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ESTONIAN SOCIETY OF CARDIOLOGY

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EESTI ENDOKRINOLOOGIA SELTS
ESTONIAN ENDOCRINE SOCIETY

7th Baltic Atherosclerosis Society Congress

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7th Baltic Atherosclerosis Congress
April 6-7, 2018 Tallinn, Estonia

Program of the 7th Baltic Atherosclerosis Congress

FRIDAY, APRIL 6	
8:00 - 8:45	Registration Open / Arrival Tea and Coffee
8:45 - 9:15	**OPENING OF THE CONGRESS** **Chair:** Alberico Catapano (IT), Gustavs Latkovskis (LV), Bela Merkely (HU), Margus Viigimaa (EE) Welcome speech by Mr. Jüri Ratas, Prime Minister of Republic of Estonia
9:15 - 10:45	**PLENARY SESSION I** **Lipid management in prevention of cardiovascular disease** **Baltic Atherosclerosis Society – European Atherosclerosis Society joint session** **Chair:** Maciej Banach (PL), Alberico Catapano (IT), Margus Viigimaa (EE)
9:15 - 9:45	Lipid-lowering therapy: present and future developments. Keynote lecture. *Alberico Catapano (IT)*
9:45 - 10:05	Novel pathways of atherogenesis and challenging therapeutic targets. *Rimvydas Slapikas (LT)*
10:05 - 10:25	Statin intolerance definition, diagnosis and management in 2018. *Maciej Banach (PL)*
10:25 - 10:45	Current development of lipid management in Baltic countries. *Margus Viigimaa (EE)*
10:45 - 11:15	Coffee break, Press conference
11:15 - 12:30	**PLENARY SESSION II** **Cardiovascular risk in diabetes** **Chair:** Peter Nilsson (SE), Lars Ryden (SE), Vallo Volke (EE)
11:15 - 11:45	Cardiovascular outcome trials in type 2 diabetes. Lessons learned from the perspective of a cardiologist. Keynote lecture. *Lars Ryden (SE)*
11:45 - 12:05	Antidiabetic drugs and cardiovascular risk – endocrinologist's point of view. *Vallo Volke (EE)*
12:05 - 12:30	Cardiovascular risk management in diabetes and hypertension. *Peter Nilsson (SE)*
12:30 - 13:30	Lunch

13:30 - 15:10	**SATELLITE SYMPOSIA**
13:30 - 14:15	**AMGEN** **Integrating anti-PCSK9 therapy into secondary prevention of CVD** **Chair:** Margus Viigimaa (EE), Gustavs Latkovskis (LV) ▪ FOURIER: PCSK9 inhibition decreases CV events in high-risk patients. *Terje Pedersen (NO)* ▪ Effectiveness and safety of very low LDL-c values with evolocumab: lowest is best. *Alberico Catapano (IT)* ▪ Which patients could benefit from treatment in clinical practice? *Alberico Catapano (IT)*
14:20 - 15.05	**Berlin-Chemie Menarini** **Chair:** Margus Viigimaa (EE) ▪ The newest guidelines on hypertension: focus on tight blood pressure control. *Margus Viigimaa (EE)* ▪ Uncontrolled hypertension – time to act. Lessons learned from case studies. *Karlis Trušinskis (LV)* ▪ Discussion

15:10 - 16:40	**PLENARY SESSION III - Atherosclerosis and heart** **Baltic Atherosclerosis Society – European Society of Cardiology joint session** **Chair:** Bela Merkely (HU), Aleksandras Laucevicius (LT), Terje Pedersen (NO)
15:10 - 15:30	Lipid-lowering therapy in the future: Will statins still be the basis? *Terje Pedersen (NO)*
15:30 - 15:50	Prevention of sudden cardiac death - the role of implantable devices. *Bela Merkely (HU)*
15:50 - 16:10	Is metabolic syndrome high or moderate cardiovascular (cardiometabolic) risk entity: results of Lithuanian High Cardiovascular Risk (LitHiR) programme. *Aleksandras Laucevicius (LT)*
16:10 - 16:30	How to improve BP Control? Novel Initiatives. *Serap Erdine (TR)*
16:30 - 16:40	Discussion
16:40 - 17:00	Coffee break

17:00 - 18:40	**SATELLITE SYMPOSIA**
17:00 - 17:45	**Boehringer Ingelheim** **Anticoagulation Management In Special Situations- Innovative or Conservative Treatment?** ▪ Rewire your thinking on AF ablation. *Karlis Trusinskis (LV)* ▪ Improving care decisions after coronary revascularization. *Elena Baranova (RUS)*
17:50- 18.35	**AstraZeneca** **Treat to success or treat to failure. What does real life tell us about Type 2 DM?** *Karlis Trusinskis (LV), Kristine Ducena (LV)*

18:40 - 19:50	**PARALLEL SESSION I** **Familial hypercholesterolemia** **Chair:** Gustavs Latkovskis (LV), Michal Vrablik (CZ)
18:40 - 19:00	Three-year experience of the Latvian Registry of Familial Hypercholesterolemia: challenges and achievements. *Gustavs Latkovskis (LV)*
19:00 - 19:20	Familial hypercholesterolemia screening: International and national initiatives. *Žaneta Petrulioniene (LT)*
19:20 - 19:40	FH management: expectations and reality. *Michal Vrablik (CZ)*
19:40 - 19:50	Discussion: Familial Hypercholesterolemia registries in Europe and in Baltic countries

18:40 - 19:50	**PARALLEL SESSION II** **Coronary atherosclerosis: physiology and management** **Chair:** Sergei Nazarenko (EE), Karlis Trušinskis (LV)
18:40 - 19:05	Vascular restoration therapy: the role of intravascular imaging guided plaque modification prior drug eluting stent or bioresorbable scaffold implantation. *Andrejs Erglis (LV)*
19:05 - 19:30	Vascular Protection by Factor Xa Inhibition in Patients with Coronary and/or Peripheral Artery Disease. *Karlis Trusinskis (LV)*
19:30 - 19:50	FDG-PET imaging of atherosclerotic plaques. *Sergei Nazarenko (EE)*
20:00 - 22:00	Welcome reception

SATURDAY, APRIL 7	
9:00 - 10:00	**PLENARY SESSION IV** **Cardiovascular risk factors and management** **Chair:** Irina Chazova (RU), Iveta Mintale (LV)
9:00 - 9:20	Impact of chronic stress on atherosclerosis process. *Dovile Karciauskaite (LT)*
9:20 - 9:40	Arterial hypertension and atherosclerosis: data from Russian national registry. *Irina Chazova (RU)*
9:40 - 10:00	Lifestyle management in cardiovascular prevention. *Iveta Mintale (LV)*

10:00 - 11:20	**PLENARY SESSION V** **Goals in blood pressure, lipids and glucose. Are we treating well?** **Chair:** Serap Erdine (TR), Andrejs Erglis (LV), Rimvydas Slapikas (LT)
10:00 - 10:20	Goals in blood pressure. *Peter Nilsson (SE)*
10:20 - 10:40	Goals in lipids. *Gustavs Latkovskis (LV)*
10:40 - 11:00	Goals in glucose. *Mart Roosimaa (EE)*
11:00 - 11:20	Coffee break

11:20 - 11:50	**PLENARY SESSION VI** **History and future of the Baltic Society of Atherosclerosis. General Assembly** **Chair:** Zita Kucinskiene (LT), Gustavs Latkovskis (LV), Margus Viigimaa (EE)

11:50 - 12:50	**PLENARY SESSION VII** **Personalised diagnostics and treatment of atherosclerotic disease** **Chair:** Valdis Pirags (LV), Peeter Ross (EE)
11:50 - 12:10	From Biobanking to Precision Medicine and beyond: the Estonian Experience. *Andres Metspalu (EE)*
12:10 - 12:30	Using stratified medicine to individualize treatment. Experience from the Latvian Genome Data Base. *Valdis Pirags (LV)*
12:30 - 12:50	Importance of data quality in nation-wide e-health system for personalized medicine decision support applications. *Peeter Ross (EE)*

12:50 - 13:00	Closing remarks
13:00:00	Say Goodbye Coffee

1. ORAL ABSTRACTS

101. Lipid-lowering therapy: present and future developments

Alberico Catapano
Department of Pharmacological and Biomolecular Sciences, University of Milan and IRCCS Multimedica

Dyslipidaemias are a major risk factor for cardiovascular disease (CVD), in particular high levels of low density lipoprotein cholesterol (LDL-C) have been associated to a higher cardiovascular risk. Reducing LDL-C levels decreases the risk of coronary heart disease (CHD), and the greater the LDL-C reduction, the greater the cardiovascular risk decrease. Although statins represent the first line lipid-lowering therapy, many patients do not reach the recommended goals or exhibit adverse side effects leading to therapy discontinuation, or continue to experience cardiovascular events; even in the presence of well controlled LDL-C levels, due to Alteration in other lipid/lipoprotein classes, including triglycerides and high-density lipoprotein cholesterol.

These conditions require further therapeutic interventions to achieve the recommended lipid goals. Several drugs have been developed to address these needs. Recent studies have shown that the association of ezetimibe with rosuvastatin or atorvastatin results in a better hypolipemic effect; beside this, PCSK9 inhibitors significantly reduce LDL-C levels and cardiovascular events.

Additional novel approaches to the development of drugs that can be used either in monotherapy or in combination will also be discussed.

102. Novel pathways of atherosclerosis and challenging therapeutic targets

Rimvydas Slapikas
Lithuanian University of Health Sciences, Kaunas, Lithuania

Despite a significant focus of many researchers on atherosclerosis in humans, the mechanisms of this disease are still not fully understood and atherosclerotic vascular disease remains the most important cause of myocardial infarction, stroke, and heart failure. Numerous studies have shown that compendium of elevated serum low-density lipoprotein with other major risk factors – smoking, hypertension, diabetes, obesity and low physical activities is an ideal environment for the initiation and progression of atherosclerosis. However, it is important to define other risk factors, which could influence the process of atherogenesis. TNT (Treating to New Targets) and IDEAL (Incremental Decrease in Clinical Endpoints Through Aggressive Lipid Lowering) trials suggested that despite treatment with high-dose atorvastatin and relevant reductions in LDL-C levels, the risk of cardiovascular events remains high, suggesting the existence of "residual cholesterol risk" which might me further diminished with PCSK9 (proprotein convertase subtilisin/kexin type 9 inhibitors) therapy. Major cardiovascular events were significantly reduced in patients without overt hyperlipidemia but with elevated high-sensitivity C-reactive protein (hs-CRP) levels when treated with rosuvastatin in JUPITER trial. The results of the trial confirmed the relevance of "residual inflammatory risk" and the possibilities as well as the need of additional therapies targeting atherosclerosis. Basic studies demonstrated that inflammation plays an inevitable role in all the stages of

atherosclerosis though its pathogenesis is complicated and still remains enigmatic. Clinical trials provided evidence for the therapeutic values of COX-2 inhibitors, antibiotics, low-dose methotrexate and colchicine. Modulation of regulatory proteins of inflammation, including costimulatory pathways and cytokines, including interleukin-1, interleukin-6 and tumor necrosis factor-a (TNF-a) are explored as therapeutic strategies to prevent atherosclerosis. The results of CANTOS (The Canakinumab Anti-inflammatory Thrombosis Outcomes Study) trial showed that antiinflammatory therapy targeting the interleukin-1β innate immunity pathway with canakinumab at a dose of 150 mg every 3 months led to a significantly lower rate of recurrent cardiovascular events than placebo, independent of lipid-level lowering. From biological perspective the data of available clinical trials demonstrate the need for further investigation of inflammatory mediators of atherothrombosis.

103. Statin intolerance definition, diagnosis and management in 2018

Maciej Banach
Department of Hypertension, WAM University Hospital in Lodz, Medical University of Lodz; Polish Mother's Memorial Hospital Research Institute, Lodz; Cardiovascular Research Centre, University of Zielona Gora, Zielona Gora, Poland

Statins are the gold standard for managing dyslipidemia in patients with elevated cardiovascular (CV) risk. Discontinuation of statin therapy/therapy non-adherence is associated with significant increase in CV events. The most important reasons of statin non-adherence are statin-associated side effects (SASE) – most commonly – statin-associated muscle symptoms (SAMS) responsible for 95% or more of all SASE. In fact, the causality has been confirmed for three of them: myalgia/myopathy, temporary elevation of alanine aminotransferase (ALT) and diabetes mellitus (=new onset diabetes mellitus [NODM]). Throughout the world patients frequently discontinue statin therapy (even 50-60% after 2 years) without medical advice due to perceived side effects, and consequently increase their risk for CV events. Thus, an important issue in the management of patients with statin intolerance is the need to avoid statin discontinuation. Options include step-by-step reduction of the statin dose (dechallenge), switching to a different statin, or using intermittent dosages (alternate-day therapy). Another includes reduction of doses and adding of ezetimibe or fibrate (especially in case of high triglycerides), in severe cases even with application in monotherapy. New non-statin agents, as well as alternative therapy with nutraceuticals (such as: red yeast rice, phytosterols, bergamot, soy products or PUFAs) with or without a non-statin drug, may help to improve therapy adherence and reduce the risk for patients with true statin intolerance. Further studies in statin intolerant patients are necessary to confirm the effectiveness and safety of nutraceuticals as well as their effect on cardiovascular outcomes (CVOTs). In addition, these agents will have to be tested in long-term randomized controlled trials (RCTs) to more definitively assess.

