



CONFERENCES

S1-1

Utility of ambulatory blood pressure measurement in general practitioner 's offices

Ardeleanu Elena*, Dorobanțu Maria**

*University of Medicine and Pharmacy "Victor Babeș" Timișoara

** University of Medicine and Pharmacy "Carol Davila" București

The diagnosis and treatment of hypertension should remain in many cases a primary care function. The traditional office blood pressure (BP) measurement is limited in the amount of information that it can provide for an adequate management of hypertension. Out-of-office BP measurement with home blood pressure measurement (HBPM) and ambulatory blood pressure measurement (ABPM) are important adjunct to office BP, ABPM being considered superior to other methods. As hypertension is common in clinical practice, ABPM must be encouraged in general practice, being indispensable for the diagnosis and treatment of patients. ABPM offers informations about BP during daily activities and sleep. The difference between mean daytime and nighttime BP allows the identification of high-risk patients, independent of the BP obtained in the office. ABPM is correlated better than office BP or HBPM with organ damage and the prediction of cardiovascular morbidity and mortality. ABPM is indicated to be used in general practitioner 's offices when there is considerable variability of office BP over the same or different visits and discordance between office BP and HBPM. ABPM offers a substantial benefit to the diagnosis of white-coat, masked, resistant hypertension, suspected preeclampsia in pregnant women and the identification of hypotension. ABPM is useful for the evaluation of treatment adequacy and appropriate timing of medication. The use of ABPM can become in general practice a largely used method, being cost-effective and cost-saving, due to improved diagnostic accuracy and fewer hypertensive patients treated inappropriately. For a widely use of ABPM in general practice there is necessary to establish appropriate educational process and to improve the methods of analysing ABPM data.

S1-2

Evaluation and monitoring of patients with arterial hypertension and diabetes mellitus in the office of the general practitioner

Valeria Herdea

Romanian Association for Education in Hypertension (ARE-HTA)

Globally, 1 of 4 adults suffer from high blood pressure (HBP). In Romania the prevalence of diabetes mellitus (DM) reaches 11%, compared to 8.5% in the EU. The value of BP > 130/80 mmHg, remains a prognostic indicator in patients with DM. Uncontrolled hypertension and diabetes, are predictors of the occurrence and causes of chronic kidney disease (CKD). The prognosis is "command" by the intervention of risk factors: stress, smoking, uncontrolled diet, inactivity, obesity, dyslipidaemia, non-compliance to medical recommendations.

The monitoring model applied in GP's practice, is presented comparing two patients similar as gender, age, educational level, monitored for hypertension and diabetes approx. 7-year, having Score risk for CVD = 15. Particularity- different compliance for medical advices and treatment

Case 1- Reluctant to lifestyle chagement recommendation, made by medical staff, evolve with myocardial infarction (MI), stroke, CKD.

Case 2- compliant to medical recommendations, hypertension and glycemc control, preserved kidney function to 7 years after diagnosis of DM.

Management of the patient with hypertension and diabetes focuses on:

a. Initial evaluation

- Target organ damage;
- Risk level;
- Management plan: risk improvement, response assessment, therapy adjustment.

b. Active monitoring of the cardiovascular high risk patient

- Periodic evaluation- therapeutic control;
- complications;
- treatment

Essential in Gp's office:

- Patient education: understanding and active control of the disease (HBPM, blood sugar and weight control) complications prevention

- Early detection and correct diagnosis of target organ damage, personalizing patient monitoring,
- Psychological support for social reinsertion of the patient

Keyword- hypertension, diabetes, education, partnership, interdisciplinary team

S1-4

The crucial role of general practitioners for the detection and follow-up of arterial hypertension in pregnancy

Ileana Brînză

Romanian Association for Education in Hypertension (ARE-HTA)

Taking the pregnant women into evidence during the first weeks of pregnancy and monitoring her by an interdisciplinary team: general practitioner, gynecologist and cardiologist is essential in case of hypertension induced by pregnancy.

Ambulatory BP monitoring predicts more accurately the evolution of the patient.

Dynamically measuring proteinuria allows to establish the therapeutic behavior according to the type of preeclampsia, the health of the mother and fetus, the gestational age of the pregnancy.

The pregnancy with high obstetrical risk which is associated with gestational hypertension requires supervision adapted to each case, taking into account the form of preeclampsia, the health of the mother and fetus, the gestational age of the pregnancy, the availability of quick health services to the pregnant woman.

Early primary prevention for hypertension in pregnant women is effectively done through educational means and methods for all women of childbearing age, to undergo regular checks-ups before the pregnancy.

The general practitioner can provide a thorough history and careful monitoring of the pregnant woman for early identification of cardiovascular risk factors and correct therapy adjusted by a team of cardiologists and obstetricians. The general practitioner can also offer personalized advice on lifestyle improvement post-partum and can check the blood pressure of the patient periodically as well as other metabolic factors in order to decrease the future risk of CVD. Women who have recently given birth and presented gestational hypertension during pregnancy will be further monitored, including by the cardiologist annually, to prevent possible complications of a new pregnancy and to reduce maternal cardiac risk.

Keywords: Gestational hypertension, general practitioner, ambulatory BP monitoring, team supervision.

S1-5

Influence of risk factors on epigenetic mechanisms in hypertension

Prof. Dr. Adrian Restian

University of Medicine and Pharmacy, Carol Davila, Bucharest

Although aware of the importance of genetic factors as well as other risk factors in the occurrence of hypertension (HT), however it is not known precisely how these factors cooperate to determine the emergence and evolution of HT. Once were incriminated a series of genes that sometimes produced and sometimes not cause disease, it has been found that the expression of these genes is regulated by a number of epigenetic mechanisms depending on the environment. Thus, epigenetic mechanisms is a kind of interface between genome and environment, that is an interface between genes and risk factors involved in the occurrence of HT. The research of epigenetic showed that besides hypermethylation of any genes, the genome of patients with hypertension has a hypomethylation overall, that is an increase in the expression of many genes involved in the occurrence of HT, as well as the gene that synthesizes angiotensin converting enzyme, the gene that synthesizes the angiotensin receptors, the gene that synthesizes the norepinephrine reuptake enzyme and so on. This demonstrates that in addition to genes, which depends ultimately the structure of proteins involved as enzymes or chemical messengers in the occurrence of HT, a special importance have the epigenetic mechanisms, that regulates the gene expression according to environmental challenges, including the risk factor challenges. Therefore the paper discusses the influence of risk factors on epigenetic mechanisms of HT.

S2-4

Vitamin D and Arterial Hypertension

Sekib Sokolovic

University Clinical Center Sarajevo, Clinic for Heart, Blood Vessels and Rheumatic diseases, Medical Faculty of Sarajevo, Postintensive and Postsurgery Cardiology Care Department
Sarajevo, Bosnia and Herzegovina

Introduction: Antihypertensive effects of vit D are manifested in the suppression of Renin – angiotensin system (RAS) and parathyroid hormone (PTH) levels. Vitamin D has also renoprotective, anti-inflammatory and vasculoprotective properties. The low 25-hydroxyvitamin D is an independent risk factor for incident HTA (1) For each 10 ng/ml increase in vitamin D levels, there is 12% lower risk of developing arterial hypertension. The highest levels of vitamin D levels were associated with a 30% lower risk of developing HTA compared to the people with the lowest levels. (2)

Material and Method: The open prospectice clinical study was designed. Total of 88 patients with arterial hypertension compared to normotensives were tested for Vitamin 25(OH) D serum levels.

Results: Average blood pressure in a hypertensive group was 172/109mmHg and heart rate was 72/min. Average blood pressure in a normotensive group was 128/82mmHg and average heart rate was 89,5/min. Average vitamin D level in hypertensive patients was 16,9 ng/ml, while normotensive subjects had vitamin D 28 ng/ml.

Conclusion: The arterial hypertension in our study has been associated with a vitamin D defficiency. Normotensive subjects had a normal value of vitamin D approximately. Testing and treating patients with arterial hypertension for vitamin D deficiency should be performed.

1. Pilz S1, Tomaschitz A. Expert Rev Cardiovasc Ther. 2010 Nov;8(11):1599-608. doi: 10.1586/erc.10.142
2. Kunutsor, S. K. et al. Vitamin D and risk of future hypertension: meta-analysis of 283,537 participants. European Journal of Epidemiology 2013;28;205-221

S3-1

Subclinical cardiovascular disease assessment in primary prevention – is it necessary?!

Ovidiu Mitu*

*University of Medicine and Pharmacy “Grigore T. Popa” – Iasi

Introduction: Multiple risk charts, such as SCORE (Systematic Coronary Risk Evaluation Project) or Framingham have been proposed for cardiovascular risk estimation in general population. However, these charts have several limitations especially in intermediate risk subjects and asymptomatic population. Thus, subclinical cardiovascular disease (CVD) screening seems to represent a more precise risk evaluation in primary CVD prevention than risk charts by evaluating directly the atherosclerotic burden. Our aim was to evaluate the relationship and the accuracy of SCORE risk correlated to multiple methods for determining subclinical CVD in asymptomatic population.

