

ESH UPDATE ON HYPERTENSION AND CARDIOVASCULAR PROTECTION

Brescia (Italy), January 12-14, 2017
Highlights

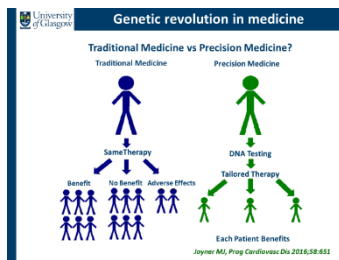
Introduction



Prof. Agabiti Rosei chairman of the symposium, opened the congress by highlighting the role of hypertension in cardiovascular morbidity and mortality. The speaker pointed out that in these last years the knowledge in pathophysiology of hypertension has been improved and new fields of research like genetics and proteomics raised. This symposium was a very important occasion for an update on hypertension and its new fields of research. This meeting was attended by many cardiologists and opinion leaders in hypertension, coming from all the world together with some young physicians and students in Medicine, with the aim to share knowledge for improving the educational skills of the young physicians in the new era of the Precision Medicine.

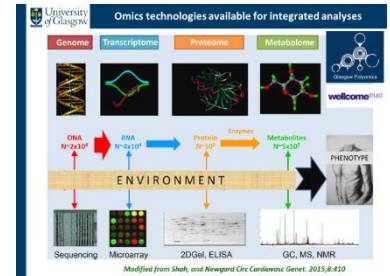
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Genetics of Hypertension and Precision Medicine

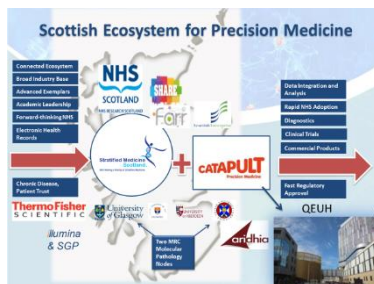


Genetic of Hypertension and Precision Medicine was the topic discussed by Prof. Dominiczak in her lecture. The speaker, coming from Glasgow (UK), went deeper in his talk by presenting data on the application of genetics in the diagnosis and treatment of Hypertension. More in particular Prof. Dominiczak spoke about the Genetic revolution in Medicine through the application of the GWAS technology and presented data given by

some studies like the Glasgow – Swedish GWAS of HTN study, a trial designed for the study of uromodulin and its activity on the regulation of sodium homeostasis in the kidney. Another very interesting study the speaker talked about, was the stratified clinical trial, a study running in three university: Glasgow, Edinburgh and Dundee on the repurposing of Torasemide based on a genetic make-up. In the second part of her presentation, the speaker talked about



the omics technology available for integrated analyses and, more in particular on proteomics and its application in many studies like the one running in pregnant women for the detection of new risk factors in blood and urine. Finally, Prof. Dominiczak spoke about the stratified Medicine Scotland -Innovation Centre and its 6 exemplars going on thanks to a very strong collaboration between Academy, Health System and Industry. In conclusion, the speaker highlighted that the application of precision medicine could produce a significant rise in the value of health.

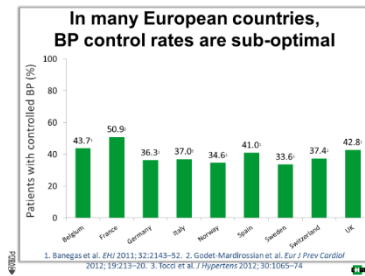


- What are the subgroups Precision Medicine is based on, from the speaker point of view?
- What's about the methodology to be applied for genome-wide associations studies?
- What are the 30 new associations across BP and HTN > 100 in total?
- What's about the exome chip analyses for the identification of the Genetic risk score?
- What are the main results of the Glasgow – Swedish GWAS of HTN study?
- What is the molecular pathways affecting sodium transport in the kidney, presented by the speaker?
- What's about uromodulin and Loop Diuretics?
- What are the Omics technologies available for integrated analyses?

