΔQTc: controll = –39 msec; DM1 = –56 msec; AN = 45 msec). QRS duration did not change during any phase of the ergometry.
Conclusion: Our ergometry system may be helpful for evaluating cardiac complications related to autonomic neuropathy. Further involvement of patients is necessary to investigate whether the severity of autonomic neuropathy could correlate with the ECG markers of repolarisation.

5

The effect of autonomic neuropathy on the frequency of hypoglycaemia in type 1 and insulin-treated type 2 diabetic patients

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Background and aims: Autonomic neuropathy (AN) may play an important role in the pathogenesis of hypoglycaemia, but the relationship between autonomic dysfunction and low glucose levels in the clinical practice is poorly documented. The aim of our study was to evaluate the incidence and severity of AN and to assess the risk and awareness of hypoglycaemia in our patients with long-standing type 1 and insulin-treated type 2 diabetes (DM) with unstable glucose metabolism.
Materials and methods: 52 diabetic patients (40 type 1 and 12 type 2 insulin-treated DM patients, age: 46.4 ± 2.3 years, disease duration: 18.5 ± 1.5 years; HbA_{1c}: 8.3 ± 0.2 %; mean ± SE). 10 healthy subjects were included as controls. The five standard cardiovascular reflex tests were performed to determine AN. Tissue glucose values were monitored by subcutaneous continuous glucose monitoring (CGM) for 6 days.
Results: Significant AN was demonstrated in the patient group (AN score: 2.5 ± 0.2 vs. 0.9 ± 0.2; p < 0.05, heart rate change during deep breathing: 18.2 ± 1.3 vs. 32.6 ± 3.8 beats/min; p < 0.01; DM vs. control). The mean frequency of hypoglycaemic episodes measured with CGM over a 6-day period was 4.5 ± 0.5, while 2 ± 0.3 events were reported by the patients only. There was no correlation between AN and frequency of hypoglycaemia awareness. The incidence of hypoglycaemia was not correlated with DM duration, but DM duration was associated with more severe AN (DM duration–AN: r = 0.29; p < 0.05). Higher HbA_{1c} was found in patients with less hypoglycaemia (r = –0.30, p < 0.05) and with more severe AN (r = 0.51; p < 0.01).
Conclusion: Hypoglycaemic episodes are common in our long-standing type 1 diabetic and insulin-treated type 2 diabetic patients, but more than half of the episodes are silent. In this patient group, hypoglycaemia was less frequent in the presence of higher HbA_{1c}. As a key finding, autonomic neuropathy associated with longer disease duration and higher HbA_{1c} did not affect the frequency of hypoglycaemia awareness in this study.

6

Comparison of erectile dysfunction prevalence among novel diabetes subgroups

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Aims: The novel diabetes subgroups differ in risk for complications but the risk for erectile dysfunction (ED) has not been investigated yet. Since inflammation is associated with ED, we hypothesised that the prevalence of ED is highest in the severe insulin-resistant diabetes (SIRD) subgroup which is characterised by an increased inflammatory state.

Methods: A total of 351 male participants from the German Diabetes Study with recent-onset diabetes (< 1 year) were included. ED was assessed with the International Index Erectile Function questionnaire. Logistic regression was used to estimate associations between diabetes subgroups and the odds of ED adjusting for the variables used to define diabetes subgroups (age, BMI, HbA_{1c}, HOMA2-B, HOMA2-IR and GAD antibodies) and hsCRP.

Results: The overall prevalence of ED was 23 %. The presence of ED was highest within SIRD (52 %), lowest within the severe autoimmune diabetes (SAID) (7 %) and intermediate within the severe insulin-deficient diabetes (SIDD), mild obesity-related diabetes (MOD) and mild age-related diabetes (MARD) subgroups (31 %, 18 % and 29 %, respectively). Individuals in SIRD had 4.62 (95 % CI 1.21 – 17.65) times greater odds of having ED than individuals in MOD. The odds of having ED were lower in SAID compared with SIDD (OR 0.11; 95 % CI 0.01 – 0.71) or SIRD (OR 0.09; 95 % CI 0.01 – 0.63).

Conclusion: The high prevalence of ED among men in SIRD suggests the role of insulin resistance in ED pathogenesis.

7

Follow-up of cardiovascular autonomic neuropathy in insulin pump-treated type 1 diabetic patients

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Abstract: Insulin pump treatment is considered in case of unstable glycaemic control in type 1 diabetes (DM). The instability of glucose metabolism can facilitate the development of cardiovascular autonomic neuropathy (CAN), while CAN may improve with better glycaemic control.