Material and Methods: A cross-sectional study was performed and included one hundred and twenty subjects randomized from the general population. The individuals were aged 35-75, completely asymptomatic and under no chronic medical therapy. Cardiovascular risk factors were evaluated and the SCORE risk was computed. Subclinical atherosclerosis was assessed by various methods: intima-media thickness (cIMT) and plaque detection by carotid ultrasound; aortic pulse wave velocity (aPWV); left ventricular mass index (LVMI) and aortic atheromatosis (AA) by echocardiography; ankle-brachial index (ABI).

Results: Mean age was 52.01 ± 10.73 years and SCORE value was 2.95 ± 2.71 , 76% being in low to intermediate risk class. 64% of all individuals had markers of subclinical CVD and SCORE risk correlated positively with all parameters of subclinical CVD, except for ABI. In SCORE < 5, 60% had evidence of subclinical CVD. In multivariate analysis, only cIMT over 0.9 mm and increased aPWV significantly predicted high SCORE risk (OR 4.14, 95% CI: 1.42-12.15, $p=0.009$; respectively OR 1.41, 95% CI: 1.01 to 1.96, $p=0.039$). Positive linear relationship was noticed between 3 territories of subclinical CVD (cIMT, LVMI and aPWV) and SCORE risk (p for trend = 0.00005).

Conclusions: Increased SCORE values are associated with most atherosclerotic markers. As 60% of subjects in the low and intermediate risk class had subclinical CVD abnormalities, a more tailored subclinical CVD primary prevention should be encouraged.

S3-2

Comparison of Early-vs-Delayed Oral Beta-Blockers in Acute Coronary Syndromes and Effect on Outcomes

Bugiardini R, Cenko E, Ricci B, Vasiljevic Z, Dorobantu M, Kedev S, Vavlukis M, Kalpak O, Puddu PE, Gustiene O, Trninic D, Knežević B, Miličić D, Gale CP, Manfrini O, Koller A, Badimon L

Previous studies mainly focused on oral beta-blockers as part of therapy in the secondary prevention of acute coronary syndromes and consistently showed a reduction in long term cardiovascular mortality after discharge. The use of oral beta-blockers is currently under scrutiny as recent investigations have questioned its influence on short term outcomes after acute coronary syndromes.

The aim of this study was to determine if earlier administration of oral β blocker therapy in patients with acute coronary syndromes (ACSs) is associated with an increased short-term survival rate and improved left ventricular (LV) function. We studied 11,581 patients enrolled in the International Survey of Acute Coronary Syndromes in Transitional Countries registry from January 2010 to June 2014. Of these patients, 6,117 were excluded as they received intravenous β blockers or remained free of any β blocker treatment during hospital stay, 23 as timing of oral β blocker administration was unknown, and 182 patients because they died before oral β blockers could be given. The final study population comprised 5,259 patients. The primary outcome was the incidence of in-hospital mortality. The secondary outcome was the incidence of severe LV dysfunction defined as an ejection fraction $<40\%$ at hospital discharge. Oral β blockers were administered soon (≤ 24 hours) after hospital admission in 1,377 patients and later (>24 hours) during hospital stay in the remaining 3,882 patients. Early β blocker therapy was significantly associated with reduced in-hospital mortality (odds ratio 0.41, 95% CI 0.21 to 0.80) and reduced incidence of severe LV dysfunction (odds ratio 0.57, 95% CI 0.42 to 0.78). Significant mortality benefits with early β blocker therapy disappeared when patients with Killip class III/IV were included as dummy variables. The results were confirmed by propensity score-matched analyses. In conclusion, in patients with ACSs, earlier administration of oral β blocker therapy should be a priority with a greater probability of improving LV function and in-hospital survival rate. Patients presenting with acute pulmonary edema or cardiogenic shock should be excluded from this early treatment regimen.

What this study adds: Early oral beta-blocker administration within 24 hours after clinical presentation is a strong, independent predictor of survival and reduced incidence of severe left ventricular dysfunction. Benefits were independent of an invasive management strategy, but disappeared when patients with frank acute pulmonary edema or cardiogenic shock were included in the analysis. The timing of oral beta-blocker administration is important in the therapeutic strategies of an acute coronary syndrome as more favorable outcomes were observed with early delivery even after adjustment for concurrent adjunctive antithrombotic and anticoagulant therapy.

S3-3

Hypertension and Chronic Kidney Disease : Beyond the Guidelines

Delia Salaru

University of Medicine & Pharmacy “Gr. T. Popa” Iași

Hypertension (HTN) and chronic kidney disease (CKD) are closely associated in a cause and effect relationship. Declines in kidney function are typically associated with rises in blood pressure (BP), and sustained elevations in BP hasten the progression of kidney function decline.

Blockade of the renin-angiotensin system and aggressive blood pressure control are the mainstays of current management guidelines to retard the progression of most chronic kidney diseases, with additional specific therapy for associated comorbidities. However, many patients still progress to end-stage renal disease or die from cardiovascular causes despite effective medication use. This is particularly relevant to the population with chronic kidney disease in whom masked daytime or nocturnal hypertension and blood pressure lability are both widely prevalent and more difficult to control. Consequently, it is possible that the limited success currently being achieved in preventing or attenuating chronic kidney disease progression may be attributable in part to suboptimal 24-hour blood pressure control. Current issues in HTN patients with CKD include altered circadian rhythm of BP, timing of antihypertensive medication, dosing, BP targets, diagnostic challenges in evaluating secondary forms of HTN, and the role of salt restriction in CKD.

The interdependence between CKD and HTN complicates both diseases. Despite many advances in the management of hypertensive chronic kidney disease patients, there are still several gaps in our knowledge. The subject remains an important area for future research.

S4-2

Against renal denervation

Pr. Sverre E. Kjeldsen

Department of Cardiology, University of Oslo Hospital, Oslo (Norvegia/Norway)

Following the publication of the randomized controlled but open-label trial Symplicity HTN-2, catheter-based renal sympathetic denervation was proposed as a novel treatment for drug-resistant hypertension. Thousands of procedures were routinely performed in Europe, Australia and Asia, and many observational studies were published. A sudden shift from overoptimistic views to radical scepticism occurred later, when the large US randomized sham-controlled trial Symplicity HTN-3 failed to meet its primary blood pressure lowering efficacy endpoint. Experts are divided on the reasons accounting for the large discrepancy between the results of initial studies and those of Symplicity HTN-3 along with other randomized studies like OSLO, PRAGUE, SYMPPLICITY-F and SYMPPLICITY-J. Indeed, the blood pressure lowering effect associated with renal denervation was overestimated in initial trials due to various patient and physician-related biases, whereas it could have been underestimated in Symplicity HTN-3, which was well designed but not rigorously executed. Still, there is a large consensus on the need to further study catheter-based renal denervation in more controlled conditions, with particular emphasis on identification of predictors of blood pressure response. US and European experts have recently issued similar recommendations on design of upcoming trials, procedures, drug treatment, patient population and inclusion–exclusion criteria. Application of these new standards may represent a second chance for renal denervation to demonstrate—or not—its efficacy and safety in various patient populations. With its highly standardized treatment regimen, the French trial DENER-HTN paved the way for this new approach and may inspire upcoming studies testing novel renal denervation systems.

S5-3

Diuretics in hypertension – which, when, how much?

Paul Gusbeth-Tatomir, MD, PhD

Fresenius Nephrocare Dialysis Center and Doctor Luca Medical Center, Pitesti, Romania

One of the main pathogenic mechanisms in hypertension is salt and water retention. Diuretics are major antihypertensive drugs in the treatment of hypertensive diseases. Although extensively recommended by current clinical practice guidelines, diuretics are to some degree underutilized in the day-to-day clinical setting.

The author extensively reviews the main classes of diuretics in terms of action mechanisms, pharmacologic properties and clinical usefulness. Unfortunately, with the exception of thiazide and thiazide-like diuretics, other classes of diuretics rarely have a clear-cut indication in the vast majority of hypertensive patients. The case for first-line diuretic and for combination therapy in diabetic and non-diabetic hypertension are discussed. Thiazide and thiazide-like diuretics have almost no compelling counterindications and have shown significant impact in preventing heart failure, including related hospitalization and cardiac death.

In chronic kidney disease, loop diuretics are a mainstay in the therapy of the frequently severe hypertension. The role of kalium - sparing diuretics in resistant hypertension is also reviewed. Finally, potential significant adverse effects, often overrated, with thiazide diuretics such as new-onset diabetes mellitus, hypokalemia and hyponatremia are extensively discussed.