104. Current development of lipid management in Baltic countries

Margus Viigimaa
North Estonia Medical Centre, Tallinn University of Technology, Estonia

The Baltic countries (Estonia, Latvia, and Lithuania) are profoundly affected by cardiovascular disease. Therefore, there is currently a vital need to implement preventative measures for combating well-known CVD risk factors, including high cholesterol. However, the usage of lipid-lowering drugs in Baltic countries is more than two times lower compared to Nordic countries. Vast majority of drugs are statins, fibrates and unfortunately also ezetimibe are rarely

SOODUSTUSEGA[2]
75-90%
DIAGNOOSIKOODID I10-I13, I15

SANORAL
AMLODIPIIN+OLMESARTAAN

olmesartaani + amlodipiini kombinatsioonravim
2 TOIME-AINET[1]

Kombinatsioonravim essentsiaalse kõrgvererõhktõve raviks![1]

- Üks Sanoral **40 mg / 5 mg** tablett sisaldab 40 mg olmesartaanmedoksomiili ja 5 mg amlodipiini.[1]
- Üks Sanoral **40 mg / 10 mg** tablett sisaldab 40 mg olmesartaanmedoksomiili ja 10 mg amlodipiini.[1]

Näidustus[1]:
Essentsiaalne hüpertensioon.
Kombineeritud ravim on näidustatud täiskasvanutel patsientidel, kellel olmesartaanmedoksomiili või amlodipiini monoteraapia ei taga piisavat vererõhu langust.
Pakend. 28 tabletti pakendis. **Retseptiravim.**

Annustamine[1]: Täiskasvanud: Sanorali soovitatav annus on 1 tablett ööpäevas. Enne fikseeritud kombinatsioonile üleminekut on soovitatav ravimi individuaalsete komponentide annuseid järk-järgult kohandada. Kliinilise näidustuse korral võib kaaluda ka kohest üleminekut monoteraapialt fikseeritud kombinatsioonile. Kasutamise hõlbustamiseks võib olmesartaanmedoksomiili ja amlodipiini monoteraapiana saavatele patsientidele määrata samade annustega Sanorali kombineeritud ravimit. Sanorali võib võtta koos toiduga või ilma.

Vastunäidustused[1]: Ülitundlikkus toimeainete, dihüdropüridiini derivaatide või abiainete suhtes. Raseduse teine ja kolmas trimester. Raske maksapuudulikkus ja sapipais. Sanorali samaaegne kasutamine aliskireeni sisaldavate ravimitega on vastunäidustatud suhkurtõve või neerukahjustusega (GFR < 60 ml/min/1,73 m^2) patsientidele. Ravimis sisalduva amlodipiini tõttu on Sanoral vastunäidustatud veel järgmistel juhtudel: raske hüpotensioon, šokk (sh kardiogeenne šokk), vasaku vatsakese väljavoolu takistus (nt kõrgema astme aordi stenoos), hemodünaamiliselt ebastabiilne südamepuudulikkus pärast ägedat müokardiinfarkti.

Reklaam on suunatud ravimite väljakirjutamise õigust omavatele isikutele, proviisoritele ja farmatseutidele.
Reklaam kinnitatud juulis 2017.
Kood EE_SAN-02-2017.

BERLIN-CHEMIE MENARINI

1. Sanoral (olmesartaan, amlodipiin) ravimi omaduste kokkuvõte.www.ravimiamet.ee (kinnitatud mais 2017).
2. Kokkuvõtlik tabel ravimisoodustustest. https://www.sm.ee/et/ravimite-hinnastamine-ja-huvitamine (vaadatud 18.05.2017)

Müügiloa hoidja: Menarini International Operations Luxembourg S.A.1, Avenue de la Gare L-1611 Luxembourg, Luksemburg

Täiendav teave müügiloa hoidja Eesti esindusest: OÜ Berlin-Chemie Menarini Eesti, Paldiski mnt. 29, Tallinn 10612

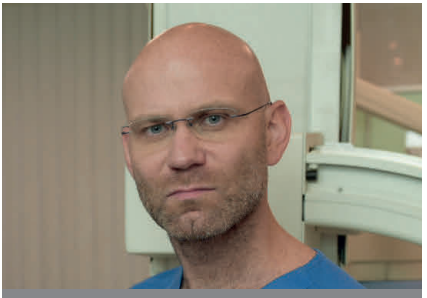
Boehringer Ingelheim Satellite Symposium

Anticoagulation management in special situations- Innovative or conservative treatment?

06.04.2018
Sokos Hotel Viru (Viru Väljak 4)
Grande hall

Boehringer Ingelheim

Prof. Elena Baranova
Professor of the Department of Internal Diseases with the course of Endocrinology, Cardiology and Functional Diagnostics, Head of the Research and Scientific Institute of Cardiovascular Diseases, Pavlov First Saint Petersburg State Medical University, Saint Petersburg



Ass. Prof. Karlis Trusinskis
Cardiologist Latvian Centre of Cardiology Pauls Stradins Clinical University Hospital, Assistant Professor Riga Stradins University, President, Latvian Society of Hypertension and Atherosclerosis Riga, Latvia

Topics:

- 17.00-17.20 **"Rewire your thinking on AF ablation"**. Ass. Prof. Karlis Trusinskis
- 17.20-17.40 **"Improving care decisions after coronary revascularization"** Prof. Elena Baranova
- 17.40-17.45 Closing and questions

ET/PRA/0318/00097

used. Combating dyslipidemia and other well-known CVD risk factors such as obesity and hypertension is vital to reduce the exceptionally high risk for CVD mortality seen in the Baltic countries.

We have performed the DYSIS study with the aim of aim to analyse the dyslipidemia treatment in a large dataset from the Baltic countries. Patients in primary care centers across the Baltic countries were enrolled into the cross-sectional, observational study. We enrolled 1797 patients ≥45 years old treated with statins for at least three months. Our findings indicate that many statin-treated patients in Estonia, Latvia and Lithuania did not meet target lipid levels and had a very high risk of CVD. Multivariate analyses indicated that a BMI ≥ 30 kg/m^2 (OR, 2.12; 95% CI, 1.45–3.08) and hypertension (OR, 2.43; 95% CI, 1.1 6–5.10) were strongly associated with dyslipidemia (involving all three lipids) during statin therapy while age ≥70 years (OR, 0.63; 95% CI, 0.42–0.94) and female gender (OR, 0.48; 95% CI, 0.33–0.68) conferred reduced risk. LDL-C was not at target level for 80.7%; low HDL-C levels were observed for 26.0%, and elevated TG levels were found in 35.0% of all patients.

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Viigimaa M, Erglis A, Latkovskis G, Mäeots E, Petrulionienė Z, Slapikas R, Gocentiene A, Bramlage P, Brudi P. Prevalence of dyslipidemia in statin-treated patients in the Baltic states (Estonia, Latvia, and Lithuania): Results of the Dyslipidemia International Study (DYSIS). Medicina 2014;50(1):44-53.

105. Cardiovascular outcome trials in type 2 diabetes - Lessons learned from the perspective of a cardiologist

Lars Rydén
Department of Medicine K2, Karolinska Institutet, Stockholm, Sweden

Cardiovascular disease is a major threat to people with diabetes. Attempts have since long been made to lower the cardiovascular risk by means of glucose lowering treatment. Initially it seemed that this possibility was an option but subsequent trials could not verify the original observations and concern was raised that some glucose lowering drugs may indeed cause cardiovascular harm. This caused medical product agencies in the US and Europe to require major outcome trials before accepting new glucose lowering drugs. The least requirement was non-inferiority compared to existing treatment modalities.

A large number of cardiovascular outcome trials (CVOT) have been performed or are ongoing including more that 100 000 patients with type 2 diabetes. Drug classes investigated are basal insulin, Di peptidyl peptidase-4 inhibitors (DPP-4 inhib), glucagon-like peptide-1 receptor agonists (GLP-1RA) and sodium-glucose co-transporter-2 inhibitors (SGLT-2) inhibitors.

The lecture will discuss these trials and reasons why some of them ended with neutral results (non-inferiority). In contrast the surprising and highly rewarding impact of SGLT-2 inhibitors (EMPA-REG OUTCOME and CANVAS trials) and GLP-1 receptor agonists (LEADER and SUSTAIN-6, trials) have led to a shift in the way CVOTs are viewed. These trials have led to a growing appreciation that type 2 diabetes is a disease that extends beyond hyperglycaemia. The so far rather glucocentric treatment approach needs to be abandoned and numerous other considerations taken into account when considering the best management.

The precise mechanisms by which SGLT-2 inhibitors and GLP-1RAs lead to beneficial effects on the cardiovascular system are still not fully understood, and the impact of the new data on diabetes management is a topic of intense debate.

The audience will be brought on a journey through a number of lessons on diabetes care strategies from a cardiologist's perspective, beginning with the history of glucose-lowering trials, progressing to recent CVOTs in diabetes, and concluding with some recommendations for changes in diabetes care.

106. Antidiabetic drugs and cardiovascular risk – endocrinologist's point of view

Vallo Volke
Tartu University, Tartu University Hospital

Cardiovascular complications of hyperglycemia are among the most important concerns of patients with diabetes. Until recently the best evidence indicated that good glycemic control of diabetes can postpone cardiovascular disease, but treatment needed to be in place, literally said, for decades. Clinical trials aiming at very strict glycemic control resulted in disappointing lack of effect on macrovascular complications, or clear harm. Surprisingly enough, the game-changing results were obtained from trials primarily designed to prove cardiovascular safety of new diabetes drugs. Collectively, we have now 3 drugs/drug classes with proven cardiovascular benefit. One must not forget the first and oldest of these, pioglitazone. While the first study of pioglitazone was not able to demonstrate benefit in terms of primary outcome, the recent study in stroke patients was clearly positive.

We are now left with couple of questions which are worth further clarification.

1. Where will be the optimal position of the drugs with CV benefit?
2. In patients with substantial CV morbidity, will metfromin will remain the first choice?
3. What will be the optimal strategy combining the drugs with CV benefit, will some combinations result in additive efficacy?

With all of the positive results we still must recognize the potential side-effects of the drugs.

From that viewpoint, it seems that pioglitazone has the most problematic side-effect profile and GLP-1 receptor agonists have so far demonstrated surprisingly few safety problems.

To conclude, we are now in a position where we can provide better value for our patients with high CV risk and, sometimes, build a more tailor –made treatment schemes.

107. Cardiovascular risk management in diabetes and hypertension

Peter M Nilsson
Lund University, Skåne University Hospital, Malmö, Sweden

Hypertension in diabetes is a common, treatable and cost-effective risk factor to intervene on, based on evidence from many randomized controlled studies, as recently summarized in a number of important meta-analyses and reviews [1-3]. Most antihypertensive drugs can be used, preferred as combination therapy, to prevent the patients from micro- and macrovascular complications, as well as renal impairment and cognitive decline. An additional benefit is to reduce the risk of diabetic eye complications and retinopathy according to the UKPDS study. An interesting aspect is the timing of drug intake. In one Danish study, the intake of antihypertensive drugs in patients with type 2 diabetes and non-dipping was more effective for 24-h blood pressure control if randomized to bed-time versus morning intake [4].

A sensitive and much debated issue is the blood pressure (BP) goal in patients with type 2 diabetes. European guidelines from ESH/ESC 2013 have recommended a BP target below 140/85 mmHg, but the American Diabetes Association (ADA) recommends (2018) a BP goal below 140/90 mmHg in most such patients, but less than 130/80 mmHg in subgroups (younger patients tolerant to BP lowering without adverse effects) [5]. It should be noted that the ADA disregards the much debated SPRINT trial because it did not include any patients with diabetes at all. Recently the

American Heart Association, together with other US organisations, have proposed a new definition of hypertension (> 130/80 mmHg) in all subjects with elevated BP, irrespective of diabetes status. These organisations also recommend the lowering of BP to below 130/80 mmHg in all patients, including diabetes patients [6]. During 2018, a new set of European guidelines have been announced to be published.

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6. Whelton PK et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 Nov 13 (e-publication).

108. Lipid-lowering therapy in the future: Will statins still be the basis?

Terje R. Pedersen
Oslo University Hospital, Oslo, Norway

Since 1994 statins have been established as the main class of drugs for prevention of atherosclerotic cardiovascular disease (ASCVD). Until recently other classes of lipid interventions have played a relatively small part. Fibrates are losing their role as preventive treatment modality with only small effect on clinical events in randomized trials. Ezetimibe has rarely been used in more than 5% of patients with established ASCVD in most countries but this may change when ezetimibe comes off patent and the price will fall. Recently inhibitors of PCSK9 have been introduced as a powerful treatment modality to lower LDL cholesterol, but the relatively high cost has so far prevented widespread use. In the next future inclisiran and bempedoic acid will likely be introduced as other effective alternatives. In the meantime statins have come under attack because of an increasing reputation of causing side effects, in particular muscle problems. However, the statin class remains the best documented treatment in current cardiovascular medicine with 28+ large randomized clinical trials. In addition new lipid interventions have been tested in patients who have been receiving a background therapy with statins. In contrast to medical practice double-blinded trials with statins have not shown an excess of myopathy or muscle pain compared with placebo. On the other hand there is evidence from clinical trials that statins may increase the risk of type 2 diabetes. Although the risk is small, patients with risk factors for developing type 2 diabetes might experience an increase in levels of HbA1c into the diabetic range. This does not counteract the beneficial effect on ASCVD prevention. The merits of statins from clinical trials together with their decreasing price level confirm their role as the fundament of ASCVD prevention, both in primary and secondary prevention.

109. Prevention of sudden cardiac death - the role of implantable devices

Bela Merkely
Heart and Vascular Center, Semmelweis University, Budapest

Sudden cardiac death (SCD) is still accountable for approximately 25% of 17 million cardiovascular deaths per, inspite

of continously improving prevalence. Risk of SCD increases with aging, most important etiological factors are ischemic heart disease, heart failure and structural heart diseases in the elderly, while chenellopathies, cardiopathies are the most prevalent causes among the young.

Implantable cardioverter defibrillators are used in primary and secondary prevention of SCD for more than 30 years. Nowadays transvenous systems are the most widespread, they can be combined with cardiac resynchronization therapy (CRT) as well.