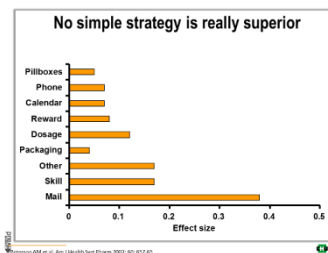
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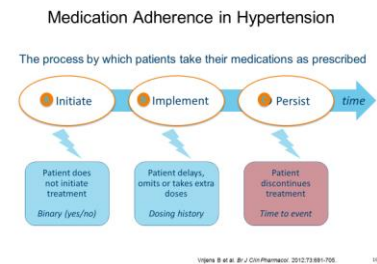
Adherence to antihypertensive treatment



patients take their medications as prescribed, by highlighting three key points: the initiation of the therapy, its implementation and the patient persistence by time. Talking about initiation Prof. Burnier pointed out the from 20% to 30% of patients do not initiate a new prescription and more in particular the speaker discussed about the methods to be implemented for improving drug adherence, starting from its measurement. In the main part of his presentation, Prof. Burnier raised a key question:



Prof. Burnier from Lausanne (CH), spoke about antihypertensive treatment and patient adherence, by presenting very interesting data on the BP control rates and the strategies to be implemented in order to improve patients' adherence to the antihypertensive treatment. More in particular the speaker talked about the process by which



“when a patient is not responding to therapy what is the problem?” The answer was divided into three points: non-responder, non-adherer and non-persistence. Finally, the speaker talked about the strategies for improving drug adherence. In conclusion Prof. Burnier pointed out that more health benefits would result from improving adherence to existing treatments than developing any new medical treatment.

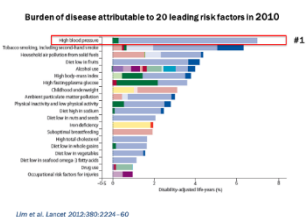
- What is the persistence to treatment in newly diagnosed hypertensive patients?
- What are the risk factors for poor adherence?
- What is the effect of renal denervation at six months based on the data presented by the speaker?
- How can we improve drug adherence?
- What are the methods of measuring adherence?
- What else can be done to support our patients in taking their treatments?

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Epidemiology of hypertension and related diseases. The use of big data

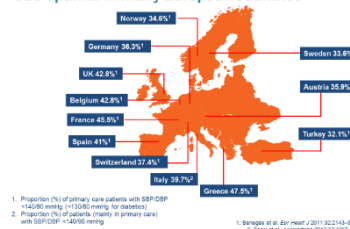
Disease and injury attributable to major risk factors, worldwide in 2010



The use of big data for the epidemiology of hypertension and related diseases, was the topic Prof. Redón spoke about in his talk. The speaker coming from Valencia (ES), presented a huge amount of data on Prevalence, Awareness, Treatment, and Control of Hypertension. More in particular Prof. Redon highlighted that in Europe is not easy to know how the hypertension is really controlled and in general there is

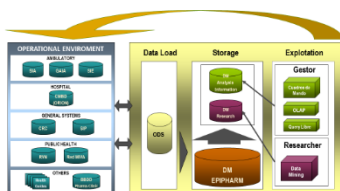
a large room for the improvement of BP control in all the european countries. In the main part of his presentation, the speaker talked about the methods to be applied for the improvement of BP control, by presenting data about the application of “Big Data” in

Room for improvement: BP control is sub-optimal in many European countries



health and more in particular in CVD prevention and control. These data are given by the Electronic Health Recording (EHR) in the Valencia Community program and more in particular, Prof. Redón presented a lot of data on the burden of risk factors, the surveillance of disease burden and costs, the attributable impact of CV risk factors and on the time-derived studies. Finally, the speaker talked about the potential of the EHRs to be applied in all the Europe countries and the challenges to be won.