S5-4

Hypertensive Emergencies in Advanced Chronic Kidney Disease

Zorila Eugenia Corina ¹, Oana Stirbu ²

¹ Western University "V. Goldis" Arad, Emergency County Hospital Arad, 2th Clinic of Internal Medicine,

² Emergency County Hospital Arad, Nefrology

Fueled by a global pandemic of atherosclerosis and cardiovascular diseases, chronic kidney disease is a pressing public health challenge. Progression of chronic kidney disease depends on the control and evolution of hypertension. Marked elevation in systolic and diastolic blood pressure (BT), usually above 180/120 defines emergencies or urgencies. Hypertensive emergencies can occur in a known chronic renal hypertension within a renal parenchymal disease, by superimposing a renovascular hypertension or an acceleration of essential hypertension. The pathogenic mechanisms include excess fluids, and activation of the sympathetic and RAA system. The typical structural changes are fibrinoid necrosis of small arteries and arterioles in the brain and kidney. Other findings show injury of the affected organs, e.g. cerebral edema and rarely thrombotic microangiopathy, in particular if associated a collagen disease (scleroderma). In chronic hypertension an emergency does not affect target organ because of autoregulation. This mechanism is present in the brain and kidneys and involves L-type calcium channels

The diagnostic evaluation for hypertensive emergencies and urgencies includes the history of the patient, repeated BT measurements, physical examination, laboratory tests, electrocardiography, renal ultrasounds, and further investigation brain CT or MRI, echocardiography, etc

For the treatment the use of parenteral antihypertensive agents may be initiated in emergency room, the mean BP should be reduced by no more than 20-25% compared with the initial values within the first hour. The diastolic BP target is between 100-110mm Hg, with the assesment of the patient's volume status .Exceptions to these treatments recommendation include the patients with acute stroke, and with aortic dissection who should have their systolic BP less than 100mmHg.

S8-1

The role of perivascular fat in arterial function in hypertension and diabetes.

**Sophie Saxton, Charlotte Bussey, Ben Clark, Robert Aldous,
Sarah Withers, Anthony Heagerty**

Institute of Cardiovascular Sciences, The University of Manchester, Core Technology Facility,
46 Grafton Street, Manchester M13 9NT UK

There is increasing interest in adipocyte tissue depots because they represent highly efficient cells which are producing a large variety of substances including vaso-constrictor and dilator molecules. In consequence perivascular adipose tissue (PVAT) may have a haemodynamically important role to play in health which may be disordered in diseases such as hypertension and diabetes. Our initial work in small arteries from healthy humans has demonstrated that PVAT can release adiponectin and induce relaxation. This appears to be mediated by the stimulation of β_3 -adrenoreceptors located on the adipocyte plasma membrane which induce the production of adipocyte derived nitric oxide and downstream this increases the bioavailability of adiponectin. This sequence of events can be reproduced using stimulation of endogenous sympathomimetic nerve fibres found to be running through the adipose tissue depot. In obesity this mechanism is deranged and the relaxation is lost which will lead to an increase in tone with a rise in blood pressure and insulin resistance. Subsequent studies have demonstrated that obese PVAT is inflamed and the cytokines responsible for this are interfering with the bioavailability of adiponectin. Our most recent studies have looked at weight reducing surgery in humans and small animal dieting to reduce obesity, both of which have been demonstrated to improve PVAT function with a fall in blood pressure and an improvement in insulin resistance.

S8-3

Metabolic effects of antihypertensive medication

Cornelia Bala

“Iuliu Hațieganu” University of Medicine and Pharmacy,
Department of Diabetes, Nutrition and Metabolic Diseases, Cluj-Napoca, Romania

Hypertension, obesity and metabolic syndrome often coexist. According SEPHAR II, over 40% of hypertensive patients have obesity (BMI>30 kg/m²), over 60% abdominal obesity, 19.4% diabetes and 56.6% metabolic syndrome (NCEP ATP III). In this context, metabolic effects of long-term treatment with antihypertensive drugs have an important clinical significance.

The most important metabolic effect of antihypertensive medication is sought to be insulin resistance through impairment of microcirculation and reduced rate of intracellular glucose utilization. Nevertheless, the metabolic effects are different among antihypertensive drug classes, with some being considered neutral, others deleterious or even protective.

“Pure” beta blockers reduce glucose utilization and are associated with worsening of glucose tolerance and dyslipidemia. By contrast, the newer vasodilating beta blockers having an alpha blocking effect or releasing nitric oxide have neutral or even favorable metabolic effects.

Use of diuretics and metabolic risk still is the subject of debate, mainly because the heterogeneity of this class. Hydrochlorothiazide (HCTZ) was considered to have the worst metabolic profile, but a recent meta-analysis on head-to-head comparisons have found no detectable differences between HCTZ and indapamide. Nevertheless, the potential risk of new-onset diabetes should be considered with this class.

RAAS Inhibitors displayed favorable metabolic effects on rate of new-onset diabetes, blood glucose, HDL cholesterol and triglycerides and were shown to attenuate negative effects of thiazides when used in combination. Calcium channel blockers are metabolically neutral and became preferred in combination with RAAS inhibitors when combined therapy is needed. Less is known about metabolic effects of other antihypertensive drugs. Moxonidine and the related agent rilmenidine have been shown to have positive effects on glucose tolerance, insulin resistance and lipid profile in patients with metabolic syndrome, but current guidelines do not recommend them as first-line therapy in this subset of patients.

S8-4

Modern antihypertensive treatment in diabetic patients.

Ass Pr Dr Călin Pop

Emergency County Hospital Baia Mare, West University Vasile Goldis- Faculty of Medicine Arad

In the last guidelines from ESH/European Society of Cardiology the target from BP in diabetic patients is < 140/ 85 class I A indication. Low salt diet, weight loss, exercise and alcohol restriction, as nonpharmacological treatment has been shown in meta-analyses to lower blood pressure (BP). Lifestyle interventions should be encouraged in all patients but antihypertensive drugs are usually need to reach the BP target. Thiazide diuretics, β -blockers, calcium channel blockers (CCBs), ACEis and angiotensin II receptor blockers (ARBs) are recommended for initiation and maintenance of antihypertensive treatment either as monotherapy or in selected combinations. Treatment should be individualized according to concomitant risk factors and diseases, and depend on age, biochemical and hemodynamic conditions of the patients. A blocker of the renin-angiotensin system (RAS) should almost invariably be included because of the evidence of its superior protective effects, especially in patients with diabetic nephropathy. Large hypertension and heart failure trials have also reported an impact on diabetes development in favor of RAS blockade. The patients receiving both ARBs and ACEis had an increased risk of adverse side effects, and the ARB/ACEi combination is not recommended. Thiazid and thiazide like diuretics reduce BP especially by reversing the tendency to volume expansion in hypertensive diabetic patients. Low-diuretic dose treatment and combination treatment with other drugs (other than β -blockers) should be preferred to reduce metabolic unwanted effects. A combination of thiazide and a RAS blocker increases the antihypertensive effect of RAS blockers reducing the production of angiotensin II as the hypovolemia-induced rise in renin secretion. Loop diuretics are not used as routine antihypertensive treatment, except in patients with impaired renal function and/or heart failure. CCBs are very effective in lowering BP and have no adverse effects on lipid or carbohydrate metabolism. Compared with RAS blockers, CCBs are shown to be less effective in preventing heart failure. CCBs are well tolerated and are often needed to achieve a target value of BP, especially in combination treatment. β -blocker, usually not used as first line treatment, is a useful add-on antihypertensive agent, especially in patients with coronary artery disease, tachycardia and heart failure. However, β 1-selective blockers with vasodilating action (β 2-agonist or α -blockers) may be preferred in order to avoid metabolic interference. Aldosterone antagonists (especially spironolactone) is a very effective third or fourth line antihypertensive drug in selected patients, especially in those with low serum potassium. Other antihypertensive are not recommended as first line treatment: α -blockers in older men with symptomatic prostatism, it may be a useful add-on therapy. Combination therapy usually using two agents may also be considered as initial treatment of severe hypertension (i.e., SBP is 20 mmHg or DBP is 10 mmHg above target). Recommendation is based on the consideration that high-risk individuals like diabetic patients may experience an event soon



after treatment initiation and timely BP control is desirable. In light of the ACCOMPLISH trial results, a combination of an RAS blocker and CCB should probably be used as first-line combination treatment. A combination of a RAS blocker and a thiazide diuretic are also often recommended. New devices and techniques such as renal denervation are not included in standard treatment. Most recommendations in guidelines and trial results are based on office BP. However, the ESH/ESC guidelines recommend for diagnostic of hypertension widely utilization of ambulatory and home BP measurements.