ICD therapy was first introduced for secondary prevention of SCD. Among patients with history of aborted SCD, ventricular fibrillation (VF) or haemodinamically unstable ventricular tachycardia (VT) ICD therapy for more beneficial in reducing arrythmogenic death than antiarrythmic medications based upon results from AVID, CIDS and CASH trials.

ICD therapy is effective in the primary prevention of SCD as well, when no malignant ventricular arrythmia is present in the previous history, but the risk is highly elevated. The most common such population is heart failure patients with severly reduced ejection fraction. The optimal medical therapy of heart failure significantly decreases the risk of SCD, however in MADIT-II and SCD-HeFT trials further decrease in arrythmogenic and all-cause mortality was observed in both ischemic and dilated cardiomyopathy.

Novel direction of device development is subcutaneous ICD (S-ICD), where electrodes are located subcutaneously encompassing the heart, outside the thorax. The main advantage of S-ICD is the lack of transvenous intracardiac electrodes, and thus the freedom from electrodes complications. S-ICD is effctive in prevention of SCD, therefore can be a real alternative for transvenous ICD in patients not requiring bradycardia-, biventricular-, or antitachycardia-pacing (ATP).

Wearable cardioverter-defibrillator (WCD) is an external ICD integrated into a vest, which might be beneficial for patients temporarily increased risk of SCD, with chance to recovery (acute myocarditis, peripartum cardiomyopathy, bridge to transplant).

110. Is metabolic syndrome high or moderate cardiovascular (cardiometabolic) risk entity: results of Lithuanian High Cardiovascular Risk (LitHiR) programme

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According to the European guidelines for hypertension and cardiovascular (CV) prevention, metabolic syndrome (MetS) is considered to reflect moderate CV risk. It is estimated that the presence of MetS means 5 times elevated risk of development of diabetes and 1.5-2 times elevated CV risk.

National Lithuanian High Cardiovascular Risk (LitHiR) prevention programme is running in Lithuania from 2006. Two level approach is applied: primary level health care institutions (PHCI) and specialized cardiovascular prevention units (CVPU). Subjects with high CV risk are assessed in detail in CVPU. Among other subjects, individuals with MetS (modified NCEP ATP III) are identified and referred to a specialized CVPU. These subjects are reassessed in the CVPU in order to re-assign them to moderate or high CV categories.

We analyzed the data obtained from 5691 subjects with MetS. Number of components of MetS was distributed as follows: 3 of 5 components were present in 42%, 4 of 5 – in 38.2% and 5 of 5 – in 19.8%

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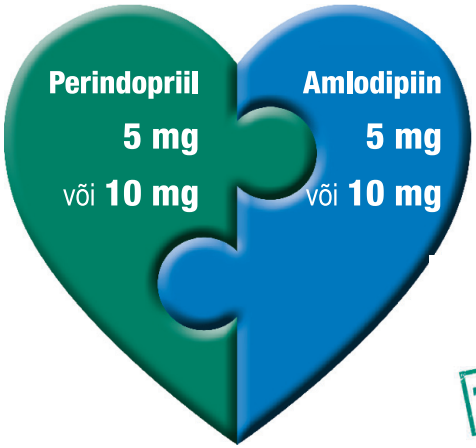

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of subjects. Apart from the components of MetS, additional CV risk factors were estimated. Elevated LDL Ch > 3 mmol/l was found in 85.5%, elevated hsCRP (> 3) – in 34.1%, microalbuminuria – in 7.4%, left ventricular (LV) diastolic dysfunction in 63.4%, LV hypertrophy - in 49.8%, enlarged left atrium – in 48.7%, presence of atherosclerotic plaques in catid arteries - in 40.3%, carotid-femoral PWV > 10m/s – in 18.6%. The MetS subjects who, in addition to the classical MetS components, had at least one additional risk factor, mentioned above, were reclassified by us from moderate to high CV risk. In order to distinguish these patients from the moderate CV risk subjects, we propose to use the term "elevated cardiometabolic risk subjects."

Furthermore, in the cohort of 170 subjects with MetS, we examined the the influence of the aerobic physical training on the dynamics of aortic stiffness. In 75 of these subjects, who underwent a heart rate controlled aerobic physical training, a statistically significant improvement of aortic stiffness (lowering of carotid-femoral pulse wave velocity) was observed. This positive dynamic was not present in the control group of 75 subjects for whom only recommendations for physical activity were provided. This result suggests that a supervised aerobic training is a reliable measure for lowering cardiometabolic risk.

111. How To Improve Blood Pressure Control? Novel Initiatives

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The primary aim of antihypertensive treatment is to reduce blood pressure (BP) to guideline-recommended targets in order to maximise the long-term reduction in the risk of cardiovascular (CV) events. Nonetheless, despite the well-established relationship between hypertension and the increased risk of CV morbidity and mortality, BP control rates remain suboptimal. In developed countries, estimates show that only 11% and 17% of male and female hypertensive patients, respectively, are achieving BP control. In Europe, data from the Cardio-Monitor survey of physician visits has indicated that the proportion of hypertensive patients achieving BP control varied from 31–46%.Suboptimal BP control rates impose a substantial global health burden. An estimated 7.6 million premature deaths worldwide were attributed to hypertension, with approximately 17% of all disability adjusted life years lost in European countries being due to CV disease. In addition, uncontrolled BP also contributes to a significant burden on the economy as the annual cost of CV disease in the EU is an estimated €192 billion.

Evaluation of predictors of CVD is essential for early detection, prevention, and treatment. Modern guidelines on screening, detection, evaluation, and treatment of hypertension repeatedly stress the importance of appropriate BP control in high-risk patients. An observational study from Turkey, TRES-1 showed that, blood pressure control was poorer in patients with 3 or more risk factors or diabetes mellitus compared to patients with no additional risk factors or 1-2 risk factors.

Poor patient compliance and adherence with prescribed antihypertensive medication makes a major contribution to the development of suboptimal blood pressure (BP) control. The asymptomatic nature of hypertension, side effects of medication, treatment complexity and high pill burdens all have a negative impact on patient compliance. It is important to address the issue of poor patient compliance as studies have shown that good compliance is associated with improvement of BP control and positive health outcomes.

Therapeutic adherence is a multifactorial issue influenced by patient-,

physician-, and therapy-related factors. Patient-related factors include demographic characteristics (e.g., age, gender, socioeconomic status), cognitive function (e.g., dementia, depression), patient's lack of insight in to the illness and missed appointments.

Retrospective analyses have suggested that about 40% of newly diagnosed patients with hypertension discontinue their antihypertensive therapy in the first year of treatment. In addition, according to the WHO report on adherence to long-term therapies, >50% of the patients treated for hypertension drop out of care entirely within a year of diagnosis and, of those who remain under medical supervision, only about 50% take ≥80% of their prescribed medication.

There is growing evidence that physician inertia is also an important cause of poor BP control. Physician can contribute to the problem by not explaining the regimen, effects and side effects properly, not learning patient's characteristics and lifestyle, poor knowledge about the cost of medications and insurance coverage of available formularies, failing in patient-physician conversation and some physicians are willing to treat hypertension aggressively.

Adherent patients have a lower predictive relative risk of adverse cardiovascular outcomes compared with these who were non-adherent and good compliance has been shown to be associated with successful BP control. There are various ways in which compliance may be improved, such as raising awareness of the dangers of hypertension, improving patient education, encouraging patients to become more accountable for their own health, and treatment simplification.

Electronic communication with the physician (use of telemetry for transmission of recorded home values, maintaining contact between patients and physicians) may provide an acceptable alternative to improve adherence to treatment. Providing continuous education and information on disease, treatment, and objectives (information material, programmed learning,computer-aided counselling) is also crucial for improving BP control.

Panaceastar is the first and unique platform in medicine which establishes link between key opinion leaders, physicians and patients via internet.

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One of the most important tasks of Panaceastar is to increase the awareness and prevent the chronic diseases and its risks by giving advices on lifestyle changes to improve the quality of life.

In conclusion,control of BP remains a challenging issue and novel strategies may become a viable option for those patients with uncontrolled hypertension.

112. Three-year experience of the Latvian Registry of Familial Hypercholesterolemia: challenges and achievements

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Latvian Registry of Familial Hypercholesterolemia (FH) was established in February 2015 as a research project within frames of the Latvian State Research Programme BIOMEDICINE, and it is carried out by the Latvian Institute of

Cardiology and Regenerative Medicine, University of Latvia in collaboration with Pauls Stradins Clinical University Hospital. The aim of the Registry was to improve diagnosis and management of FH patients in order to cost-effectively prevent cardiovascular morbidity and mortality among these very high risk patients.

Before year 2015 very few FH cases were recognized by physicians in Latvia due to very low professional awareness of the disease despite the fact that estimated number of such patients was at least 8000 in the whole country. Public awareness was virtually non-existent.

The activities of the Registry first and foremost included education of cardiologists, general practitioners, endocrinologists, internists and other specialists on the clinical signs and diagnosis of FH. The public awareness was effectively raised in close collaboration with cardiovascular patient organization ParSirdi.lv. An important key to the success was involvement of a dedicated team consisting of enthusiastic cardiologists and young doctors.

All patients referred to the Registry were evaluated according to the Dutch Lipid Clinic Network criteria. Management of patients included further risk stratification and lipid-lowering as well as cascade screening that was initiated for the first-degree relatives in cases of probable or definite FH of index patients. Within three years 416 individuals have been included in the database, and 176 of them have been diagnosed with FH. Thus, according to our estimation, approximately 2.2% of all FH patients in Latvia have been diagnosed at the Registry by the end of December 2017. Another 151 patients have possible FH, and a proportion may be reclassified to probable or definite FH after further evaluation. All patients were consulted regarding further management with follow-up recommendations. Collaboration with general practitioners was set as a top priority.

Regrettably, our data also revealed that management of most FH patients before involvement in the Registry was far from optimal. Half (46%) of FH patients were not on any kind of lipid-lowering therapy at the time of inclusion in the Registry, and only 23% were on maximal atorvastatin or rosuvastatin doses despite mean age of 51.4 years. Only 3% and 6% of high- and very high-risk FH patients had their LDL-C levels below goal before inclusion in the Registry. One third (36%) had history of premature coronary heart disease. The youngest individual with diagnosed asymptomatic coronary atherosclerosis was 27 years old. These and other observations of the Latvian Registry of FH are convincing proofs to our professional community how critical is the need for such registries and specialized care of FH patients. State funds should clearly be allotted for these purposes.

113. Familial hypercholesterolemia screening: International and national initiatives

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Familial hypercholesterolemia (FH) is commonest co-dominantly inherited condition. Mutations in one of three genes result in life-long elevations in LDL cholesterol and development of premature atherosclerotic cardiovascular disease. FH is underdiagnosed and undertreated in most countries. There is urgent need to improve diagnostics and treatment of FH in Baltic countries, create national registries and join international initiatives. Lithuania is among participants of EAS Familial Studies Collaboration (FHSC) project. Main rationale and design of the global EAS-FHSC initiative of European Society of Atherosclerosis is pooling and expanding registries of familial hypercholesterolemia to assess gaps in care and improve disease management and outcomes. Agreements with National

Coordinators have already been signed; preparation of documents for regional Biomedical Research Ethics committee, close collaboration with coordinating center in Imperial College London has been successfully started. Another international activity is Screening Project for Familial Hypercholesterolemia in Central, Southern and Eastern Europe (ScreenProFH). Certificate of National Coordinator has already been signed, preliminary data have been published. Textbook "Familial hypercholesterolemia" (written by Richard Cask) has been translated to many languages (to Lithuanian as well). It will help to increase educational level of knowledge about FH.

At the national level Competence centre of Lipidology (member of MetabERN; network coordinator Maurizio Scarpa) has been established at Vilnius University Hospital Santaros Clinics (together with Centre of Pediatrics and Coordinating Centre of Children's rare Diseases). MetabERN (the European Reference Network for Hereditary Metabolic Diseases) is one of the 23 approved European Reference Networks For Rare Diseases. MetabERN gives excellent possibility for cardiologists, pediatricians and other specialists to work together in the field of hereditary metabolic diseases and dyslipidemia.

Screening of familial hypercholesterolemia and FH registry in Lithuania has been started on the basis of nationwide cardiovascular primary prevention programme. There are thousands of lipidograms of the middle-aged Lithuanian men and women in the database for the detailed lipid profile analysis. Cases of severe dyslipidaemia and possible FH are extracted and analyzed. Another important national activity is creation of FH databases and FH follow-up systems in Vilnius University Hospital Santaros Clinics Electronic case reports system (with data protection): one database is created under supervision of Competence center of Lipidology and dedicated for adult and pediatric patients with rare and severe dyslipidaemia, another database - for adult patients with early acute coronary syndrome and possible FH. Delegated users with their passwords and usernames are allowed to connect those systems. Cascade screening of index case families has already been started. Cardiologists, pediatricians, geneticists, apheresis specialists, family doctors, laboratory diagnostic specialists, dermatologists and even plastic surgeons (when needed) are involved in the management of FH patients. Vilnius University Hospital Santaros Clinics is coordinating center for FH screening initiative. Dutch Lipid Clinic Network criteria are recommended and applied for the FH index case diagnosis. Lipid lowering drugs (statins, ezetimibe, fibrates) are available and reimbursed in Lithuania. PCSK9 inhibitors are available, but not reimbursed. Lithuania actively participated in PCSK9 trials: ODDYSSEY and FOURIER. There are several apheresis centres in Lithuania, but LDL apheresis is not available currently and not reimbursed. Genetic testing of FH has been successfully implemented and reimbursed in Vilnius University Hospital Santaros Clinics. Lithuanian Heart Association and Lithuanian Society of Cardiology take active part in national FH initiatives.