Objectives: The aim of the study was to describe the characteristics of the cardiovascular autonomic function at initiation of insulin pump treatment and 2 months as well as 6 years later.

Methods: 13 patients (7 women and 6 men) with type 1 diabetes were involved. Their disease started in childhood or puberty (duration of DM at baseline: 16.5 ± 2.7 years, age at baseline: 27.8 ± 2 years). All patients received intensive insulin therapy right after their diagnosis until the insulin pump therapy. CAN was assessed at the first application of insulin pump and 2 months as well as 6 years later by cardiovascular reflex tests (CRT).

Results: We found a correlation between the duration of DM and the impairment of CRTs. Moderately severe AN was proven which decreased 2 months later (overall CAN score: 2.85 ± 0.3 vs. 1.23 ± 0.3, $p < 0.01$). The CAN score increased to the initial value by the 6th year of pump treatment (CAN score: 2.85 ± 0.47). The change of CRTs was not significant during the observational period. The mean HbA_{1c} decreased by 0.7 % after 2 months and became lower 6 years later.

Conclusion: In type 1 diabetic patients a moderately severe CAN was detected at the initiation of insulin pump treatment. The severity of the parasympathetic involvement correlated with the duration of DM. A short-term insulin pump treatment might achieve some beneficial effects on the autonomic function, while a 6-year period delays the progression of CAN in type 1 diabetic patients.

8

Cerebral and peripheral microcirculation in T2DM and obesity, influence of neuropathy and C-peptide level

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Microcirculation is damaged in diabetic patients and it has also been observed in obesity.

Our aim was to investigate the cerebral and peripheral microcirculation, peripheral neuropathy and to find any association between them and with C-peptide and VEGF levels in obesity and type 2 diabetes.

Participants (diabetic group: 16 female and 24 male, mean age: 50.9 ± 6.9 years, BMI: 32.9 ± 5.1 kg/m^2; obesity group: 18 female and 14 male, mean age: 51.4 ± 1.0 years, BMI: 38.8 ± 6.0 kg/m^2) were involved after a written consent was obtained.

Tc99m HMPAO dynamic SPECT/CT studies were performed to assess cerebral and peripheral microcirculation and neurometer was used to determine neuropathy.

Leg perfusion was significantly lower in the diabetic group ($p < 0.001$) and it correlated with BMI (rho = 0.36). According to the presence and severity of neuropathy a significant difference in lower limb microcirculation was detected independently of diabetes and obesity. Surprisingly the results in the severe neuropathy group were only non-significantly decreased compared to patients without neuropathy ($p = 0.18$). However, significant differences between mild neuropathy and no neuropathy groups, nevertheless between mild and severe neuropathy groups were revealed ($p = 0.036$ and $p = 0.042$. respectively).

Regarding C-peptide level a significant difference between mild and severe neuropathy groups was found ($p = 0.0066$).

The quantity of lower limb microcirculation correlated significantly and positively with C-peptide ($p < 0.05$, rho: 0.29), but not with VEGF level. There was also a positive correlation between C-peptide level and cerebral microcirculation ($p < 0.05$, rho: 0.27).

C-peptide highly contributes to the changes of lower limb microcirculation in patients with neuropathy.

9

Farming, compared to walking and sports, is more efficient on metabolic parameters and level of depression in Transilvanian type 2 diabetes patients

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Background and aims: The beneficial effect of physical activity (PA) in type 2 diabetes (T2DM) is well established, however the impact of different types of PA on metabolism and mood was less investigated. Our goal was to investigate the influence of different PA categories in T2DM patients on metabolic parameters and depression in a mostly rural Transilvanian region.

Materials and methods: The cross-sectional, observational study was conducted in Mures County, a representative Transilvanian region. We recorded anthropometric, diabetes related data, and metabolic parameters. Habits of PA were recorded by using a questionnaire, referring to duration, intensity, type, frequency of activity. Mean physical activity index (PAI)/week was calculated. The different types of PA were walking (1), farming/working on field type activity (2), profession related activity (3) and sports or leisure physical exercise (4). Depression symptoms were evaluated using the Beck Inventory – short version.