Conclusions: Early detection and treatment of hypertension in diabetic patients decrease the total cardiovascular risk. ACEis and ARBs, diuretics, β -blockers, CCBs, can all be used, but most often a combination of two or more drugs is needed. A blocker of the RAS it is recommended to be a regular component of combination treatment and the one preferred when monotherapy is sufficient. Treatment strategies should consider interventions against others cardiovascular risk factors, such as lipid lowering, smoking cessation and normalization of hyperglycemia

S10-2

If the milligrams are the same, does adherence make the difference?

Daniela Bartos

Internal Medicine Department, Clinical Emergency Hospital Bucharest, Romania

In spite of the numerous available pharmacologic and non-pharmacologic methods for arterial hypertension (HTN) management, compliance and adherence to treatment remains a major challenge. Moreover, non-adherence appears as one of the most important factors leading to 'resistant' HTN.

There are several factors that lead to non-adherence such as social and economic-related factors (age, race, medication costs), patient related factors (frailty, level of disability, forgetfulness, anxiety) as well as medication related factors (length of treatment, complexity of treatment, unwanted side effects). Detecting non-adherence can be cumbersome and a few methods have been developed to objectively detect it such as urine analysis. Even though there is a long way until the routine use of these methods, studies up to date using objective measurements of adherence have shown that not complying with blood pressure (BP) lowering medication is frequent and more so in patients with suboptimal BP control as well as in patients referred for interventional anti-HTN treatment.

Therefore, efforts should be made to improve compliance to anti-HTN medication. There are now studies showing that simplification of treatment is the most effective intervention such as using extended-release formulations, multidrug pill and avoiding complicated schedule for drug administration. Along with these measures, several motivational strategies can be used such as reminder charts, telephone apps, electronic medication aid caps and so on.

Currently available data suggest a significant improvement in long-term cardiovascular outcome associated with high adherence to anti-HTN treatment which underscores the importance of patient education in the management of HTN.

S10-3

Time is blood pressure control!

Elisabeta Badila

Internal Medicine Department, Clinical Emergency Hospital Bucharest, Romania

Blood pressure (BP), like many other physiological variables, is under the influence of the circadian cycle, displaying a normal variability during the 24 hours of the day. Ambulatory automated BP measurement is a useful tool in describing the BP circadian rhythm and has allowed the identification of normal night time BP deeping with a morning rise and fluctuations related to daytime activity. Several major studies have shown a prognostic importance of alterations in BP circadian rhythm and is now well established that non-dipper pattern and isolated night time hypertension are predictors of worse cardiovascular outcome as well as that excessive BP morning surge is associated with an increased incidence of target organ damage, especially stroke. Therefore, normalisation of 24 hour BP pattern has become a new target in hypertension management and is associated with improved BP control and cardiovascular outcome. Chronotherapy is a branch of pharmacology who aims at increasing the efficacy and decreasing side effects of drugs by administering them at a certain time of day such that their 24-hour serum concentrations are synchronized with the biological rhythm that we want to influence. Chronotehrapy has become an important tool in managing hypertension with solid scientific data showing that the administration of one antihypertensive drug at night can improve BP control, can aid drug resistant hypertensive patients reach BP targets and can positively influence the dipping pattern. Therefore, chronotherapy has important practical applications and should routinely be considered in the management of hypertensive patients.

S11-1

Hypertension prevalence in Romania: preliminary results from sephar III survey

Maria Dorobantu

University of Medicine & Pharmacy “Carol Davila”

The two SEPHARs cross-sectional national surveys carried out in the last seven years, revealed that the tendency of HT's prevalence among romaninan adult population seems to be a descending one, with an increase in awareness, treatment and control of this condition. Still HT in Romania at this time still remains an “unsolved equation”. A recent analysis of SEPHAR II data regarding factors influencing BP control in romanian hypertensive patients concluded that increasing the awearness and level of education in regard to HT of general population will positively impact the trend of BP controll. In this current situation, Romanian Society of Hypertensions has organised a series of actions targeting the increase in the awearness and the level of education in regard to HT and continuos medical educational programs both for physicians and for nurses offering medical care to hypertensive patients.

However, in this moment, having only two national representative evaluations does not enable us to estimate a trend in HT prevalence, treatment, and control in Romania, that has a crucial importance for the development of prevention strategies at national level. Also, we need to know if RSH's actions had the estimated impact on HT prevalence, treatment, and control.

Those were the main premises for designing and conduction of a new epidemiologic national survey SEPHAR III, on a representative sample of approximately 2000 adults selected by means of a multi-stratified proportional sampling procedure (criteria for sample selection were: territorial regions (Romania's territory was divided in 7 regions plus the capital city Bucharest, based on the National Statistics Institute recommendations), locality type (cities with over 200 000 inhabitants, cities with 50 000-200 000 inhabitants, cities with less than 50 000 inhabitants, Commune), gender (male and female), age groups (18-24 years, 25-34 years, 35-44 years, 45-54 years, 55-64 years, 65-75 years, 75-80 years)

SEPHAR III Survey Conduction

The 2 study visits (at 4 days interval) took part in a special "medical caravan" entitled SEPHAR BUS - fully equipped with all the medical equipment and proper facilities for the conduction for the study, that also allow the team to travel across the country in all the recruitment sites.

The fieldwork team was made of cardiologists as primary investigators and senior residents in cardiology and nurses as sub-investigators, and a series of nurses designated by the central laboratory, responsible for blood and urine samples collection and their transport to the central laboratory.

Compared to SEPHAR I and II surveys, SEPHAR III's design brought the novelties of a complete target organ damage evaluation (by means of transthoracic echocardiography and Doppler ultrasound examination of the carotid arteries and measurement of ABI) , the inclusion of the MoCA, Epworth,

Morinski and depression questionnaires in the case report form, and the estimation of 24h urinary sodium excretion from morning sport urine samples.

SEPHAR III Preliminary results

Between November 16th – November 23rd 2015 and February 15th – April 25th 2016, a total number of 2065 adult subjects (18 – 80 years) who gave written informed consent to participate in the study were enrolled.

This interim analysis was performed on the data from 1776 enrolled subjects (86%).

Hypertension was defined as study SBP \geq 140mmHg and/or study DBP \geq 90mmHg at both study visits, or previously diagnosed HT under treatment during the last two weeks, regardless of BP values, were study SBP/DBP was calculated as the arithmetic mean of the 2nd and 3rd BP measurement of each study visit.

Hypertension control was defined as SBP < 140mmHg and DBP < 90mmHg in hypertensive subjects who were under treatment for at least 2 weeks before, taking into account the maximum value between the two SBP/DBP values from each visit.

Preliminary results revealed a HT general prevalence of 47.5%, in the majority previously diagnosed HT – 39.9%, and a general awareness of HT of 84%. While treatment of HT was recorded in 80.3% of the hypertensive patients, BP control of the treated hypertensive patients was 30.1%.

CONCLUSIONS

Hypertension prevalence in Romania is increasing, although together with an increase in awareness, treatment and control. Possible explanations of this trend might be unhealthy life-style and diet, increased salt-intake and increase in obesity and diabetes mellitus.

SEPHAR III data will offer an estimation of a real 11 – years trend in HT's prevalence, treatment, and control (2005-2016) and will serve as base for future prevention strategies urgently needed in our country!

S11-5

Arterial stiffness and myocardial ischemia

Darabont Roxana Oana – associate professor,

University of Medicine and Pharmacy “Carol Davila”, Discipline of Internal Medicine and Cardiology –
University Emergency Hospital, Bucharest

The effects of arterial stiffness on subclinical organ damage or cardiovascular mortality have been widely studied in the last years. There are physiopathological premises, experimental studies and epidemiological data which are sustaining the correlation of arterial stiffness with myocardial ischemia. During this lecture there will be presented: the pathological determinants and consequences of arterial stiffness - including myocardial ischemia, and the studies that have highlighted the association of arterial stiffness with myocardial ischemia. Arterial stiffness is characteristic for old patients, but, in certain conditions, can occur earlier in life (EVA - early vascular aging). Increased arterial stiffness leads to high pulse pressure (PP), especially of the central in regard with the brachial one, explained by the rise of systolic and the fall of diastolic blood pressure. As a consequence, myocardial ischemia can be induced by an imbalance between the high systolic workload and the decreased subendocardial flow supply. In experimental studies, like those conducted by Watanabe et al., more than 20 years ago, have been assessed the effects of a decreased aortic compliance on coronarian flow reserve, in the presence and the absence of epicardial coronary arteries stenosis. More recently, a series of studies have emphasized the prognostic implications of arterial stiffness in acute coronary syndromes. In acute myocardial infarction with ST elevation pulse wave velocity in aorta (PWVao) was identified as predictor of recovery of left ventricular infarction (Imbalzano et al., Int J Cardiovasc Imaging, 2015) and PP proved to be the stronger predictor of 30-day mortality among different blood pressure indices (Ma WF et al., Am J Hypertens., 2015). Moreover, in another study, PWVao was found as an independent risk factor of MACE for all STEMI and NSTEMI patients (Akkus O et al., Scientific World Journal, 2013).