114. FH management: expectations and reality

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Familial hypercholesterolemia is the most frequent genetic disorder associated with premature atherosclerotic cardiovascular disease (CVD). Several international and

national guidelines have emphasised the need for early identification and aggressive management of FH, which have been proven effective in reducing CVD risk.

Despite the vast evidence and guidance, identification rate of FH individuals in most populations remains low and attainment of therapeutic goals is suboptimal. Thus, we designed non-interventional, retrospective, open-label, multicentre disease registry for patients with heterozygous familial hypercholesterolemia in the Czech Republic and Slovakia (the PLANET registry).

The aim of the PLANET registry was to assess the attainment of therapeutic target LDL-C level in the settings of everyday medical practice. The second goal was to characterize lipid-lowering therapy patterns in FH patients in the real life and to characterize cardiovascular events observed in this patient population.

1755 patients were enrolled and analysed. 1421 patients were enrolled in 24 Czech sites and 334 patients were enrolled in 8 Slovak sites, all members of the nationwide network of specialized FH (MedPed) centres. The mean LDL-C observed in all 1755 subjects was 3.52 mmol/l (SD=1.51). LDL-C in the subgroup with target value ≤ 1.8 mmol/l resp. ≤ 2.5 mmol/l was 3.32 mmol/l (SD=1.48) resp. 3.67 mmol/l (SD=1.52). The mean in the subgroup with attainment of target value resp. without attainment of target value was 1.80 mmol/l (SD=0.54) resp. 3.82 mmol/l (SD= 1.42). Participating patients were treated with monotherapy (49%) or combination of lipid lowering medications (43%). Some of observed subjects were newly diagnosed patients (8%) without therapy to date. Statins were used by 1578 patients (98%). At least one cardiovascular event experienced 16.8% patients from the PLANET registry population (n = 1739).

The PLANET registry documents insufficient intensity of management of the FH patients whose LDL-C target values attainment remains low. Despite high penetration of statin therapy in the population studied, we have documented inadequate dose titration and lack of combination therapy use. Periodical evaluation of treatment patterns highlighting gaps in the management of FH patients is an important tool to improve standards of care even in the specialized care setting.

ACKNOWLEDGEMENT

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115. Vascular restoration therapy: the role of intravascular imaging guided plaque modification prior drug eluting stent or bioresorbable scaffold implantation

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Second-generation drug-eluting stents (DES) have revolutionezed treatment of obstructive coronary artery disease by reducing the rate of restenosis and the need for repeat revascularization when compared to bare-metal or first-generation DES. Bioresorbable vascular scaffold (BVS) represents a new concept of providing transient vessel support with drug delivery capability but theoretically without the long-term limitations of metallic DES.

The left main (LM) – the most proximal part of the left coronary artery – is the most important structure in the human arterial vascular tree. The majority of patients with LM disease are symptomatic and have a very high risk of major cardiovascular events. During the last decade, many technological improvements have been made for percutaneous coronary intervention (PCI) and many studies have been conducted to evaluate the efficacy of different revascularisation methods in patients with LM lesions.

Since 2002 we have enrolled all consecutive patients with LM stenosis who underwent PCI at the Latvian Centre of

Cardiology in the registry to evaluate the real-world outcomes of LM PCI. The analysis of 965 patients showed that one year cardiovascular survival rate was higher in patients with intravascular ultrasound (IVUS) guided LM stenting compared with patients without IVUS guided LM stenting. One year total and cardiovascular survival rates were significantly higher in patients with plaque modification with cutting balloon before stent implantation compared with others. In the latest European guidelines on myocardial revascularization the indication of PCI of LM with low or moderate angiographic risk has been equated to coronary artery bypass grafting, however the appropriateness of PCI in high risk LM anatomy, including true bifurcation lesions requiring double stenting, remains an area of controversy. Our hypothesis is that applying modern diagnostic (intravascular imaging guiding and optimization) and treatment (plaque pre-treatment prior stenting, new generation DES, BVS, adjunctive pharmacotherapy) strategies could improve PCI outcomes in patients with high risk anatomy. Therefore, recently we initiated a pilot, prospective, consecutive, one centre registry analysing feasibility of IVUS-guided and optical coherence tomography-optimized two stent technique using DES from LM to the main branch and BVS in the side branch for the treatment of distal LM true bifurcation stenosis. The study is on-going and results will be presented.

116. Vascular Protection by Factor Xa Inhibition in Patients with Coronary and/or Peripheral Artery Disease

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Dual antiplatelet therapy has been ACS pharmacological strategy for decades. Dual pathway inhibition concept by blocking Xa factor on the top inhibited platelets was successfully tested in ATLAS ACS-TIMI trial. Mortality and morbidity rates in patients with multifocal atherosclerosis are still high. Recent trial data showed effectiveness of combination of vascular dose of rivaroxaban and aspirin stable coronary artery disease and peripheral artery disease patients.

117. Role of 18F-FDG-PET/CT in Management of Atherosclerotic Plaque: Current Evidence

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Objective: Management of atherosclerotic plaque and inflammation stays in the focus of clinical management of patients with atherosclerosis and dyslipidemias. Increasing availability of 18F-FDG-PET/CT in standard hospital settings for different clinical applications has raised the interest in possible role of this method in detection and assessment of inflammatory capture of atherosclerotic plaque.

Methods: In our report, we provide an overview about current evidence on 18F-FDG in management of atherosclerotic plaque.

Results: Use of 18-F-FDG-PET/CT is usually not included into current guidelines for clinical practice. This is also the case with 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias, and with the 2016 European Guidelines on cardiovascular disease prevention in clinical practice. However, a number of publications is dedicated to this topic.

Importance of this issue is emphasized by the clinical reality where 18F-FDG-PET/CT studies may be performed not only as a dedicated study in patients with atherosclerosis or dyslipidaemias, but inflammatory atherosclerotic plaques may present them as occasional findings

Levemir® (detemirinsuliin) **on näidustatud suhkurtõve raviks täiskasvanutel, noorukitel ning 1-aastastel ja vanematel lastel.** **Annustamine ja manustamisviis:** Levemir® on pika toimeajaga analoog-insuliin, mida kasutatakse basaalinsuliinina. Toimeaeg on kuni 24 tundi sõltuvalt annusest, mis võimaldab ravimit manustada üks või kaks korda päevas. Kombineeritult suukaudsete diabeediravimitega ja lisatuna liraglutiidile soovitatakse Levemir'i kasutada üks kord päevas, algannuses 0,1...0,2 Ü/kg või 10 Ü täiskasvanud patsientidel. Kui Levemir'i kasutatakse basaalboolusrežiimis, tuleb seda manustada üks või kaks korda päevas, lähtudes patsiendi vajadustest. Annus tuleb kindlaks määrata individuaalselt. Manustatakse subkutaanselt, süstides seda kõhuseina, reide, õlavarde, deltalihasesse või tuharasse. Ei tohi manustada intravenoosselt, sest see võib põhjustada rasket hüpoglükeemiat. Ei tohi kasutada insuliinipumpades. Levemir'i tõhusust ja ohutust ei ole uuritud alla 1-aastastel lastel. **Vastunäidustused:** ülitundlikkus detemirinsuliini või ükskõik millise abiaine suhtes. **Hoiatused:** ebaadekvaatne annustamine või ravi katkestamine, eriti I tüüpi diabeedi puhul, võib põhjustada hüperglükeemiat ja diabeetilist ketoatsidoosi, mis võib lõppeda surmaga. Ühe söögikorra vahelejätmine või ettekavatsematu pingeline füüsiline tegevus võivad põhjustada hüpoglükeemiat. Patsientidel, kelle veresuhkru kontroll on märgatavalt paranenud, näiteks intensiivse insuliinravi tulemusena, võivad harjumuspärased hüpoglükeemia hoiatavad sümptomid muutuda ja neid tuleb sellest teavitada. Raske hüpoalbumineemiaga patsiente on soovitav hoolikalt jälgida. Kasutamisel koos pioglitasooniga tuleb patsiente jälgida südamepuudulikkuse, kaalutõusu ja tursenähtude suhtes. Pioglitasoonravi tuleb lõpetada, kui ilmneb mõne kardiaalse sümptomi halvenemine. **Koostoimed teiste ravimitega:** insuliinivajadust võivad vähendada suukaudsed diabeediravimid, MAO inhibiitorid, beetablokaatorid, AKE inhibiitorid, salitsülaadid, anaboolsed steroidid ja sulfoonamiidid. Insuliinivajadust võivad suurendada: suukaudsed rasestumisvastased ravimid, tiasiidid, glükokortikoidid, kilpnäärmehormoonid, sümpatomimeetikumid, kasvuhormoon ja danasool. Alkohol võib insuliini hüpoglükeemilist toimet intensiivistada või vähendada. **Rasedus ja imetamine:** Rasedusaegset Levemir-ravi võib kaaluda, kuid hinnata tuleb võimaliku saadava kasu ja võimaliku rasedusele kahjuliku toime riski suurenemise vahekorda. Turuletuleku järgselt täiendavalt 250 raseda kohta saadud andmed näitavad, et detemirinsuliin ei põhjusta kõrvaltoimeid rasedusele ning ei põhjusta vääraregnuid ega avalda kahjulikku toimet lootele/vastsündinule. **Kõrvaltoimed:** Kõige sagedamini esinenud kõrvaltoime on hüpoglükeemia. Süstekoha reaktsioonid (valu, punetus, lööve, põletik, muljumisjäljed, turse ja sügelus süstekohas) esinevad sageli, kuid on enamasti kerged ja mööduva iseloomuga. Insuliinravi alguses võivad tekkida refraktsioonianomaaliad ja turse. Need nähud on tavaliselt ajutise loomuga. Süstekohas võib tekkida lipodüstroofia. Pidev süstekoha vahetus sama süstepiirkonna ulatuses võib aidata vähendada selliste reaktsioonide tekkeriski. Allergilised reaktsioonid, võimalikud allergilised reaktsioonid, urtikaaria, punetus, lööve esinevad aegajalt, kui Levemir'i kasutatakse basaalboolus raviskeemis. Anafülaktilised reaktsioonid esinevad väga harva, kuid võivad olla eluohtlikud. Glükeemilise kontrolli kiire taastumisega võib kaasneda akuutne valulik neuropaatia, mis on enamasti pöörduv. Intensiivse insuliinravi ja glükeemilise kontrolli järsu paranemisega võib kaasneda diabeetilise retinopaatia ajutine halvenemine, kuigi pikaajaline hea glükeemiline kontroll vähendab diabeetilise retinopaatia süvenemise riski. **Levemir® FlexPen® on retseptiravim.** Levemir® FlexPen® 100 Ü/ml süstelahus pensüstlis. Toimeaine: detemirinsuliin. Pakend: 5x3 ml.

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Vasodilatatiivsete omadustega beetablokaator [2,3]

Näidustused[1]**:** Essentsiaalne hüpertensioon. Stabiilse kerge ja mõõduka kroonilise südamepuudulikkuse ravi lisaks standardravile 70-aastastel ja vanematel patsientidel.
Retseptiravim. Pakend: 5 mg tabletid, 28 või 90 tk.

Annustamine[1]: Essentsiaalne hüpertensioon.
Täiskasvanud: Üks tablett (5 mg) ööpäevas, eelistatult alati samal kellaajal. Tablette võib manustada söögi ajal. Vererõhku alandav toime ilmneb 1-2 nädalat pärast ravi alustamist. Mõnikord saavutatakse optimaalne toime alles nelja nädala pärast. (Vt täiendavalt ravimi omaduste kokkuvõte. www.ravimiamet.ee (kinnitatud juulis 2014)).

Vastunäidustused[1]**:** Ülitundlikkus toimeaine nebivolooli või abiainete suhtes. Maksapuudulikkus või maksatalitluse häire. Äge südamepuudulikkus, kardiogeenne šokk või südamepuudulikkuse dekompensatsiooniepisoodid, mis vajavad i.v. inotroopset ravi.

Nagu ka teiste beeta-adrenoblokaatorite kasutamine, on Nebileti kasutamine vastunäidustatud, kui esineb: siinussõlme nõrkuse sündroom (ka sinuatriaalne blokaad); 2. ja 3. astme atrioventrikulaarne blokaad (ilma südamestimulaatorita); varem esinenud bronhospasmid ja bronhiaalastma; ravimata feokromotsütoom; metaboolne atsidoos; bradükardia (südamefrekvents vähem kui 60 lööki minutis enne ravi algust); hüpotensioon (süstoolne vererõhk <90mmHg); rasked perifeerse verevarustuse häired.

Reklaam on suunatud ravimite väljakirjutamise õigust omavatele isikutele, proviisoritele ja farmatseutidele.
Reklaam kinnitatud augustis 2017. EE_NEB-04-2017.

- **Antihüpertensiivne toime säilib ka pikaajalise ravi korral** [1]
- **Ei mõjuta diabeetikutel veresuhkru taset** [1]
- **Veresoonte laienemine tänu otsesele stimulatsioonile, mis viib endoteelistsõltuvale NO vabanemisele** [2,3]

ANNUSTAMINE[1]

ESSENTSIAALNE HÜPERTENSIOON
5 mg x 1

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on 18F-FDG-PET/CT studies in patients with oncological or neurological problems.

Available data provide useful hints for the interpretation of 18FDG uptake in vascular wall. At the same time, available data point to the need of further systematic studies of the role of 18F-FDG-PET/CT in assessment of atherosclerotic plaque, as well as to the need of fine tuning of PET/CT studies for the assessment of an atherosclerotic plaque.

Conclusions: Role of 18F-FDG-PET/CT in assessment and management of atherosclerotic plaque cannot be disregarded due to increasing availability of this method. It may be used for detection of inflammatory processes, for evaluation of prognosis and treatment results. And it should be correctly reported when occasionally detected in imaging due to other diseases.