Results: Study population included 412 T2DM patients; mean age was 63.17 ± 10.05 years. The distribution of activity type chosen by patients was walking: 55.1 %, farming: 31.3 %, profession related activities: 10.3 %, sports only in 3.3 % of cases. PAI/week was the highest in the 2. and 3. group ($p < 0.001$, CI 0.45–0.25). In those mainly gardening compared to those mainly walking BMI (27.68 ± 4.7 vs. 29.78 ± 5.6 kg/m^2, $p < 0.01$), waist circumference (98.0 ± 17.1 vs. 105.0 ± 17.2 cm, $p < 0.00$), HDL cholesterol (48.59 ± 12.2 vs. 42.4 ± 9.9 mg/dl, $p < 0.01$), triglycerides (158.6 ± 107.6 vs. 191.2 ± 98.0 mg/dl, $p < 0.00$), depression score (10.18 ± 6.6 vs. 18.9 ± 11.4, $p < 0.00$) and depression worsening score (9.6 ± 5.7 vs. 13.2 ± 8.9, $p < 0.00$) were significantly better. HbA_{1c} did not differ between the two groups.

Conclusion: In the studied region BMI, WC, HDL cholesterol, and level of depression were far better with farming or professional activities than with walking.

10

10 years follow-up of cardiac and diabetes-specific complications in young type 1 diabetic patients

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Introduction: The observation of the cardiac and microvascular conditions in type 1 diabetic patients supplies facts about the nature of the parallel progression.

Objectives: The aim of our study was to characterise and follow up the neuronal, renal, ophthalmic and cardiac complications during 10 years.

Materials and methods: 21 young type 1 diabetic patients with long-term disease (age: 28.9 ± 1.5 years, duration of DM: 13.5 ± 1.7 years, HbA_{1c}: 8.2 ± 0.4 %, BMI: 23.3 ± 0.7 kg/m^2; mean ± SE) were involved. Autonomic neuropathy (AN) was assessed by cardiovascular reflex tests (CRTs). The peripheral sensory function was detected with neurometer. Cardiac morphology and function were measured with conventional and Doppler echocardiography. The urinary protein content, the kidney function and the state of the retina were also determined. The tests were started in 2008 and repeated 10 years later.

Results: Left ventricular (LV) muscle mass increased prominently during 10 years (141 ± 10 vs. 172 ± 11 g, $p < 0.05$, baseline vs. follow-up, increased in 19 from 21 patients). From the CRTs the heart rate response to breathing worsened frequently (25.5 ± 2.4 vs. 18.5 ± 1.6 beats/min, $p < 0.01$, decreased in 17 from 21 patients). The current perception threshold (CPT) of the large myelinated fibres at the peroneal nerve became higher in 14 from 21 patients (CPT: 3.18 ± 0.4 vs. 4.35 ± 0.4 mA, $p < 0.05$). All of the 17 patients with worsened heart rate response to breathing had an increase in the LV muscle mass as well. The urinary protein excretion and severity of retinopathy progressed less frequently (increase in protein excretion: in 11 from 21 patients, worsening retinopathy in 4 from 21 patients).

Conclusions: Worsening of parasympathetic dysfunction and the increase in the left ventricular muscle mass were frequently found and these complications had a parallel progression in young type 1 diabetic patients. The progressive impairment of the large myelinated fibre function at the lower extremity was also a characteristic finding, while the kidney and retina were a less frequently altered during 10 years.

11

Interplay between CXCL chemokine family and matrix metalloproteinase-2 (MMP-2) in streptozotocin induced diabetic rat heart

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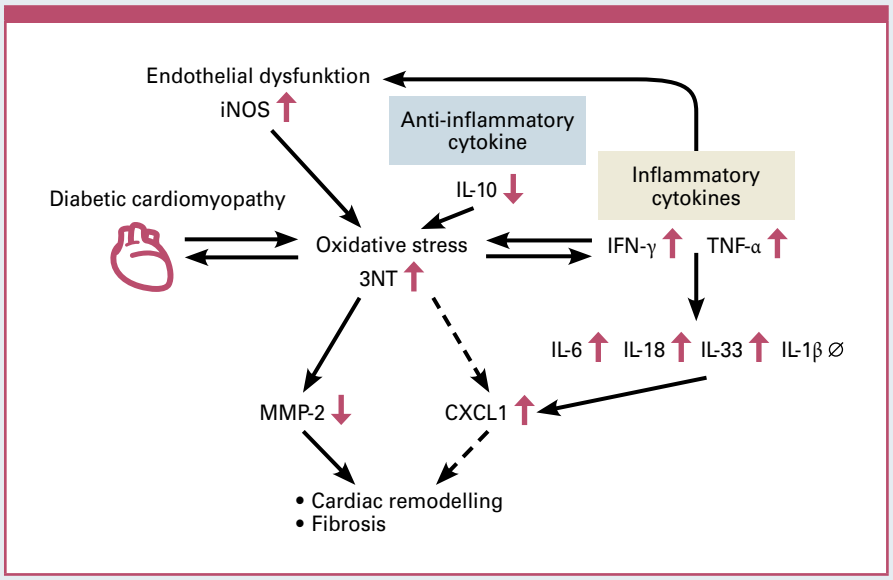
Cardiovascular disease (CVD) is the most prevalent cause of morbidity and