S13-4

„The lower the better” also in HBP – an already old „novelty” – arguments offered by ABPM

Horia Balan, Livia Popescu

UMPh „CAROL DAVILA” – Bucharest, ROMANIA

The year 2013 seems to bring a new paradigm in HBP diagnosis and management.

In such a major health problem, that is expected to affect more than 1,5 billion subjects in 2025 all over the world, a proper diagnostic and management strategy being critical for a real prognostic improvement.

The most important scientific and media impact had SPRINT study, that showed (n = 9.361) a 25% reduction in the mortality and a 33% reduction in CV event rates by a more intensive BP lowering therapy, especially in those with significant co-morbidities, elderly ones, obese ones, etc.

But previous data/guidelines, as 2013 ISC guidelines (2013 ABPM guidelines for the diagnosis of adult hypertension, assessment of cardiovascular risk, and attainment of therapeutic goals), the results of the ongoing Hygia trial, of MAPEC trial (over 3.000 subjects with DM), 19 trials including more than 45.000 participants, offered the same conclusions: intensive BP lowering significantly induced major cardiovascular benefic effects, the greatest being obtained in those with DM or METS, CKD, obstructive sleep apnea/other sleep disorders. elderly, those with secondary or resistant hypertension, those with a Framingham risk assessment for CVD of $\geq 15\%$ over 10 years; and we must underline that even those considered to have a higher fraility (over 75 years) tolerated „at least as well” as younger ones the intensive treatment.

Thus, we will have to extrapolate the BP thresholds/results offered by these studies/guidelines in general population.

S14-4

Safety of antihypertensive drugs in the elderly

Cătălina Arsenescu Georgescu^{1,2}, MD, PhD, FESC, Larisa Anghel¹, MD, PhDs

¹ Cardiovascular Diseases Institute „Prof. Dr. George I. M. Georgescu” Iași, România, ² University of Medicine and Pharmacy „Grigore T. Popa” Iași, România

Worldwide, the population is aging and the elderly are the fastest growing population. Heart problems, including hypertension, become increasingly common with advancing age and may affect quality and also length of life. The elderly are not only a high-risk group in terms of prognosis but also have an increased risk of treatment related complications, because of the narrow therapeutic window which significantly affects their management. Taking into account that with aging there is a reduction in the total numbers of functioning nephrons and thereby a parallel decline in glomerular filtration rate and that many of the cardiovascular drugs are primarily excreted by the kidney, all drugs should be administered with caution. The elderly have also other comorbidities that could negatively influence the bioavailability of the antihypertensive drugs administered.

A diuretic and also a calcium channel blocker may be a good first step in treating hypertension in the elderly, but nevertheless taking into account some adverse effects that may occur more frequently at this age, such as hypotension, electrolyte disturbances or uremia. An ACE inhibitor or an angiotensin II receptor blocker may be given as a first step when there are signs of heart failure or left ventricular hypertrophy. The other antihypertensive drugs such as centrally-acting sympathetic agonists, have little role in the elderly, because of the side-effects.

Therefore, the appropriate use of cardiovascular drugs in the elderly requires knowledge of age-related changes in pharmacokinetic and pharmacodynamic effects of drugs and also the medical history and previous medication experiences.

S16-2

Small Arteries Disease In Hypertension Target Organs: What's New

Enrico Agabiti Rosei

Clinica Medica, Dept. of Clinical and Experimental Sciences, University of Brescia, Italy

It is now widely accepted that structural abnormalities of resistance vessels are common alterations associated with chronic hypertension. An increased arterial wall thickness together with a reduced lumen in small resistance arteries (internal diameter $< 350 \mu\text{m}$) may play an important role in the increase of vascular resistance, and may also be an adaptive response to the increased haemodynamic load. In the last years, many experimental studies have indicated that changes of small artery structure in hypertension are the consequence of either eutrophic or hypertrophic remodeling (re-arrangement of the same amount of wall material around a narrowed lumen or smooth muscle cell hypertrophy/hyperplasia, respectively). Mechanisms involved in the development of microvascular remodeling are still poorly understood; however, recently, an important role of the innate and adoptive immune system was demonstrated.

The interest of the researchers recently focused also on the anti-contractile properties of perivascular fat. These properties, probably mediated by the local production of adiponectin, seem to be lost in obesity and in other clinical conditions characterized by an increase in oxidative stress/low-grade inflammation.

Structural alterations of small resistance arteries, as indicated by an increased media to lumen ratio were demonstrated to be powerful predictor of cardiovascular events in a high risk population of patients with primary and secondary hypertension. The demonstration of prognostic importance of structural alterations of subcutaneous small resistance arteries was extended to patients with essential hypertension at low-moderate cardiovascular risk, and is present also when only major cardiovascular events (myocardial infarction, stroke and sudden death) are considered. The possible regression of vascular alterations is an appealing goal of antihypertensive treatment. A complete normalization of small resistance artery structure was demonstrated in hypertensive patients, after prolonged and effective therapy with dihydropyridine calcium channel blockers, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. No effect was observed with beta-blockers and diuretics despite similar blood pressure reduction. Recent data suggest also the presence of a prognostic relevance of the extent of the regression of vascular structural alterations. However, prospective studies, possibly with less-invasive approaches, are needed in order to clarify whether structural alterations in small resistance arteries may be definitely considered a surrogate endpoint in the evaluation of the effects of antihypertensive treatment. Recently, a non invasive evaluation of retinal arteriolar morphology by Scanning Laser Doppler Flowmetry was proposed. The information provided seems to be similar to those obtained with invasive assessments, thus opening interesting clinical perspectives in terms of risk stratification in hypertensive patients.

References

- 1) Mulvany MJ, Aalkjaer C. Structure and function of small arteries. *Physiol Rev* 1990; 70: 921-971
- 2) Folkow B. Physiological aspects of primary hypertension. *Physiol Rev* 1982; 62: 347-504.
- 3) Rizzoni D, Porteri E, Boari GEM, De Ciuceis C, Sleiman I, Muiesan ML, Castellano M, Miclini M, Agabiti-Rosei E. Prognostic significance of small artery structure in hypertension. *Circulation* 2003; 108: 2230-2235
- 4) Agabiti-Rosei E, Heagerty AM, Rizzoni D. Effects of antihypertensive treatment on small artery remodelling. *J Hypertens* 2009; 27:1107-1114.
- 5) Agabiti Rosei E, Rizzoni D. The effects of hypertension on the structure of human resistance arteries. In: *Comprehensive Hypertension*, Lip GYH and Hall JE Eds, Mosby Elsevier 2007, chapter 47, pp.579-590.
- 6) Agabiti Rosei C, Withers SB, Belcaid L, De Ciuceis C, Rizzoni D, Heagerty AM. Blockade of the renin-angiotensin system in small arteries and anticontractile function of perivascular adipose tissue. *J Hypertens* 2015; 33:1039-1045.

S17-4

Clinical imaging in hypertension

Carmen Ginghina, Professor MD PHD

University of Medicine & Pharmacy “Carol Davila”, Bucharest, Romania

Hypertensive heart disease (HHD) is the target organ response to systemic arterial hypertension. Imaging in HHD revolves around assessment of concentric hypertrophy, myocardial fibrosis and diastolic function of the left ventricle. Increased left ventricular mass (LVM), as related to the cardiac remodeling process in hypertension, is strongly associated with significant cardiovascular morbidity and mortality, independent of traditional risk factors, including hypertension itself. Myocardial fibrosis, a common end-point in HHT, has been incriminated in the development of diastolic dysfunction, whereas the latter has been shown to represent a link between hypertension and heart failure.

Estimation of LVM and diastolic function can be achieved by several imaging modalities, among which 2D echocardiography, despite its limitations, remains the pillar of imaging for the HHD. 3D echocardiography is a superior alternative, since it does not rely on geometrical assumptions, but its use is limited by lack of availability and user proficiency. Cardiovascular magnetic resonance is currently the gold standard in the imaging artillery of HHD, providing not only accurate measurements for the LVM, but also assessment of myocardial fibrosis, diastolic dysfunction and comprehensive investigation of a suspected cause of hypertension. Cardiac computed tomography also allows precise measurement of LVM, but it is less employed due to radiation exposure. SPECT can also be employed in LVM assessment, particularly in patients with concomitant coronary artery disease. Despite its ubiquitous use, chest X-ray is not routinely recommended in patients with uncomplicated hypertension, since cardiothoracic ratio is an unreliable indicator of left ventricular hypertrophy.