118. Impact of chronic stress on atherosclerosis process

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Atherosclerotic cardiovascular diseases remain the major cause of death worldwide. Since the death rates from cardiovascular diseases are generally higher in Lithuania than in Western European countries and traditional risk factors not always explain this higher morbidity, other atherosclerosis risk factors have to be considered. Psychological factors have significant impact on pathogenesis, progression and complications of atherosclerosis, but mechanisms underlying these associations are not completely clear. In our work we sought to examine effects implicated by chronic psychological stress on several pathogenetic pathways: dyslipidemia, oxidative stress and inflammation. The evaluation of chronic stress was made not only by using specific questionnaires, but also by measuring cortisol concentration in hair, which reflects perceived stress over certain period of time. Malondialdehyde, total antioxidant activity and concentration of carotenoids in blood were measured as biomarkers of oxidative stress. Inflammation was evaluated by a high sensitivity C-reactive protein, interleukin-6 and cyclophilin A.

In our study we included 161apparently healthy volunteer men, aged 25-55 years. Most significant finding was that cortisol concentration in hair was positively correlated with age, body mass index, waist circumference, systolic and diastolic blood pressure, as well as with total and low-density lipoprotein cholesterol. However, hair cortisol levels were not related to the markers of inflammation and oxidative stress.

The results of our study suggest that chronic stress increases atherosclerosis risk through metabolic changes. However, the impact of stress on other pathways, such as inflammation and oxidative stress, has to be address in further more detailed studies.

119. Arterial hypertension and atherosclerosis: data from Russian national registry

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Objective: Arterial hypertension (AH) is a leading cause of morbidity and mortality both worldwide and in Russia.

Methods: Data from Russian national registry of Arterial Hypertension.

Results: Data from the multicenter observational study ESSE-RF (Epidemiology of Cardiovascular Diseases and their Risk

Factors in Regions of Russian Federation) showed that the prevalence of AH was 48,1% in men and 40,7% in women. On the other hand according to the Russian national registry of Arterial Hypertension, which is in place since 2010 and covers 33 571 patients, the majority of them tends to have high and very for CVD events – 38% and 56% respectively, 4% - low-risk and 2% - middle-risk CVD patients. According to the registry 32,4% of hypertensive patients had coronary heart disease, 19,5% had myocardial infarction, 5% - stroke and 58% - peripheral arterial disease. Prevalence of obesity was 38,3% and abdominal obesity - 44%.

According to epidemiological ESSE-RF study in the total sample 60,6% of participants had elevated levels of cholesterol (> 4,9 mmol/l) and 73,5% of patiens with AH, high LDL-C level (>3,0 mmol/l) – in 58% and in 70,4%, low HDL-C level (<1,0 mmol/l) – in 18,8% and in 21,6%, hypertriglyceridemia (>1,7 mmol/l) – in 24,9% and 36,6% respectively.

Conclusions: Data from the epidemiological studies and the Russian national registry of Arterial Hypertension shows high prevalence of dyslipidemia in patients with AH, that leads to cardiovascular events, such as coronary heart disease, myocardial infarction, stroke and peripheral arterial disease, therefore to a high and very high CVD risk profile.

120. Lifestyle management in cardiovascular prevention

Iveta Mintale
Cardiology centre, P.Stradins Clinical university hospital, Latvian University

Lifestyle management is a serious tool in CV prevention, particularly in high risk patients. No smoking, Med diet, regular physical activity, which help to maintain normal body weight. Easy to say, difficult to perform…

In the CV Prevention Guidelines there are several pages dedicated to behavioral changes – how to facilitate them from 3 sides: individuals, medical stuff and authorities. All of them have high level of evidence (IA, IB).

Healthy diet is one of the most important tasks. The guidelines say: diet – low in saturated fat with a focus on wholegrain products, vegetables, fruit and fish. To tell this to patient means to say nothing – no one knows how to translate this into products and meals…

What does it mean – healthy diet in real life? First of all high quality products, then – optimal size of the plate, and last, but not least – high quality fats (preferably olive oil). This is real life Meditterranean diet which has a huge amount of evidence after PREDIMED trial, which is easy to follow for a long time, which can help to lose weight. High adherence to Med diet can significantly reduce the risk of MI, stroke and peripheral artery disease, diabetes, atrial fibrillation… This can reduce a .carotis media thickness and even incidence of invasive breast cancer.

Let's look at one of the CV risk factors – obesity! The concept of 'metabolically healthy obesity (the absence of metabolic dysfunction), individuals with excess adiposity are not at greater cardiovascular risk, has been controversial. A recent pan-European case-cohort study (European Prospective Investigation into Cancer and Nutrition study (EPIC-CVD)), observed higher cardiovascular risk with increasing general and central adiposity. It is crucial – to maintain normal body weight in order to reduce BP, dyslipidemia and risk of developing type 2 DM, and thus improve the CV risk profile (IA). Mediterranean diet is the best eating style (keeping in mind that low-fat diet has no CV benefits), which can reduce CV risk even in high risk persons.

It is not easy to change the lifestyle in 40ie or 50ies. Definitely education on good health should start in the family from the early age.

We should encourage our patients to define the meaning of good health for themselves to make changes easy to rediscover the joy, energy, movement or happiness. To be healthy!

121. Goals in blood pressure

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The search for a practical, cost-effective and evidence-based blood (BP) goal in hypertension is a much debated and hot issue over the last few years. Observational studies have indicated a more or less linear relationship between lower BP and lower risk, especially for stroke. However, some data from randomized, controlled studies indicate a J-shaped curve for risk of cardiovascular events in relation to achieved BP in patients on drug treatment for hypertension. The European view, as manifested in the European Society of Hypertension (ESH) and European Society of Cardiology (ESC) Guidelines on Arterial Hypertension from 2013 recommend a BP goal below 140/90 mmHg office BP for most patients, but less than 140/85 mmHg in patients with diabetes [1]. However, in a recent set of recommendations from the American Heart Association and related organizations from November 2017, hypertension is defined as a mean BP over 130/80 mmHg and BP goals for risk patients should, according to these recommendations, be below 130/80 mmHg [2]. One argument in favor of this more ambitious goal is the benefits shown in the SPRINT study in the treatment arm randomized to a BP goal lower than 120 mmHg, even if adverse effects also increased [3]. It should be noted that the methodology for measuring BP in SPRINT was unusual, with the patient sitting alone in a quiet room and using self-monitoring. According to critical arguments, this unusual method corresponds to BP levels 15 mmHg higher based on standard office BP measurements [4].

The debate goes on, but the paradox is that so many risk patients still are not below the target BP of 140/90 mmHg (a "reasonable" goal) while experts debate over a "perfect" BP goal. This is an example on the importance to focus on subjects at high risk before focus is put on subjects with relatively low risk. Additional problems involve compliance with drug intake, adverse effects and high costs (for visits, not drugs) when lower BP goals are recommended for a great number of the adult population. One way for better BP control and compliance is to encourage patients to use home BP measurements more and also trust patients to adjust their own antihypertensive drug medication to achieve a better control [5]. European guidelines will be updated during 2018.

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122. Goals in lipids

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The recommendations of the European guidelines on cardiovascular prevention and management of dyslipidemias both published in 2016 clearly state that low-density lipoprotein cholesterol (LDL-C) remains the primary lipid target. In contrast to 2013 ACC/AHA guidelines which focused more on intensity categories of statin therapy in context of risk, the latest European guidelines have integrated absolute levels and percentage reduction as goals of LDL-C management in various risk groups. The goals in very high- and high-risk groups are defined as LDL-C less than 1.8 mmol/l (and at least 50% reduction those with baseline levels 1.8-3.5 mmol/l) and less than 2.6 mmol/l (and at least 50% reduction those with baseline levels 2.6-5.1 mmol/l), respectively. The optimal goal in low- to moderate-risk patients is less than 3.0 mmol/l, but the decision about therapy initiation should be individualized and carefully balanced and discussed with patient. The secondary targets include non-high density lipoprotein cholesterol (non-HDL-C), apolipoprotein B and total cholesterol, but only non-HDL-C optimal goals are defined as follows: less than 2.6 mmol/l, 3.3 mmol/l and 3.8 mmol/l in very high-, high- and moderate-risk patients, respectively. Triglycerides are not a target, but levels above 1.7 mmol/l indicate higher risk. Due to recent genetic and intervention studies HDL-C cannot be regarded as a lipid target anymore. It remains to be determined what are optimal lipid goals in various risk groups and what should be regarded as physiologic normal lipid levels. Studies with statins, ezetimibe and PCSK9 inhibitors indicate that it is safe to lower LDL-C levels to well below 1 mmol/l, even as low as 0.3-0.5 mmol/l, and there is an incremental beneficial effect on atherosclerosis non-progression and event reduction with such low levels.

123. Goals in glucose

Mart Roosimaa
North Estonia Medical Centre

Both type 1 and type 2 diabetes are known cardiovascular risk factors. Patients having diabetes are considered to be either high or very high cardiovascular risk by European Society of Cardiology depending on complications and other risk factors. Optimal glucose control is one of the key targets for reducing these risks. Current guidelines suggest glycated haemoglobin (HbA1c) of less than 7% as a target for most patients, together with fasting plasma glucose of 4,4 to 7,2 mmol/L. These targets are based on data from randomized controlled trials assessing different levels of glycaemic control (UKPDS, DCCT, ACCORD, ADVANCE, VADT) and their observational follow-up studies. In these trials up to 30% reduction in cardiovascular events has been observed after long-term (25 to 30 years) follow-up without the use of GLP-1 receptor agonists, DPP-4 and SGLT2 inhibitors. Even though there is clear cardiovascular benefit from optimal glycaemic control there is a marked lag time between adequate treatment and risk reduction. Therefore, more relaxed glycaemic targets, usually HbA1c less than 8 to 8,5%, are suggested by guidelines to be appropriate for patients with advanced complications, multiple comorbidities, recurrent hypoglycaemia, limited life expectancy or patients living in long term care facilities. While there have been no major changes in glycaemic targets in over a decade and the choice of medications has expanded rapidly, still at least one third of patients will not meet their targets both in USA and Europe.

124. History of the Baltic Atherosclerosis Society

Margus Viigimaa
North Estonia Medical Centre, Tallinn University of Technology, Estonia

The Baltic Atherosclerosis Society was founded during the 1st Baltic Lipid Conference on the 15th of April, 1998 in Tallinn. The mission of the Baltic Atherosclerosis Society is "...advancing and exchanging knowledge concerning the causes, natural history, treatment and prevention of atherosclerotic disease..." and it could be achieved by the "...concerted scientific and clinical discussions of new developments in basic research, diagnosis and therapy of atherosclerotic disease". "Atherosclerosis Memorandum" was approved on this congress and addressed to all Presidents and Prime ministers of three Baltic countries. The Memorandum has stressed very high cardiovascular mortality in Estonia, Latvia and Lithuania and has demonstrated urgent need to improve cardiovascular prevention including lifestyle changes and statin treatment.

The first Board members of the Society were: Margus Viigimaa (President, Estonia), Zita Kučinskienė (President-elect, Lithuania), Janika Kõrv (Secretary, Estonia), Guntis Bahs (Latvia), Andrejs Kalvelis (Latvia), Aleksandras Laucevičius (Lithuania) and Arvo Mesikepp (Estonia). Baltic Atherosclerosis Society has started to publish the Baltic Atherosclerosis Journal, which has been merged with the journal Seminars in Cardiovascular Medicine in 2001.

Next congresses of the Baltic Atherosclerosis Society were organized as follows. The 2nd Baltic Atherosclerosis Congress took place in Vilnius, Lithuania (2001) the 3rd in Riga, Latvia (2004), the 4th in Tallinn, Estonia (2007), the 5th in Vilnius, Lithuania (2010), the 6th in Riga, Latvia (2013). The 7th Congress of the Baltic Atherosclerosis Society is taking place in Tallinn on April 6-7, 2018.

125. From Biobanking to Precision Medicine and beyond: the Estonian Experience

Andres Metspalu
The Estonian Genome Center, Institute of Genomics, University of Tartu, Estonia

The Estonian Biobank was founded in 2000 as a population-based biobank. 18 years later, the biobank includes a collection of health and genetics data of around 52 000 people and by the end of the 2018 it will be increased to 152 000, or approximately 15% of the adult population. All participants of the biobank have donated blood samples for purification of DNA and plasma. The whole cohort of 152 000 will be genotyped with Illumina GSA array (currently 52 000). The Human Genes Research Act (from year 2000) allows regular updating of data through linkage to national registries enabling long-term follow-up of the cohort and to re-contact the gene donors. In the past few years increasing amount of attention has been placed on translating the results of genetic research to improve public health. A nationwide technical infrastructure (X-road) for the secure electronic exchange of medical data has also been established and is maintained by the state. This allows creating the disease (or life!) trajectories on all gene donors from the birth in the Estonian Biobank, where all contacts with the medical systems incl. ICD-10 diagnoses, prescriptions, lab data and EMR are included. Recently, we have completed the deep sequencing of the (~30X coverage, PCR-Free) whole genomes of 2,500 gene donors and in addition 2500 whole exomes. Using these data, we have demonstrated in the case of familiar hypercholesterolemia that "the genetics first approach" can discover many new FH patients not seen by medical system

before and over 50% of cases the treatment was changed. The initial cohort of 52 000 has been characterized for sequence variations (SNV) and imputed using the Estonian reference. We are conducting several pilot projects in order to work out the best ways to return the heath related research data - genetic risks scores (GRS) back to people in the biobank who are asking for it. For that purpose, we have developed the decision support tools for several major diseases like CAD, T2D, breast cancer etc. During the first contact with the genetic counsel and/or medical geneticist the rapport will be explained and if needed further recommendation given. It will be transferred to the medical system in next year and together with the RITA program on personalized medicine in two largest hospital in Estonia the personalized medicine as 4P medicine (personal, predictive, preventive and participatory) has reached to the point of no return.