EHR in the Valencia Community (ABUCASIS) General Structure

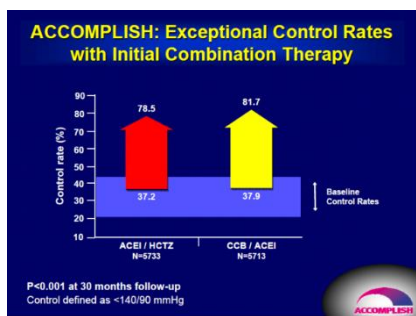


- Why the trend of decreasing BP values is lower in Europe than in other western countries?
- What’s about the awareness, treatment and control rates in England and Canada?
- What is the definition of Big Data in Health, from the speaker point of view?
- What are the main opportunities for CVD prevention/control with big-data from HER?
- What’s about the EHR in the Valencia Community (ABUCASIS) Program?
- What are the main examples from EHR of the Valencia Community Program?
- What are the key elements for a correct health system approach from the speaker point of view?

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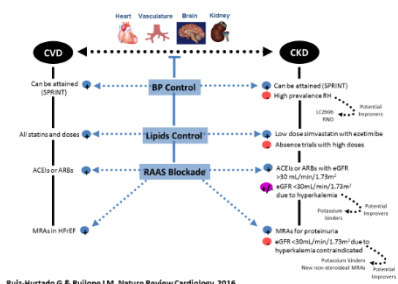
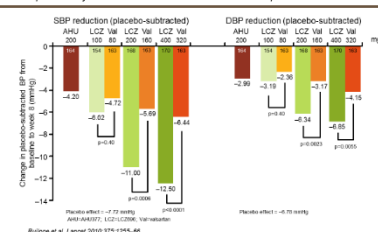
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Old and new drugs in hypertension



people starting from SBP levels about 140 mmHg, have no benefit in outcome with a further drop in BP levels, the speaker pointed out. Prof Ruilope went deeper in his lecture by highlighting the necessity of the combination therapy implementation for more than the 50% of hypertensive patients and in order to give a strong demonstration of this concept, presented a huge amount of data given by many clinical trials on antihypertensive combination-therapy. In the last part of his presentation, the speaker talked about the correlation between BP control, cardiovascular outcome, diabetes and chronic kidney disease.

LCZ696 in mild-to-moderate hypertension: Complementary effects of NEP inhibition and AT1 receptor blockade

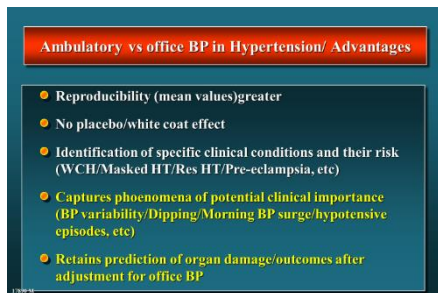


- What's about the Cardio Renal continuum?
- What are the grades of BP as defined by current guidelines?
- What's about the differences in BP control between Office and ABPM in treated hypertensives?
- What are the control rates with initial combination therapy in the ACCOMPLISH trial?
- Why we do not get a better BP control from the speaker point of view?
- What's about LCZ696 in mild-to-moderate hypertension?

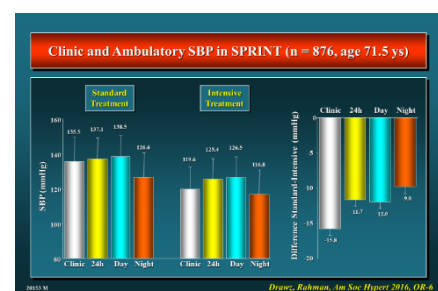
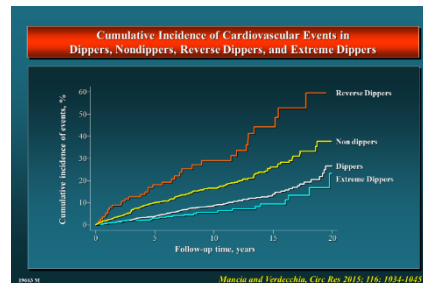
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Present status and future prospects of blood pressure measurement research