S18-1

Erectile dysfunction: the cardiologist's point of view

Michael Doulas, Associate Professor of Medicine

Thessaloniki, Greece and Washington, DC

Erectile dysfunction has been traditionally managed by urologists and psychiatrists. However, recent advances in the pathophysiology and therapy of erectile dysfunction have attracted the attention of other specialties, including cardiologists. Cardiologists need to pay attention in patients' sexual life for several reasons, including: a) increased prevalence of erectile dysfunction in cardiac patients, b) to avoid poor adherence to cardiovascular medications, c) drug interactions, d) the opportunity to identify asymptomatic coronary artery disease, and e) to provide proper sexual counseling in cardiac patients.

Erectile dysfunction is of vascular origin in the vast majority of cases, due to structural and vascular alterations of the penile arteries (diffuse atherosclerosis, reduced nitric oxide bioavailability). It is thus of no surprise that erectile dysfunction is highly prevalent not only in patients with overt cardiovascular disease (coronary artery disease, myocardial infarction, stroke, congestive heart failure) but also in patients with cardiovascular risk factors (arterial hypertension, diabetes mellitus, dyslipidemia, obesity).

Several cardiovascular drugs have been implicated into the development of erectile dysfunction. The association seems to be strong with some antihypertensive drugs, especially with centrally acting agents, diuretics, beta-blockers and aldosterone antagonists. Erectile dysfunction severely affects the quality of life of patients and their sexual partners, and frequently leads to drug discontinuation or poor adherence. Therefore, drugs with neutral or even positive effects on erectile function (nebulolol, angiotensin receptor blockers) are attractive options either as first choice for patients valuing sexual health or as substitutes for patients exhibiting erectile dysfunction with older drugs.

PDE-5 inhibitors are the cornerstone of erectile dysfunction management. PDE-5 inhibitors increase nitric oxide bioavailability and thus possess vasorelaxant properties. PDE-5 inhibitors usually exert weak hemodynamic effects, but occasionally hypotension might occur in a minority of patients. The co-administration of PDE-5 inhibitors and nitrates is absolutely contra-indicated due to the risk of severe hypotension and fainting, while the co-administration with alpha-blockers is no longer contra-indicated but requires precaution.

Erectile dysfunction usually precedes the occurrence of coronary artery disease by 2 to 5 years. This might be attributed to the smaller diameter of penile compared to coronary arteries, according to the artery size hypothesis. Therefore, erectile dysfunction provides a unique and excellent opportunity to identify asymptomatic coronary artery disease. There is no consensus as to when and how to screen for heart disease; however, it seems rational to perform screening as soon as erectile dysfunction appears (within 6 months) and to carry a stress test in moderate and high-risk patients.



Erectile dysfunction is a form of physical exercise. Therefore, high-risk patients need to visit a cardiologist and perform a treadmill exercise before engaging in sexual intercourse. Patients with overt cardiovascular disease, especially after an acute event, need sexual counseling by an experienced cardiologist as to when to restart sex, the intensity and the positions permitted, and the potential use of PDE-5 inhibitors.

Based on the above, it seems obvious that cardiologists are at the epicenter of sexual health, and the role of cardiologists is of paramount importance in the management of erectile dysfunction. Unfortunately, many cardiologists are not familiar with sexual health and feel reluctant to discuss about it, mainly due to restricted education (pre- and post-graduate).

S18-2

Prostate cancer in men - a motive of pre-surgery, especially post-surgery tension

Belinski Catalin – MD, urologist, FECSM

Prostate cancer is the most frequent form of cancer in men. In Europe, 1 in 10 men will have prostate cancer at one point. In 2008, 65 men out of 100.000 have been diagnosed with prostate cancer. In the incipient phases it is asymptomatic and the diagnostic is made with the help of prostate-specific antigen (PSA). This is a test recommended for all men above 50 years, annually or after 45 years for those who have a relative of first degree diagnosed with prostate cancer.

In Romania the prostate cancer diagnose has improved and at the same time treatment have diversified, the most utilised therapeutic method for patients in incipient stages is radical prostatectomy (open, laparoscopic or robotic), with very good results from an oncological point of view, but with a risk of between 25% and 75% of erectile dysfunction.

This presentation analyses the cause, but also technical possibilities of prevention and treatment, which will ensure the best quality of life possible for the patient.

S18-3

Sexual dysfunction - a couple's tension

Calomfirescu Adrian – clinical psychologist, psychotherapist, ECPS

Sexual dysfunction is one of the factors which severely influences a couple's relationship. Either as a main health cause, either secondary associated with another health problem, in many cases sexual dysfunction is a mixt problem (medical and psychological) in a more complicated context than that of the patient, the relationship of the couple. From a psychological point of view sexual dysfunction influences negatively both cognition and emotions, and can lead up to depression and anxiety. Both in turn cand further maintain ad aggravate the dysfunction. Up until the moment the patient comes for a consultation there has passed a sufficient amount of time in which this problem started to manifest itself and started to deteriorate the relationship. In this moment psychological support and therapy is necessary to rewind the changes that appeared on a personal and relationship level. A simple medical treatment can't repair months, if not years of personal and relationship dysfunction.

S18-4

Male hypogonadism and type 2 diabetes mellitus

Dr. Mihalca Radu – MD., PhD., endocrinologist, andrologist, FECSM

Sanamed Hospital, Bucuresti, Romania

Survival of the human species depends directly on the reproductive capacity and this is controlled by a complex network which involves the hypothalamus, the pituitary gland, gonads and the internal and external genital organs. The initiation of the process starts at the level of the central nervous system with neuroendocrine mechanisms integrated mainly at the level of the hypothalamus. The GnRH hypothalamic production induces in the pituitary gland the secretion of FSH and LH, in turn responsible for the steroidogenesis and the gonadic gametogenesis. Any chronic pathological condition has a direct effect on the reduction of production or action of GnRH and a reduction of the secretion of FSH and LH, also on a reduction of the gonadic production of testosterone (mixed hypogonadism). The reduction of sexual steroids in men has been correlated with an increase in morbidity and mortality, total but also cardio-vascular. Hormonal replacement therapy could have a double function, of catalyst of sexual function, but also of cardio-metabolic protection.

S18-5

Which are the treatment strategies when phosphodiesterase-5 inhibitors fail?

Sebastian Voinea

"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Center for Urology and Renal Transplantation, Fundeni Clinical Institute, Bucharest, Romania

Phosphodiesterase-5 (PDE5) inhibitors are the most frequent used treatment in patients with erectile dysfunction. In 20-60% of cases the patients fail to respond to PDE5 inhibitors. The purpose of the presentation is to describe a number of salvage techniques for these patients. First line techniques consist of: correct dose titration, correct timing, food issue, risk factor management and using testosterone in hypogonadic patients. The second line techniques consist of: continuous dosing and switching patients to other PDE5 inhibitors. When patients with erectile dysfunction fail to respond to PDE5 inhibitors this techniques should be used before initiating invasive therapies.

S18-6

Case study: Hypertension in a couple

Calomfirescu Nicolae MD., PhD., urologist, sexologist

This chosen case presents a couple in which both partners are undergoing treatment for hypertension. Taken with life, children, businesses, they didn't notice that sexually they don't function anymore. After many years and several discussions later they ask for a couple's sexology consultation. How was it possible that 12 years have passed? It shouldn't surprise us. There are solutions to this problem but they need to be accessed. This is a very frequent and true story of ignorance and denial of reality.

S19-2

Renal involvement in severe sepsis. Hemolytic uremic syndrome

Mihaela Balgradean

UMF Carol Davila. Clinical Emergency Hospital for Children “M.S. Curie”

Despite of the decrease in mortality caused by sepsis in the latest years pathology still remains a major cause of morbidity and mortality for the children younger than five years old. The kidney is involved, bacterial infections being the main cause. Author presents the renal involvement in the hemolytic uremic syndrome (HUS) with prodromal diarrhea, typical SHU, caused by Shiga-like toxins produced by enterohemorrhagic, invasive, type of Ecoli EHEC- Stx. HUS is a thrombotic microangiopathy defined by hemolytic anemia, thrombocytopenia and acute renal failure AKF. HUS, the most frequent and severe form of AKF during childhood, is not only a kidney disease, but a systemic one, it is responsible for severe complications and still high mortality rates during the acute phase of the disease. Stx are produced inside the intestine by enterohemorrhagic type of Ecoli and afterwards delivered into the blood flow. They are the main aggressive factors, being responsible for the endothelial microvascular lesions noticed in HUS. Endothelial tumefactions, accumulation of fibrinoid material and arteriolar thrombosis take place in afferent arterioles and, less frequent, in the efferent arterioles. The mortality rates is constantly associated with extrarenal involvement of the disease, with multiple organ failure, and mainly central nervous system involvement(cerebral edema, vascular injuries, intracranial hypertension) followed by seizures and other neurological signs early in the course of the disease. Some other HUS major complications are also described: colonic strictures, intestinal perforations, intussusception, billiary lithiasis, pancreatitis, diabetes, cardiac, pulmonary and muscle impairment, hypertension, and progressive renal disease or ESRD, in 4% of cases who need dialytic therapy.