126. Using the principles of stratified medicine to individualize treatment strategies for diabetic patients. Experience from the Latvian Genome Data Base

Valdis Pīrāgs
Hospital, University of Latvia, Pauls Stradiņš Clinical University

The main task of the stratified medicine is to identify subgroups of patients with particular responses to treatments. The Latvian Genome Data Base (LGDB) established in 2006 recruits volunteer patients from several hospitals as well as healthy volunteers. Currently it contains more than 33,000 tissue samples and phenotype data entries (1,5% of population). Our aim is to create a reliable and open resource for focused clinical trials in main diseases threatening the life expectancy and life quality, including cardiovascular and cerebrovascular diseases, oncology, diabetes and other metabolic diseases as well as certain monogenetic pathologies, e.g. familial hypercholesterolemia.

In 2008, we started the prospective follow–up study OPTIMED as a part of the Latvian National Research Program "Development of new prevention, treatment, diagnostics means and practices and biomedicine technologies for improvement of public health" involving 42 endocrinologists from health care centers and hospitals. The project was primarily focused on drug naïve Type 2 diabetes (T2D) patients. One week following the drug prescription, the doctors consulted their patients via phone in order to collect information about possible episodes of drug intolerance, the second visit was planned after 3 months, all following visits - every 6 months.

After we found an association between side-effects of metformin and two genetic variants of the organic cation transporter 1 (OCT1), additional recruitment of T2D patient with known history of metformin use and available HbA1c measurements (RetroOPTIMED study) was started. Altogether more than 600 patients were enrolled. Additionally, three novel genetic variations in the upstream region of organic cation transporter 2 (OCT2) and organic cation transporter 3 (OCT3) coding genes were shown to be associated with short-term efficiency of metformin therapy. In cooperation with international consortium MetGen a variation in the glucose transporter gene SLC2A2 associated with glycemic response to metformin was discovered.

127. Importance of data quality in nation-wide e-health system for personalized medicine decision support applications

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Implementation of Estonian nation-wide health information system (EHIS) in 2008 has paved the way for a development of new e-health services during the last decade. Besides of traditional e-services like digital prescription, electronic health record, patient portal, etc., also more personalized services are emerging – among of others, digital decision support systems (DDSS) for personalized medicine.

The architecture of EHIS allows secure internet-based data exchange between several health care data repositories. Against this backdrop, different queries and decision support algorithms could be applied across databases. Instead of applying DDSS on single electronic medical record only, data needed to feed algorithms could be retrieved from several databases across the country. As an example, drug-drug interaction database is applied all over Estonia since 2016 to find every single potential adverse effect while prescribing new drug.

Similar approach could be practiced to use DDSS in personalized medicine. DDSS in cardiovascular diseases or automatic risk score calculators in cancer care could be used for advising health care professionals or patient based on the genome data and medical data of the person retrieved from different repositories. Unfortunately, compared to drug-drug interaction database which is using only very limited types of data, implementation of DDSS in personalized medicine is much more complex. In later case both phenotype and genotype data are used which puts very high demands to data structuring and quality.

This presentation is to give an overview about

1. the importance of availability of structured computer readable data in electronic medical record,
2. challenges to enter high quality health and medical data by health care professionals,
3. the use of supporting DDSS applications to increase data quality,
4. secondary use of data in personalized medicine, and
5. different types of DDSS in health care.

2. POSTER ABSTRACTS

201. Genotype-first screening and management of familial hypercholesterolemia in a healthcare-associated biobank

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Large-scale biobanking efforts with extensive health records and genomic profiles provide a powerful platform to identify individuals with disease-predisposing genetic variants, to facilitate timely diagnosis and treatment. To explore the scope of genomics-guided strategy, we applied a genotype-first framework to familial hypercholesterolemia (FH), which is among the most common single-gene disorders and is significantly under-diagnosed and inadequately treated. We were able to (1) discover 29 individuals with FH-associated variants in LDLR, APOB or PCSK9 genes based on 30× whole-genome (n=2420) or 60× whole-exome sequence (n=2384); (2) via cascade screening of 64 relatives, identify 20 additional carriers; (3) via deep-phenotyping, detect overt or subclinical atherosclerosis in 57% of the variant carriers; and (4) via genetic and cardiologic counselling, provide personalized disease management and appropriate therapy initiation or modification. No FH-associated variant carriers, including those on statins, had achieved guideline-recommended LDL-C levels prior to the study. We reclassified 21 of the 42 study participants (50%) from having non-specific hypercholesterolemia or no diagnosis to having FH, including 13 (31%) who had not been recognized by routine medical care. At the end of the study, statin therapy was started or uptitrated for 67% of the carriers, and all participants were counselled on lifestyle modifications. Our systematic analysis highlights the power of genomics-guided phenotyping as a research tool to facilitate preventative clinical care within a healthcare-associated biobank.

202. Stockholm-Tartu Atherosclerosis Reverse Networks Engineering Task (STARNET) - A Unique biobank for studying the mechanisms of Coronary artery disease (CAD)

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The Aim of STARNET study is to enable systems genetic studies on layers of metabolic and vascularomics data to provide insights to the pathogenesis and

risk factors of CAD and by that to find preclinical biomarkers for early detection of patients at risk and to find novel therapeutic targets of CAD.

Methods: At cardiac surgery department in Tartu University Hospital, 1040 CAD and 260 control patients going through open heart surgery have been enrolled in the study. The STARNET database consists of extensive phenotypes (including BMI, syntax score, laboratory analysis) and the biobank of DNA, RNA and proteins from multiple tissues (blood, atherosclerosis-affected and atherosclerosis- free vessel walls, metabolic tissues- liver, skeletal muscle, omental and subcutaneous fat) collected during the perioperative period.

Results: The STARNET dataset has already proven its importance by means of being a disease-specific database for regaining and validating genetic risk loci identified by genome-wide association studies (GWAS). As an example, inference of gene regulatory single nucleotide polymorphisms (eSNPs) revealed that the known risk SNPs for LDL cholesterol and CAD linked to PCSK9 do not regulate PCSK9 expression in liver but in visceral abdominal fat emphasising the importance of obesity to understand risks and etiologies of dyslipidemias and premature CAD. However, unlike the case with PCSK9 where the associated risk SNP had a specific role in fat, most CAD risk SNPs identified by GWAS were found to have multiple Cis and Trans genes acting across several tissues whereof some also were shared between cardiometabolic diseases in regulatory-gene networks.

Conclusions: STARNET is a unique CAD-specific gene-tissue expression biobank with associated phenotypic and deep -omics data. Multiple modality disease-specific datasets like STARNET are needed to unravel the molecular networks underlying complex diseases like CAD and provide opportunities for novel diagnostic markers and therapeutic targets.

203. Endothelial progenitor cells, circulating microparticles and chemokine receptors in the evolution of acute myocardial infarction

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Objective: To compare two lipid-lowering strategies after acute miocardial infarction (AMI), concerning endothelial progenitor cells, circulating microparticles and monocyte chemokine receptors.

Methods: This is a PROBE (prospective, randomized, open label trial with blinded endpoints) study (ClinicalTrials.gov Identifier: NCT02428374). Adult patients (n=129) of both genders, ageing 18-75 years, were randomized in a 2x2 factorial design for treatment with rosuvastatin 20 mg/day or simvastatin 40 mg/day plus ezetimibe 10 mg/day as well as ticagrelor 90 mg 2x/day and clopidogrel 75 mg, in addition to conventional AMI therapy. Blood samples were collected at baseline, after one month and six months of treatment. Endothelial progenitor cells (CD34+/KDR+/CD133+) and circulating microparticles (from endothelial cells CD51+/CD105+, platelets CD42+/CD31+ and monocytes CD14+) were identified and characterized by flow cytometry. Monocyte chemokine receptors (CCR2, CCR5 and CX3CR1) were analyzed by real time PCR. Results: When compared during the six months of treatment, there were no diferences, between the four groups, in the percentage of endothelial progenitor cells, as well as for the number of circulating microparticles for the three subpopulations evaluated

(endothelial, platelet and monocytic microparticles) (p=ns, Kruskall-Wallis Test). However, considering the time of treatment (baseline x one month x six months), there were differences for endothelial and monocytic microparticles (p=0.033 and p=0.002 respectively, Friedman Test). The preliminary results related to chemokine receptors suggested an increase around 10 times in the expression of CCR2 and CX3CR1 after one month, followed by a reduction at six months of treatment, without differences for CCR5.

Conclusion: Our data suggest a time-dependent modulation of endothelial and monocytic microparticle levels, CCR2 and CX3CR1 expressions, without differences for platelet microparticles and endothelial progenitor cells. These changes do not seem to be affected by the choice of the lipid-lowering strategy.

204. A Comparison of Decision Tree Induction with Binary Logistic Regression for the Prediction of the Risk of Cardiovascular Diseases

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Abstract: The main purpose of this presentation was to compare traditional binary logistic regression analysis with decision tree analysis for the evaluation of the risk of cardiovascular diseases in adult urban men.

Subjects and methods: In our study, we used data from the Multifactorial Ischemic Heart Disease Prevention Study (MIHDPS). In the MIHDPS study, a random sample of male inhabitants of Kaunas city (Lithuania) aged 40–59 years was examined between 1977 and 1980. We analysed a sample of 5,626 men.

Results: Taking blood pressure lowering medicine, disability, intermittent claudication, regular smoking, a higher value of the body mass index, systolic blood pressure, age, total serum cholesterol, and walking in winter were associated with a higher probability of ishemic heart disease or cardiovascular diseases. Having more siblings and drinking alcohol were associated with a lower probability of these diseases.

Conclusions: The binary logistic regression method showed a very slightly lower level of errors than the decision tree did (the difference between the two methods was 0.1338 % for ishemic heart disease (IHD) and 0.1029% for cardiovascular disease (CVD), but for consumers, the decision tree is easier to understand and interpret the results. Both of these mehods are appropriate to analyze cardiovascular disease data.

205. Familial hypercholesterolemia management tool in the North Estonia Medical Centre

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Objectives: Familial hypercholesterolemia (FH) is underdiagnosed and undertreated in the general population. Our objective was to create a clinical tool which could improve correct diagnosis of FH, assemble FH patients into a clinical database and give further instructions about the best treatment approach according to individual patients Dutch Lipid Clinic Network Score (DLCNS).

Methods: An algorithm was introduced to North Estonia Centre of Medicine's IT system which made DLCNS mandatory if patients had LDL-cholesterol levels ≥5 mmol/L and they had been diagnosed

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with pure hypercholesterolemia (classified under E78.0 in ICD-10). The tool provides clinicians with a comfortable way to fill the score with explanations about each criteria and automatically groups patients into five subgroups in the clinical database according to the likeliness of FH diagnosis. Furthermore, the clinician gets clear instructions about the next steps of treatment based on individual score points.

Results: The tool launched in active use starting from 01.01.2018 and not only has it assembled first patients into the database, but also led to numerous physicians, nurses and other medical personnel seeking advice on other aspects of diagnosis and care in patients with familial hypercholesterolemia. The long term objective of this project is to spread the tool throughout other major hospitals of Estonia in order to enhance the correct diagnosis and treatment in Estonian population and prevent early morbidity and mortality in this highly susceptible and undertreated disease population.

206. Common polymorphisms are unlikely to play a major role in pseudo - FH development in Czech population

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Objective: Familial hypercholesterolemia (FH) is a serious disease, leading (if not treated) to premature myocardial infarction. FH is caused predominantly by mutations within the LDL receptor and APOB genes. Recently, gene scores have been defined, suggesting the existence of "pseudo - FH", clinically indistinguishable from classical FH, but without one causal mutation. In our study, we have analyzed 17 LDL-cholesterol associated (in general population) SNPs in Czech patients with FH.

Methods: Polymorphisms within PCSK9, NYNRIN, ST3G, SORT1 (two SNPs), ABCG8, LDLR, APOB (two SNPs), SLC22, PPP1R3, MYLIP, HFE, CETP, CILP/PBX4, BRAP and HMGCoAR were genotyped using Taqmann technology on an AB 7300 RT PCR cycler or using PCR-RFLP in 298 FH patients without the causal mutation and in 296 patients with the LDL receptor mutation.

Results: Frequencies of the individual genotypes significantly differ between two analyzed groups only in the case of CILP/PBX4 – rs1699148 ($P < 0.005$) and APOB – rs1367117 ($P < 0.005$) genes. Genotype frequencies of other polymorphisms did not differ between the analysed groups.

Conclusion: The results from our study suggest that common genetic variants will not play a major role in the "pseudo-FH" development in Czech population. Only two of seventeen analysed SNPs seem to be of clinical importance and to influence the development of the pseudo - FH phenotype.

Supported by Ministry of Health of the Czech Republic, grant nr. 15-28277A. All rights reserved.

207. Pigment epithelium derived factor in patients with type 2 diabetes: its relationship to endothelial hemostatic markers

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Introduction: Pigment epithelium derived factor (PEDF) belongs to relatively novel

adipokines, which may participate in insulin resistance and vascular damage. Aim of the study was to compare PEDF circulating levels in type 2 diabetes patients with and without metabolic syndrome (MS) to healthy controls and assess PEDF relations to risk cardiovascular factors and endothelial hemostatic markers.

Methods: Fifty individuals with type 2 diabetes (23 men, 27 women) and forty healthy controls (15 men, 25 women) were included to this pilot study. PEDF, anthropometric parameters, markers of insulin resistance and diabetes compensation were investigated in all subjects. Diabetics were divided into two groups: with (n=30; 11 men, 19 women) and without (n=20; 12 men, 8 women) MS. Von Willebrand factor (vWF), tissue plasminogen activator (t-PA) and plasminogen activator inhibitor-1 (PAI-1) served as markers of endothelial dysfunction.