Prof. Mancia talked about the present status and the future perspectives of blood pressure measurement in the field of the Clinical Research. The speaker, coming from Milan (IT), introduced his talk by presenting data on different BP measurement methods like exercise blood pressure, central blood pressure, laboratory stressors measurements and out of office blood pressure, like ambulatory or home blood pressure. In the main part of his lecture, Prof. Mancia talked about the future role of out of office BP measurements compared to office BP measurements, by presenting a huge amount of data given by many clinical trials on antihypertensive therapy as PAMELA study. In the final



part of his presentation the speaker talked about the so called “SPRINT-like BP measurements” characterized by an automatic or semi-automatic BP measurement directly controlled by the patients. In conclusion, Prof. Mancia pointed out that despite the interest raised about the new BP measurements like out-of-office BP and SPRINT-like BP, office blood pressure will remain the standard method for the BP measurement for years in the future.

- What is the impact of Peripheral and Central PP on Clinical Outcomes in CAFE Study?
- What are the advantages of ambulatory vs office BP in Hypertension?
- Should Out-of office BP replace Office BP routinely?
- What is the risk of CV death as predicted by SBP in PAMELA?
- What are the limitations of ABP prediction of Outcomes?
- Is epidemiological evidence comparable for office and out-of-office BP?
- What is the relationship between 24h and Home BP in PAMELA?
- What’s about the SPRINT-like BP measurement method?

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Hypertension in children and adolescents



Hypertension in children and adolescents was the topic of Prof. Lurbe presentation. The speaker, coming from Valencia (ES), in his presentation, talked about the 2016 ESH guidelines on this topic, by highlighting that the old ESC guidelines published in 2009, were quite unsuitable for the underestimation of the phenomenon. The speaker went deeper in his lecture, by presenting the new topics of these guidelines, like the

2016 Guidelines: What is new?

- Pros and cons of screening
- Definition of HTN at 16 years or older
- Relevance of out of office and central BP measurement
- Clinical significance of isolated systolic hypertension
- Treatment strategies
- Follow-up
- Future research

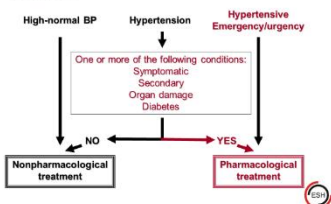
Guidelines content:
14 sections, 19 tables, 6 boxes, 4 figures



definition of HTN at 16 years or older, the relevance of out-of-office and central BP measurement, the clinical significance of isolated systolic hypertension, the treatment strategies, the follow-up strategies and finally the future research issues. Among these topics of relevance were the differences in hypertension definition for age and gender,

the recommendations for 24-hours ambulatory BP measurements, the criteria for the definition of hypertension-induced organ damage, the evaluation for secondary hypertension in very young children and adolescents, the recommendation about the time to start the antihypertensive treatment and finally, the blood pressure goals to be achieved. In the last part of her presentation Prof. Lurbe spoke about follow-up strategies and future research topics.

2016 Guidelines: When to initiate antihypertensive treatment?



- What is the purpose of the 2016 Guidelines?
- What is new in the 2016 Guidelines?
- What's about the Recommendation for screening?
- Why introduce new criteria in order to define hypertension?
- What's about the Recommendations for 24-hour ambulatory BP measurements?
- What's about Isolated systolic hypertension?
- What are the main criteria for the definition of hypertension-induced organ damage?

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Hypertension in pregnancy

Classification of hypertension in pregnancy

- pre-existing hypertension
- gestational hypertension
- pre-existing hypertension plus superimposed gestational hypertension with proteinuria
- antenatally unclassifiable hypertension