S20-3

Hypertension and stroke: failure of cerebral autoregulation?

Akos Koller

University of Physical Education, Budapest, Department of Neurosurgery and Szentagothai Res Centre, University of Pecs, Hungary and Department of Physiology, New York Medical College, Valhalla, NY, USA

The cerebral vascular network is enclosed in the rigid cranium thus increases in pressures and/or volumes could elicit increases intracranial pressure, endangering the maintenance of appropriate blood flow to the brain tissues. Thus in the brain a very efficient autoregulation is present, which is an important feature of the cerebral blood flow (CBF). It is logical to assume that autoregulation is coupled to changes in hemodynamic forces and the vascular wall itself.

Pressure sensitive vasomotor response: Autoregulation of CBF first has been explained by the pressure-induced myogenic - smooth muscle dependent - responses of cerebral arteries. This response of vessels was first described by W. Bayliss early in the 20th century. Accordingly, when systemic blood pressure increases cerebral vessels constrict, which elevates cerebrovascular resistance. Because flow relates to the 4th power of radius the increased resistance maintains CBF close to the original level, despite elevation in pressure. In contrast, when systemic pressure decreases, dilation of cerebral vessels reduce cerebrovascular resistance, thereby maintaining relatively constant blood flow.

Flow sensitive vasomotor response: During increases in systemic pressure blood flow to the brain increases, as well. This led to the hypothesis that there is a vascular mechanism, which is sensitive to changes in blood flow. Indeed, our recent studies support this idea. We have found in the isolated middle cerebral arteries that - in the presence of constant pressure - increases in flow elicited constrictions. The constrictions are mediated by 20-HETE (20-hydroxieicosatetraenoic acid, a constrictor metabolite of arachidonic acid synthesized by cytochrome P450 hydroxylases) and reactive oxygen species (ROS). Thus simultaneous increases of hemodynamic forces amplify their action to protect the brain from high pressure and volume. Unfortunately, these mechanisms are not always working properly, especially in hypertension and aging, which could be responsible for the development of stroke. Indeed, our recent experiments, on so called stroke prone hypertensive rats, showed that the arterial mechanisms sensitive to changes in hemodynamic forces are impaired leading to early stroke. We assume that similar impairment may be present patients affected by stroke.

Elucidating the “missing” vasomotor mechanisms and their molecular basis will help to develop stroke prevention therapy in high risk patients.

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S20-4

Cardiomyocyte mitochondriology: networking, retrograde signaling, quality control

Lucia-Doina Popov

“Nicolae Simionescu” Institute of Cellular Biology and Pathology of the Romanian Academy

“Mitochondriology” of the cardiomyocyte (CM) is an ongoing field of research that comprises a variety of novel attributes of this organelle including the dynamic shape changes, the regulatory function, and the pathophysiological dysfunction. Although mitochondrion is known as energy powerhouse of any cell, in CM the target of generated ATP depends on the specific intracellular location of mitochondria within the CM. Thus, generation of the cardiac action potential, CM contraction, and transcription and translation processes are directed by subsarcolemmal, interfibrillar, and perinuclear mitochondria, respectively. Recent reports demonstrate that mitochondria form interconnected filamentous networks, move towards the cellular sites where energy supply is locally demanded, act as “quality controller”, spread signals to the rest of the cell (“retrograde signaling”), scavenge excess of reactive oxygen species produced by other cellular sources, and conclude on cells survival or death. This lecture provides morphological (transmission electron microscopy) evidence on mitochondrial networking, retrograde signaling and quality control installment in diabetic left ventricle CMs aiming a connection to the newly identified molecules/ mechanisms beyond these attributes. The main issues examined here are: (i) the inter-mitochondrial connection in adjacent/distal mitochondria, (ii) the nucleus and nucleolus interactions with mitochondrion, and (iii) the consequences of physical connectivity between mitochondria and sarcoplasmic reticulum. The lecture is concluded by the benefit of delivery of biologically active molecules to dysfunctional mammalian mitochondria, along with the potential transfer of “healthy” autologous mitochondria into dysfunctional CMs.

S20-7

Immunosuppressive drugs and hypertension in chronic kidney disease

Eugen Moța

University of Medicine & Pharmacy Craiova România

Some types of kidney damage occur through activation of the immune system causing inflammation. Lupus (SLE) affecting the kidney, vasculitis, and Goodpasture's disease are all diseases in which kidney damage is caused by inflammation. So are several types of glomerulonephritis. Immunosuppressive drugs and drugs that reduce inflammation are used to treat these diseases. Immunosuppressive drugs are essential in kidney transplants to dampen the immune system and prevent rejection. Some other kidney diseases are slower but also respond to treatment of this type, for example some causes of nephrotic syndrome.

Hypertension in kidney transplant recipients is a major "traditional" risk factor for atherosclerotic cardiovascular disease.

Atherosclerotic cardiovascular disease is the leading cause

of premature death and a major factor in death-censored graft failure in transplant recipients.

Before the US Food and Drug Administration approval of cyclosporine in 1983, nearly half of all transplant recipients had hypertension, an observation attributed at the time to activation of the renin-angiotensin system of either native kidney or transplant derivation.

Presently, >90% of calcineurin inhibitor-treated kidney transplant recipients have hypertension, and in one study, only 5% of kidney transplant recipients were normotensive, defined as ambulatory BP readings <130/80 mm Hg without treatment.

Risk factors for hypertension after transplant include:

- determinants of both donor and recipient origin
- factors that relate to the transplant process and immunosuppression

Optimal management of hypertension after transplant includes:

- manipulating immunotherapy when possible (for example, patients using cyclosporine often experience improved BP control after dose reduction or conversion to either tacrolimus or sirolimus).

Nondihydropyridine CCBs that pharmacokinetic drug interactions

occur when used with cyclosporine, tacrolimus, or sirolimus

Verapamil and diltiazem are potent inhibitors of cytochrome P450 C3A4

and cause plasma levels of the latter immunosuppressive drugs

to increase sharply soon after initiation.

Some types of kidney damage occur through activation of the immune system causing inflammation. Immunosuppressive drugs and drugs that reduce inflammation are used to treat these diseases.



HTN has been reported to occur in 85% to 95% of patients with CKD (stages 3–5). With each progressive stage of CKD, the rates of hypertension increased (approximately 36% in individuals with stage 1 CKD, increasing to 84% of individuals with stage 4 or 5 CKD). At stage 3 CKD and above, individuals were more likely to have hypertension than not.

Immunosuppressive drugs are essential in kidney transplants to dampen the immune system and prevent rejection. Hypertension is almost ubiquitous in kidney transplant recipients and is a risk factor for cardiovascular disease.

S20-9

Non-steroidal anti-inflammatory drugs and arterial hypertension

Daniela Opris

Spitalul Clinic Sfanta Maria, Clinica de Medicina Interna si Reumatologie, UMF Carol Davila Bucuresti

Non-steroidal anti-inflammatory drugs (NSAIDs) are a group of highly effective agents widely used in various medical specialties due to their analgesic, antipyretic and anti-inflammatory effects.

Most of the data existent till now showed that these drugs may increase blood pressure through a variety of mechanisms, related especially to renal prostaglandin synthesis inhibition from arachidonic acid via cyclooxygenase blockade (the main mechanism of action of NSAIDs). This effect is mainly seen in hypovolemic patients (eg old individuals, patients with congestive heart failure) and is associated with increased sodium and fluid retention. NSAIDs could cause elevations in systolic blood pressure, and little or no change in diastolic blood pressure. The incidence and levels of hypertension associated with COX-2 inhibitors are within the range of those observed with nonspecific NSAIDs.

Antihypertensive medications seem to have decreased effects with concomitant NSAID administration. A special attention should be paid to hypovolemic individuals treated concomitantly with ACE inhibitors and NSAIDs since both medications could impact glomerular flow leading to decreased glomerular rate and acute prerenal failure. This could be associated to potentially detrimental effects on patients, especially since individuals over age of sixty years, comprise of an important segment of high blood pressure population and also over half of regular users of NSAIDs.

Patients at risk for hypertension should be consequently closely monitored for changes in blood pressure during NSAID treatment and, if possible, when treating this group of patients, antiinflammatory drugs should be used at lower doses and for minimal efficient interval.

S22-1

Diabetes and hypertension: the unholy alliance in the target organ damage

Maria Mota, Denissa Turneanu

University of Medicine & Pharmacy Craiova, Romania

Cardiovascular disease morbidity-mortality is greater in people with type 2 diabetes mellitus (T2DM) or metabolic syndrome (MetS). The presence of target organ damage (TOD) increases the risk of cardiovascular complications independently of the existing estimated risk.