Results: Compared to healthy controls only diabetics with MS had higher levels of PEDF [14160 (10240-16000) ng/ml versus 11120 (8560-14400) ng/ml; $p<0.05$]. In all subjects PEDF significantly ($p<0.05$) correlated: positively with BMI, waist circumference, hs-CRP, triglycerides, non-HDL cholesterol, apolipoprotein B, fasting glucose, glycated hemoglobin, C-peptide and insulin; negatively with HDL-cholesterol and apolipoprotein A1. Additionally, in diabetics with MS a negative correlation of PEDF with vWF (ρ =-0.46 $p < 0.05$) were found.

Conclusion: Patients with type 2 diabetes and MS have significantly higher levels of PEDF, which are associated with symptoms of MS and insulin resistance. A negative correlation of PEDF with vWF may point out its vascular protective role.

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208. PCSK9 Inhibitor Causes a Reduction in the Level of Oxidatively Modified Low-Density Lipoproteines in Patients with Atherosclerosis

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Objective: The effect of the cholesterol-lowering drug - inhibitor of protein convertase subtilisin/kexin type 9 (PCSK9) evolocumab of Amgen company (in a dose of 420 mg once a month) on the level of oxidatively modified LDL (ox-LDL) and the activity of antioxidant enzymes in the blood of patients with coronary atherosclerosis was investigated.

Methods: The level of oxidatively modified LDL (ox-LDL) was determined by the immunochemical method using the Mercodia Oxidized LDL ELISA test kits (Sweden).

Results: In our study the PCSK9 inhibitor reduced the LDL cholesterol level in patients with coronary atherosclerosis by more than 80% for 3 months. The level of ox-LDL progressively decreased after the administration of PCSK9 and remained at a reduced level (more than 2-fold) within 12 months after initiation of therapy. Revealed a strong positive correlation ($r = 0,79$; $p <0.01$) between the ox-LDL and LDL cholesterol levels. The activity of key antioxidant enzymes (SOD, GSH-peroxidase, catalase) in erythrocytes of patients with PCSK9 therapy did not significantly change over the whole period (12 months) of observation.

Conclusions: Thus, unlike statins, the cholesterol-lowering drug - inhibitor PCSK9 does not cause a decrease in the level of natural antioxidants and contrib-

utes to a decrease in the level of atherogenic oxidatively modified LDL.

ACKNOWLEDGMENT

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209. Plasma kynurenine pathway metabolites are associated with mortality in patients with predominantly ischemic heart failure

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Objective: Circulating concentrations of metabolites of tryptophan produced via the kynurenine pathway (kynurenines), are linked to all-cause mortality in coronary artery disease, but have not been extensively explored in patients with clinical heart failure. We aimed to compare plasma levels of kynurenines between patients with predominantly ischemic heart failure and controls, and to investigate whether kynurenines predict mortality.

Methods and results: The study included 202 patients with heart failure and 264 controls without heart disease (propensity score matched by age and gender). All participants underwent coronary angiography and cine ventriculography. Plasma kynurenines, pyridoxal 5'phosphate (PLP), C-reactive protein (CRP) and monocyte count were measured at baseline. Case-control differences were assessed by logistic regression and mortality-hazard by Cox regression. Results were adjusted for multiple testing. Ninety-four (47%) of the heart failure patients died during the follow-up period. Kynurenine (Kyn, [OR 1.65, $p < 0.001$]) and the kynurenine-tryptophan-ratio (KTR, [OR 1.63, $p < 0.001$]) were higher in patients with heart failure than in controls. KTR [HR 1.59, $p = 0.006$], 3-hydroxykynurenine (HK, [HR 1.65, $p < 0.001$]), and the ratio of HK to xanthurenic acid (HK/XA, [HR 1.67, $p < 0.001$]) were all associated with increased mortality.

Conclusion: Metabolites of the kynurenine pathway, related to innate immune activation and apoptosis, are increased in heart failure and associated with mortality. Whether these associations reflect mainly underlying causes that activate the pathway or effects of the kynurenines themselves remains undecided.

210. Comparison of atherosclerotic lesions in brachiocephalic and coronary arteries in famial hypercholesterolemia patients

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Objective: Early diagnosis of atherosclerosis in brachiocephalic arteries helps to identify very-high risk individuals among patients with familial hypercholesterolemia (FH). We explored how well does presence or absence of atherosclerosis in brachiocephalic arteries correspond to lesions in coronary arteries in FH patients.

Methods: Among 175 FH patients diagnosed at the Latvian Registry of FH, we selected patients who had undergone both coronary imaging (MS-CT or invasive

Table. Findings in brachiocephalic and coronary arteries (n=64).

Brachiocephalic arteries	Atherosclerosis in coronary arteries				
	Stenosis > 50%	Stenosis 10-50%	Plaque	No athero-sclerotic lesions	Total (100%)
Stenosis > 50%	6 (60%)	1 (10%)	2 (20%)	1 (10%)	10
Stenosis 10-50%	15 (62%)	4 (17%)	3 (13%)	2 (8%)	24
Plaque	4 (29%)	5 (36%)	2 (14%)	3 (21%)	14
No atherosclerotic lesions	4 (25%)	3 (19%)	3 (19%)	6 (37%)	16
Total	29 (45%)	13 (20%)	10 (16%)	12 (19%)	64

coronary angiography) and ultrasound of brachiocephalic arteries.

Results: The data on both coronary and brachiocephalic arteries were available for 64 patients (Table). Mean age (SD) was 53.7+13.4 years, and 20 (31.3%) were men. Among 16 (25%) patients with no evidence of brachiocephalic atherosclerosis, 10 (63%) had coronary atherosclerosis and 4 of them (25%) had a coronary stenosis >50%. Among 12 patients with no coronary lesions 6 (50%) had evidence of brachiocephalic disease. Only 6 (9.4% of all) patients had no atherosclerosis in both locations. Correlation between lesions and their severity in coronary and brachiocephalic arteries was significant (Spearman's rho=0.337, p=0.007).

Conclusions: The correlation between brachiocephalic and coronary atherosclerosis is low in patients with FH. Evidence of coronary atherosclerosis is found in majority of FH patients with normal brachiocephalic ultrasound findings. Absence of brachiocephalic atherosclerosis is not a reliable method to exclude very high risk in FH patients.

211. Targeted lipidomics of arterial stiffness and hemodynamics in atherosclerosis

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Objective: Metabolomics approach provides a detailed insight into lipid metabolism and allows to study the levels and roles of its numerous intermediates and products in the pathogenesis of cardiovascular disease (CVD). Our study aimed to investigate the relationship between the lipidomic profile, arterial function and hemodynamics in coronary artery disease (CAD) patients, peripheral arterial disease (PAD) patients and healthy controls.

Methods: We studied 52 patients with CAD, 32 patients with PAD, and 40 apparently healthy controls. All of them were male. Serum levels of 40 acylcarnitines, 76 phosphatidylcholines (PC) and 14 lysophosphatidylcholines (lysoPC) were determined with the AbsoluteIDQ™ p180 kit (BIOCRATES). Arterial applanation tonometry (Sphygmocor, Atcor Medical) was used for pulse wave analysis and

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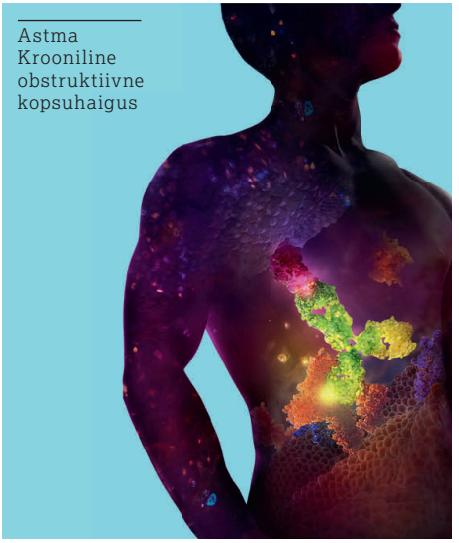

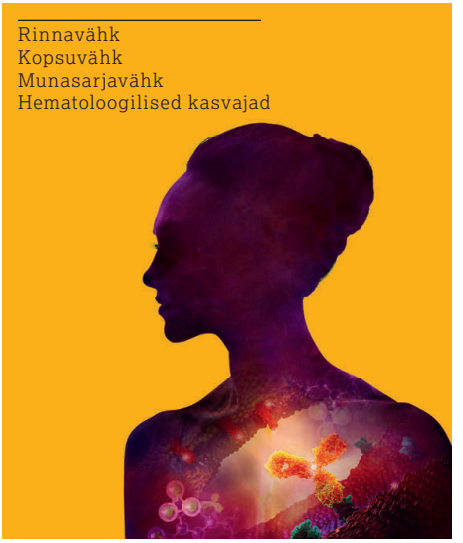

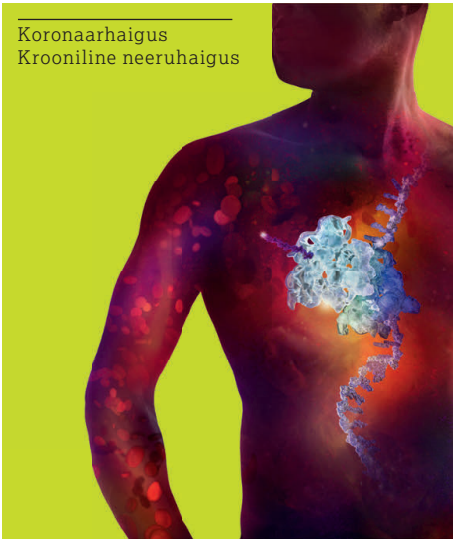

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- monoteraapiana, kui metformiin on talumatuse või vastunäidustuste tõttu sobimatu;
- lisaks teistele diabeediravimitele.

Annustamine ja manustamisviis: algannus on 0,6 mg liraglutiidi päevas. Vähemalt ühe nädala pärast tuleks annust suurendada 1,2 mg-ni. Vastavalt kliinilisele vastusele võib vähemalt ühe nädala mööduides suurendada annust 1,8 mg-ni vere glükoositaseme regulatsiooni edasiseks parandamiseks. Manustatakse üks kord päevas mis tahes kellaajal, sõltumata söögikordadest. Võib manustada s.c süstina kõhtu, reide või õlavarde. Ei tohi manustada veeni- ega lihasesiseselt. Kui Victoza't lisatakse sulfonüüluureale või basaalinsuliinile, tuleks kaaluda sulfonüüluurea annuse vähendamist, et vähendada hüpoglükeemia ohtu. Victoza® lisamisel metformiini- või metformiini ja tiosolidiindiooni kombineeritud ravile võivad metformiini ja tiosolidiindiooni annused jääda endiseks. Victoza't ei saa soovitada lõppstaadiumis neerukahjustusega või raske maksakahjustustega patsientide raviks. **Vastunäidustused:** ülitundlikkus toimeaine või ükskõik millise abiaine suhtes. **Hoiatused:** ei tohi kasutada 1. tüüpi diabeediga patsientidel ega diabeetilise ketoatsidoosi raviks. Victoza® ei asenda insuliini. Ei soovitata põletikulist soolehaigust ja diabeetilist gastropareesi põdevatele patsientidele. Kasutamise kogemus puudub NYHA IV klassi kongestiivse südamepuudulikkusega patsientide osas. GLP-1 retseptori agonistide kasutamisel on esinenud pankreatiiti. Patsiente tuleb teavitada ägeda pankreatiidi iseloomulikest sümptomitest. Kui kahtlustatakse pankreatiiti, tuleb Victoza® kasutamine katkestada. Kui ägeda pankreatiidi esinemine on tõendatud, siis ei tohi Victoza-ravi uuesti alustada. Kliiniliste uuringute käigus esines kilpnäärme kõrvaltoimeid, sh struumat, eriti eelnevate kilpnäärme haigustega patsientidel. Patsiente tuleb teavitada Victoza® gastrointestinaalsete kõrvaltoimetega kaasneda võivast dehüdratsiooni võimalikust ohust ja ettevaatusabinõudest, kuidas veekaotust vältida. **Rasedus ja imetamine:** ei tohi kasutada raseduse, raseduse planeerimise ja rinnaga toitmise ajal. **Kõrvaltoimed:** kõige sagedamini esinevad iiveldus ja kõhulahtisus. Sageli esinevad kõrvaltoimed on nina-neelupõletik, bronhiit, hüpoglükeemia, anoreksia, söögiisu vähenemine, peavalu, pearinglus, südame löögisageduse tõus, oksendamine, seedehäire, valud ülakõhus, kõhukinnisus, gastriit, kõhupuhitus, kõhu paisumine, gastroösofageaalne reflukshaigus, ebamugavustunne kõhus, hambavalu, lööve, väsimus, süstekoha reaktsioonid, lipaasi ja amülaasi taseme tõus. **Üleannustamine.** Kliinilistes uuringutes ja turuloleku ajal on teavitatud kuni 40-korda (72 mg) säilitusannust ületavatest annustest. Harilikult teatasid patsiendid raskest iiveldusest, rohkest oksendamisest ja kõhulahtisusest. Ükski patsient ei teatanud hüpoglükeemiast. Kõik patsiendid paranesid komplikatsioonideta. **Victoza® on retseptiravim.**

Viited: Marso SP, Daniels GH, Brown-Frandsen K, et al; the LEADER Steering Committee on behalf of the LEADER Trial Investigators. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2016;375(4): 311–322.

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carotid-femoral pulse wave velocity (cf-PWV) assessments.