mortality in diabetic patients, but the mechanisms are still not fully understood. The aim of the present study was to determine the role of chemokines, mainly C-X-C motif ligand (CXCL)/matrix metalloproteinase-2/nitrosative stress axis in the development of diabetic cardiomyopathy.

Male Harlan rats were randomly assigned to control and diabetic group. Rats were injected with streptozotocin (STZ, 80 mg/kg, i.p.) to induce type 1 diabetes or an equivalent volume of saline (control) and fed standard rat chow. Following 4 weeks after STZ injection hearts were isolated and perfused for 10 min at Langendorff system. Different inflammatory cytokine levels (IFN, TNF, IL-1, 6, 10, 18, 33) and CXCL-1 as a chemokine were quantified using the Legendplex multiplex bead-based flow cytometric assay. Cardiac 3-nitrotyrosine (3-NT), nitrix oxide isoforms (NOS) by ELISA and MMP-2 activity using zymography technique were also assessed.

Our results show that all inflammatory cytokines except IL1-beta increased while anti-inflammatory IL-10 decreased significantly ($p < 0.05$) in diabetic rat heart. CXCL-1 was 1.4 fold increased during diabetes. From the three distinct NO synthase isoforms only inducible isoform (iNOS) level was increased (77.4 ± 21.6 vs. 47.88 ± 17.1; $p < 0.05$) compared to control group. According to increased iNOS level, impaired NO production, the oxidative stress marker 3-nitrotyrosine was markedly increased in the diabetic heart. This was accompanied by decreased cardiac MMP-2 activity (1038.7 ± 160.1 vs. 683.2 ± 79.5).

Endothel dysfunction, oxidative stress may able to activate CXCL-1 and recruit inflammatory cells from circulation to the myocardium. However, activated inflammatory cells promote the development of cardiomyopathy by inducing the expression and release of inflammatory mediators such as IL-6, 18 and 33. It has been reported that under pathological conditions, the interleukines can damage vascular endothelial cell causing oxidative stress and dysregulation in extracellular matrix degradation. This condition is featured by reduced MMP-2 activity which leads to cardiac fibrosis associated with diabetes.

12

Is there any indication for plasmapheresis and opioid therapy in the treatment of diabetic neuropathy? – a case report

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We report a 72-year-old patient with type 2 diabetes (T2DM), he was diagnosed with diabetic neuropathy 30 years ago. During the years, he underwent coronarography, lower limb PTA and stent implantations several times due to macrovascular complications. This time, the patient was admitted to hospital because of poor glycaemic control (HbA_{1c}: 11 %) and falls. To achieve better metabolic control in the obese patient (BMI: 39.2 kg/m^2), we titrated doses of SGLT-2 inhibitor and GLP-1 receptor agonist therapy. The patient has already been on combination therapy for severe painful diabetic neuropathy including both pathogenetically oriented (benfotiamine and alpha-lipoic acid) and symptomatic (duloxetine and pregabalin) treatment options. Despite, he still suffered from typical neuropathic pain. On neuropathy examination, severe sensory impairment was confirmed on all extremities by diminished current perception thresholds (CPT) measured by neurometer (Neurotron Inc.), by the Vibratip, Tiptherm, the monofilament, the tuning fork and thermal perception thresholds detected by Q-Sense (Medoc Ltd.). Moderate cardiovascular autonomic neuropathy was also proven. Based on the neuropathy studies, the frequent falls complained by our patient might have resulted from his severe distal sensorimotor neuropathy and orthostatic hypotension (32 mmHg). As the so far administered fourfold combination therapy did not provide sufficient pain relief, the patient underwent plasmapheresis and opioid therapy was initiated with approving result.

Conclusions: Diabetic neuropathy may be characterised by extremely severe hypaesthesia and neuropathic pain simultaneously. Good glycaemic control is a cornerstone in the treatment of diabetic neuropathy. When treating painful diabetic neuropathy, both pathogenetically oriented and symptomatic therapy should be implemented. Besides, plasmapheresis and opioid supplementation should be considered for some patients.