The prevalence of hypertension (HTN) is higher in patients with T1DM than in the general population (up to 49%) and more than 60% of patients diagnosed with T2DM have HTN.

DM and HTN are additive risk factors for cardiovascular disease.

Cardiovascular target organ damage may account for a part of the cardiovascular residual risk that remains, even after control of conventional risk factors.

The 2012 Joint European Society guidelines on CVD prevention recommended that patients with DM, and at least one other CV risk factor or target organ damage, should be considered to be at very high risk and all other patients with DM to be at high risk.

The common conditions coexisting with T2DM (e.g., HTN and dyslipidemia) are clear risk factors for atherosclerotic cardiovascular disease and diabetes itself confers independent risk.

The detrimental effects of glucose already occur with glycemic levels below the threshold for the diagnosis of diabetes. Early disglycemia caused by obesity-related insulin resistance or impaired insulin secretion is responsible for functional and structural alterations of the vessel wall culminating with diabetic vascular complications.

S23-2

The Heterogeneity of the Optimal Blood Pressure Values for Prevention of Stroke

Sorin Tuță

University of Medicine & Pharmacy „Carol Davila” Bucharest, National Institute of Neurology and Neurovascular Diseases Bucharest

Arterial hypertension is the main vascular risk factor for ischemic stroke and the direct cause for 90% of cerebral hemorrhage. Stroke is a heterogeneous disease from the point of view of pathology subtypes and etiology and thus the optimal blood pressure value for stroke prevention depends on stroke subtypes (ischemic, cerebral hemorrhage), timeline (acute or post-acute stroke), mechanisms of ischemia (hemodynamic, large arteries critical stenosis or small vessel disease), some associated therapies like acute stroke thrombolysis, or revascularization (carotid endarterectomy or stenting when deleterious cerebral reperfusion syndrome depends on blood pressure values).

The last guidelines recommend values of blood pressure up to 140/90mmHg or lower for stroke prevention, but some accept higher values up to 150-160mmHg for older patients, this higher values generating some controversies. For the very old patients with cognitive impairment diastolic blood pressure under 75mmHg should be avoided.

In the first 24-48 hours from onset of ischemic stroke blood pressure should not be decreased under 220/120mmHg, unless are not tolerated due to heart disease or thrombolysis is planned, a situation when the blood pressure is decreased under 180/110mmHg. For cerebral hemorrhage the higher blood pressure values are treated more intensive than for ischemic stroke, but the lower limit for the first 24 hours is controversial, the INTERACT study recommend 140mmHg for systolic values while the recent ATACH II trial did not find any advantage for survival, or improved neurologic deficit below 160mmHg values.

S25-1

Antihypertensive Treatment: Past, Present and Future

Alberto Zanchetti, Professor Emeritus University of Milan, Milan, Italy

Scientific Director, Istituto Auxologico Italiano, Milan, Italy

The development of a mercury sphygmomanometer for practical usage by Riva-Rocci in 1896-97 opened an era in which blood pressure became a quantity in which blood pressure (BP) became a quantity measurable at the bedside and therefore an object of clinical and scientific investigation.

In spite of the availability of BP measurement devices and the increasing awareness of the cardiovascular risk of high BP, antihypertensive treatment was delayed until the 1950-60s not only because of the lack of effective BP lowering drugs, but particularly because medical thought was dominated by the prejudice that hypertension was a compensatory mechanism “not to be tampered with”. With the development of several classes of effective and well tolerated antihypertensive drugs during the second half of the 20th century, this prejudice has been disproved by a series of randomized controlled trials (RCTs) that we have recently meta-analyzed showing all major types of cardiovascular (CV) events as well as mortality are significantly reduced by antihypertensive treatment.

The relative effectiveness of different BP lowering drug classes has also been investigated by head-to-head comparison of different drugs in the same RCT. Their meta-analysis has shown that, for similar BP reductions the effect of all antihypertensive drug classes on most outcomes are similar.

Present research is mostly concentrated on investigating at what BP and CV risk levels antihypertensive treatment should be initiated and to what levels BP should be brought by treatment is not available. Also in this area our recent meta-analyses have shed some light.

The major goal of hypertension research and management in the next decades is finding realistic solutions to the worldwide problem of insufficient BP control. While an earlier treatment initiation, a wider use of fixed association preparations and, hopefully, new drugs will certainly be helpful, the major obstacles to successful control are physicians' inertia and patients' lack of adherence. The future challenge for hypertension research is finding new means, new solutions to overcome these obstacles, common, in general, to chronic disease control.

S25-3

What target blood pressure levels are the optimal for cardiovascular prevention?

Antonio Coca

Hypertension and Vascular Risk Unit. Department of Internal Medicine. Hospital Clínic (IDIBAPS),
University of Barcelona, Spain

In the last 5 years several trials and meta-analysis on this issue have been published. Concerning SBP only very few trials have specifically investigated the possible benefits of lowering SBP below given cutoffs. In a recent meta-analysis of 32 trials including 128,232 individuals relative and absolute outcome reductions were significant for SBP differences (treated vs control) across 150 and 140 mmHg cutoffs, but below the cutoff of 130 mmHg only stroke and all-cause death were significantly reduced. No evidence is available that diabetic HT patients should have SBP < 130 mmHg and the only trial that directly explored the matter, the ACCORD study, was unable to show a reduction of CV endpoints in diabetic patients whose SBP was reduced to 119 mmHg as compared to 133 mmHg. The evidence from trials in elderly HT shows that incident CV events are significantly reduced when for SBP 150-140 mmHg. In patients after stroke, a systematic review of the relationship between BP reduction and secondary stroke prevention in a combined sample size of 15,527 subjects showed significant reductions in all recurrent strokes even in normotensive subjects. The overall reductions in stroke and all vascular events were related to the degree of BP lowering achieved in the range between 140-130 mmHg, but none of these studies achieved an average SBP < 130 mmHg. The SPS3 trial included 3,020 patients with lacunar (small-vessel disease) strokes randomized to 2 different SBP targets: <150 mmHg vs. <130 mmHg. The primary outcome of recurrent stroke tended to be lower in the lower-target group but differences were not significant (HR, 0.81; 95% CI, 0.64–1.03). The only trial specifically designed to explore this issue is the ongoing Stroke in Hypertension Optimal Treatment trial (SHOT). Recently, the SPRINT trial included 9,361 participants aged ≥ 50 years (diabetics and stroke survivors were excluded) who were randomly allocated to a standard treatment with SBP target <140 mmHg vs. to an intensive treatment with SBP target <120 mm Hg. Intensive treatment reduced the composite primary outcome by 25% (fatal and nonfatal MI, stroke, HF, or CV death), and total mortality by 27% compared to the standard target. Due to several reasons SPRINT results have to be seen with caution, particularly in elderly patients over 75 years. In conclusion, the general evidence-based recommendation can be given to aim at SBP < 140 mmHg in all HT patients independently of their level of cardiovascular risk, but we have to be cautious in recommending values below 130 mmHg. Some data suggest that values slightly below 130 mmHg may have some further beneficial effects as far as stroke is concerned.

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Cardiovascular effects by anti-diabetes drugs – An update 2016

Peter M Nilsson, MD, PhD

Lund University, Skåne University Hospital, Malmö, Sweden

For many years it has been difficult to show cardiovascular benefits by treatment of hyperglycaemia in type 2 diabetes (DM2). In the UKPDS study some effects were shown by use of metformin in obese DM2 patients, but in other studies the effects have been minor, or even adverse, for example in the ACCORD trial. Some attempts have been made to show effects based on meta-analyses, and these have shown a trend for a positive effect on non-fatal myocardial infarction. Now we have learned more about cardiovascular protection by use of newer anti-diabetes drugs in recent trials. Over the two last years we have been seen publications on three trials using DPP-4 inhibitors (SAVOR-TIMI, EXAMINE, TECOS) and two trials using a GLP-1 analogue (ELIXA, LEADER). In addition there was one publication on the effects of a new SGLT2 inhibitor (EMPA-REG Outcome Study).

In the DPP-4 studies safety was shown, except increased risk of heart failure (HF) in one study, but no added cardiovascular protection. This was also true for ELIXA, but in the LEADER study a significant decrease of the primary composite cardiovascular endpoint was reported by use of liraglutide versus placebo. Other benefits included a reduced cardiovascular mortality. Also in the EMPA-REG Outcome Study similar benefits were noted for empagliflozin versus placebo. The main effect for the outcome was a reduction of HF, but the exact mechanisms are still largely unknown. In summary, for the first time in 18 years following the UKPDS Study in 1998, now two large-scale intervention trials in type 2 diabetes have shown substantial risk reductions for cardiovascular disease. However, the background for these positive effects is still not clear and it seems that a simple reduction of hyperglycaemia per se cannot explain the findings.