Results: 1) Acylcarnitine profile (CAD patients vs healthy subjects): elevated levels of C16:1, C18:1, C3-DC(C4-OH), PC aa C40:6, Met-SO/Met were observed in the CAD group compared to the healthy controls. The cf-PWV showed positive correlations with C14, C16:1, (C2 + C3) / C0, C2 / C0 and the CPT-1 ratio for the CAD group. Moreover, PCA-derived factor 3 (acylcarnitines) proved to be an independent determinant of cf-PWV for these patients. 2) PC and lysoPC profiles (CAD patients vs PAD patients vs healthy subjects): decreased serum levels of several PC and lysoPC species (e.g., PC aa C28:1, PC aa C30:0, PC aa C32:2, PC ae C30:0 and PC ae C34:2, lysoPC a C18:2) were observed for both patient groups in comparison to the healthy controls. Further, a considerable number of PCs and lysoPCs were inversely related to either cf-PWV, heart rate, asymmetric dimethylarginine (ADMA) or ADMA/arginine only for patients.

Conclusions: In addition to the classical lipid-related CVD risk markers, the intermediates of lipid metabolism may serve as novel indicators for altered vascular function and hemodynamics.

212. Severe hypertriglyceridemia: clinical and laboratory characteristics

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Objective: Severe hypertriglyceridemia (SH) is defined as plasma concentration of triglycerides above 10mmol/l, which is determined by polygenic type of inheritance in the presence of additional triggers (insulin resistance, type 2 diabetes, alcohol abuse). It is associated with the risk of acute pancreatitis, while the risk of cardiovascular complications is not significantly elevated. The aim of this study is to characterize clinical and laboratory findings in patients with SH.

Methods. A cohort of unrelated patients with at SH was selected from our patient database. In total, 58 women and 187 men were identified, with an average age of 57.0±11.6years. Biochemical parameters were determined enzymatically using an automated analyzer.

Results: The median of highest TG was 18.3±25.11mmol/l, TC 9.89±6.32mmol/l, respectively. The latest measured values in the majority of patients treated with a statin and fenofibrate had median TG 3.19±6.78mmol/l and TC 5.05±2.27mmol/l. 15% of women and 19.8% of men had at least one attack of acute pancreatitis in their medical histories. Median BMI was 29.0±4.7kg/m^2 and glycemia 6.0±4.4mmol/l. Type 2 diabetes was diagnosed in 44.9% men and 57% women.

Conclusion: Manifestation of SH is triggered by a number of factors (insulin resistance, type 2 diabetes and obesity) as documented by their high prevalence in our cohort of patients. A history of acute pancreatitis was identified in 15% women and 19.8% men. This subgroup did not differ in serum lipid concentrations from the group without this history. Identification of other factors leading to acute pancreatitis in the context of SH requires further research.

ACKNOWLEDGEMENT:

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213. Comparison of two-year clinical outcomes after implantation of first and second generation drug-eluting stents in left main coronary artery stenosis in patients with hypercholesterolemia: real-life registry sub-analysis

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Objectives: Evaluate 2-year clinical outcomes of unprotected left main (LM) coronary artery percutaneous coronary intervention (PCI) in patients with hypercholesterolemia. We compare results in two patient groups who receive first (Delta1) and second (Delta2) generation drug eluting stents (DES).

Methods: Between October 2002 and June 2011 from two databases of unprotected LM PCI (n=895) we selected 689 (n=78.0%) patients with hypercholesterolemia, analyzed clinical, angiographic results: all-cause death, cardiac death, target vessel-related myocardial infarction (MI), target lesion revascularization (TLR), target vessel revascularization (TVR), scaffold thrombosis (ST), cerebrovascular events (CVE).

Results: Man population 69.5 % (n=485), mean age 65.97 ± 10.16 years. Active smoking 15.3% (n=113), diabetes mellitus 15.3% (n=107), previous CABG 1.6% (n=11), previous PCI 47.7% (n=333). Clinical follow-up reached 80.8% (n=564) patients. Mean stent length 19.40 ± 7.56 mm. LM ostial PCI 10.5% (n=73), body PCI 13.5% (n=94), distal PCI 66.2% (n=462). All cause death 2.6% (n=2) observed in Delta1, 2.1% (n=10) in Delta2 (p=0.776). The overall rate of all reason death was 7.7% (n=6) in Delta1 group vs Delta2 (n=4) (7.7% vs. 0.8%; p<0.001). TLR was observed in 5.1% (n=4) in Delta1 vs 2.7% (n=13) in Delta2 (p=0.0236). TVR 11.5% (n=9) in Delta 1 vs 7.2% (n=35) in Delta2 (p=0.18). MI was 7.7% (n=6) vs 0.8% in Delta2 (n=4); (p<0.001). CVE was observed 2.6% (n=2) in Delta 1 vs 0.4% (n=2) in Delta2 (p=0.04). Definite stent thrombosis1.5% (n=1) only in Delta1. CABG, cerebrovascular events did not differ significantly.

Conclusions: Second generation DES showed statistically better two-year results in patients with hypercholesterolemia and LM PCI in terms of all reason death, MI and stent thrombosis.

214. Comparison of two-year clinical outcomes after implantation of first and second generation drug-eluting stents in left main coronary artery stenosis in patients with diabetes mellitus: real-life registry sub-analysis of the Latvian Centre of Cardiology

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Objective: We evaluated 2-year clinical outcomes of unprotected left main (LM) coronary artery percutaneous coronary intervention (PCI) in patients with diabetes mellitus. We compare results in two patient groups with diabetes mellitus who receive first (Delta1) and second (Delta2) generation drug eluting stents (DES).

Methods: Between October 2002 and June 2011 there were two databases registry

of unprotected left main PCI (n=895) collected at the Latvian Center of Cardiology registry, a high-volume PCI center. From these two databases, we selected 136 (15.2%) patients with diabetes mellitus for follow-up analysis. In Delta1 (n=174) and Delta2 groups (n=712), 22 patients (12.6%) and 114 patients (16.1%) were diabetics, respectively. Both branch stenting was performed 15 patients (11.0%). Elective PCI were 117 (86.0%). During follow-up, we analyzed clinical and angiographic results such as all-cause death, cardiac death, target vessel-related myocardial infarction (MI), target lesion revascularization (TLR), target vessel revascularization (TVR), scaffold thrombosis (ST), cerebrovascular events (CVE).

Results: Clinical follow-up reached 106 (77.9%) patients. One in-hospital death was observed in patient from Delta1 group. Hospital MI were detected in 3 (2.2%) patients, mostly in Delta1 group as compared with Delta2 (2 (9.1%) vs. 1 (0.9%); p=0.017). There was no in-hospital TLR, TVR, CVE. The overall rate of all reason death in follow up period were 3 (2.8%), more frequent in Delta1 group as compared with Delta2 (2 (9.1%) vs. 1 (1.2%); p=0.047). MI were observed 4 (3.8%) patients, frequently in Delta1 group as compared with Delta2 (3 (13.6%) vs. 1 (1.2%); p=0.008). TLR and TVR did not show significant difference between these groups. Definite ST were detected in 2 (1.9%) patients from Delta1 group.

Conclusions: Second generation DES showed statistically better two-year results in patients with diabetes mellitus and LM PCI in terms of all reason death, MI and stent thrombosis.

215. Stockholm-Tartu Atherosclerosis Reverse Networks Engineering Task (STARNET)- A Systems Genetic Study of Atherosclerotic Cardiovascular Disease

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Introduction: Atherosclerotic cardiovascular disease is not a single locus disease, but a systemic and progressive disease. In 2015, the global death from atherosclerotic cardiovascular disease was 17.7 million , out of which 6.7 million were due to stroke. A better understanding at molecular and cellular levels is needed and can be achieved by using Systems Genetics; applying advanced algorithms on omics data sets to disclose networks driving molecular process in diseases.

Aim: The STARNET study was started initially to study patients with coronary artery disease,but to extend the understanding of atherosclerosis systematically we have also included patients with severe carotid stenosis, which is another atherosclerotic cardiovascular disease with out good preclinical markers frequently diagnosed only after a clinical event.

Methods: 220 patients who underwent carotid endarterectomy due to severe carotid stenosis have been enrolled at the Department of Vascular surgery, Tartu University Hospital. Phenotypic data along with a biobank of DNA, RNA from multiple tissues (blood, metabolic tissues- skeletal muscle, subcutaneous fat, atherosclerotic carotid plaque) is collected during the peri-operative period. The atherosclerotic plaque is also stored in OCT media for immuno-histologic analysis. The central cellular pathway of atherosclerosis being the monocyte-macrophage-foam cell is also studied. Single cell RNA sequencing

by FACS sorting of plaques will help to refine the data analysis at the level of individual plaque cells.

Conclusion: Characterization of cell populations in Carotid plaque along with clinical correlations and deep omics data will be an important resource to better understand the molecular underpining of carotid stenosis and as such pave the way for novel therapeutic targets and to early diagnose patients at risk for stroke.

216. First Time Study On Quality Of Life In Obese Children In Estonia

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Objective: To assesse health-related quality of life (HRQOL) in schoolage obese children who participated in the Clinical-Community Childhood Obesity Intervention project „Personalized approach in child obesity management", implemented in partnership with children's hospital and Foundation.

Methods: The Pediatric Quality of Life Inventory (PedsQoL™ 4.0 SF15, Varni, Seid&Rode,1999) is a generic HRQOL questionnaire consisting of 23 items rated on a 5-point Likert Scale with 4 domains: physical , emotional, social and school functioning. Scales are standardized with scores ranging from 0 to 100, with higher scores indicating better quality of life. Special tool in assessment of children's lifestyle, child's and parent' motivation by VAS (1-10) and selection of real goals to improve lifestyle was used. Demographic information included age, sex, and anthropometric data, body mass index (BMI) percentiles by CDC norms adjusted for age and sex (CDC,2000).

Participants: 25 obese children (BMI ≥ 95 percentile) and their parents completed separately PedsQoL™ inventory in physician's office. Statistical analysis were conducted using SPSS for Windows.

Results: Mean age of children was 12±2 years, among them 63% boys and 37% girls. General PedsQoL total score in children was 16 % lower and parent proxy report score was 44% lower than in healthy children. Largest difference comparing with healthy children was found in children self –reported and parents' proxy reported emotional functioning. Item-scale correlation demonstrated that most items for child self-report and all items for parents' proxy report exceeded the minimal reliability standard of 0,7.

Conclusion: The first examination of quality of life on all aspects of obese child functioning using standardized questionnaires showed agreement between mean pediatric and mean parents' proxy-reported scores. We proposed that studies of targeted interventions to treat obesity in children should include an assessment of HRQOL.

217. Chronic and oxidative stress association with total count of endothelial microvesicles in healthy young male plasma

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Objectives: The objective of this study was to test the correlation between

oxidative and chronic stress markers and and endothelial microvesicle count in peripheral blood.

Methods: Study included 81 males who were aged between 25 and 55 years and apparently healthy. Venous blood samples were labelled with anti-CD144-FITC, anti-CD105-BV421, anti-CD42a-PerCP, anti-CD62e-PE, anti-CD31-APCy7 and anti-CD61-APC (BD, San Jose) and tested using a BD LSR Fortessa cytometer (BD, San Jose). Events were gated on forward and side-scattered light parameters. Malondialdehyde and cortisol concentrations were measured using high performance liquid chromatography.

Results: Four populations of endothelial microvesicles expressing combination of CD105+, CD31+, CD144+, CD62e with CD42a- or CD42a+ markers were examined. We found correlations between malondialdehyde concentration and hair cortisol and total count of CD144+ microvesicles, weak correlations between CD62e+ endothelial microvesicles and diastolic blood pressure (P=0.003, r=0.324), and systolic blood pressure (P=0.016, r=0.267). Predictive model showed association between CD144+ microvesicle counts with cortisol and malondialdehyde concentrations also waist circumference.

Conclusions: In conclusion, our data and predictive model showed that the total count of CD144+ endothelial microvesicles were associated with stress related parameters - cortisol and malondialdehyde concentrations; expression of CD62e in various populations of endothelial microvesicles were associated with increased diastolic and systolic blood pressure.

218. The metabolic profile of ischemic heart disease patients with or without previous MI by serum 1H NMR is similar

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Ischemic heart disease (IHD) is the most common cause of death in the world. Metabolic profiling is an innovative and reliable new method to detect more sensitive biomarkers identifying altered health conditions specifically among the variety of patients with different risk factors. We evaluated the metabolic profile of filtered serum of IHD patients (ICD10 codes I20 and I25.2) using proton nuclear magnetic resonance spectroscopy (NMR).

The filtered venous serum from age and gender matched IHD patients ICD10 coded I20 (n=12), I25.2 (n=6) and control individuals (n=18) were analyzed using one-dimensional proton nuclear magnetic resonance (1H NMR) spectroscopy. These spectra were used for metabolic profiling and concentration calibration (Chenomx Inc) followed by statistical analysis using one-way ANOVA and principal component analysis (PCA).

Chemometrics analysis showed a significant distinction between the patients and control individuals. The IHD patients were exemplified by the increased concentration of acetylacetate, choline, pyruvate, betaine, formate and by the decreased concentration of alanine, creatine, glycine, histidine, lactate, proline, urea and other

biomolecules. The major implications found in the serum of IHD patients are related to energy metabolism and potentially altered microbiome.

PCA of 1H NMR detected serum metabolites exhibit a significant difference of IHD patients and control individuals. These data demonstrate that metabolomics approach may be useful for the early detection of IHD, for detection of synergistic pathways involved in the development of altered health conditions, and molecular understanding of particular health condition. The differences of the detected metabolic profile of ischemic patients with or without previous myocardial infarction appear to be minor.

This relatively inexpensive, non-invasive and reproducible approach may be useful for the molecular understanding and early prevention of IHD, improvement of surveillance and therapy. The study emerge the need for future investigations using larger cohort and possible longitudinal sight.