Hypertension in pregnancy was the topic at the core of Prof. Cifkova presentation. The speaker coming from Prague (CR), presented very interesting data, starting from the consideration that this disease is a major cause of maternal, fetal and neonatal morbidity and mortality. “Why is it difficult to treat hypertension in pregnancy?” with this question Prof. Cifkova addressed the

audience and, with the intention to find an exhaustive answer she went deeper in her talk, by presenting a huge amount of data given by many clinical trials on hypertension in pregnancy. More in particular the speaker talked about pre-eclampsia, pre-existing hypertension, gestational hypertension, cardiovascular changes in pregnancy and the so called “antenatally unclassifiable hypertension. In the final part of her presentation, Prof. Cifkova talked about the management of hypertension in pregnancy, with

Risk factors for preeclampsia

Risk factor	RR [95% CI]
Antiphospholipid antibodies (APLS)	9.72(4.34-21.75)
Previous history of preeclampsia	7.19(5.85-8.83)
Pre-existing diabetes	3.86(2.54-4.99)
Twin pregnancy (increased risk with multiples)	2.93(2.04-4.21)
Nulliparity	2.91(1.28-6.61)
Family history of preeclampsia	2.90(1.70-4.93)
Raised BMI before pregnancy	2.47(1.66-3.67)
Raised BMI at booking	1.55(1.28-1.88)
Maternal age \geq 40 years (primipara)	1.68(1.23-2.29)
Maternal age \geq 40 years (multipara)	1.96(1.34-2.87)
SBP \geq 150 mmHg at booking	2.37(1.78-3.15)
DBP \geq 90 mmHg at booking	1.38(1.01-1.87)
Inter-pregnancy interval: 10 years	1.12(1.11-1.13)

Adapted from Queensland Clin Guidelines, 2015

a particular attention to the non-pharmacological and the pharmacological management. More in particular the speaker presented data on the antihypertensive drugs used in pregnancy and the ones usually compatible with breastfeeding. In conclusion, Prof. Cifkova pointed out that in women with a history of pre-eclampsia and/or pregnancy induced hypertension, periodic screening of hypertension and DM should be considered.

Maternal antihypertensive medications usually compatible with breastfeeding

Captopril	Nadolol
Diltiazem	Nifedipine
Enalapril	Oxprenolol
Hydralazine	Propranolol
Hydrochlorothiazide	Spirolactone
Labetalol	Timolol
Methyldopa	Verapamil
Minoxidil	

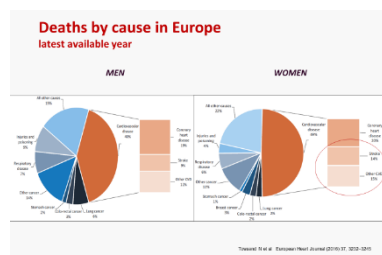
Pediatrics 2001;108:776-789

- Why it is difficult to treat hypertension in pregnancy
- What is the classification of hypertension in pregnancy?
- What are the main risk factors for pre-eclampsia?
- What are the BP thresholds for drug treatment initiation in pregnancy?
- What is the definition of hypertension in pregnancy?
- What are the principles for treatment of mild-to-moderate hypertension in pregnancy?
- What are the thresholds for drug treatment initiation?
- What are the antihypertensive drugs used in pregnancy and in breastfeeding time?

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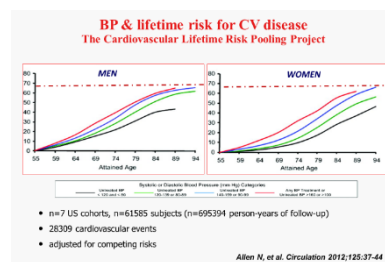
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Hypertension and organ damage in women

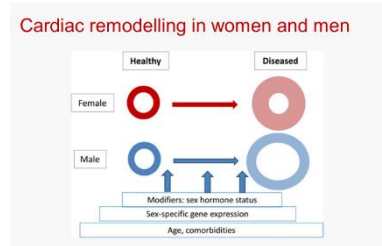


Prof. Muiesan, coming from Brescia (IT) spoke about hypertension and organ damage in women. At the beginning of his presentation, the speaker presented very interesting data on the death by cause in Europe divided between women and men where women die for more than men for stroke and CV diseases. Starting from these data, Prof. Muiesan spent the main part

of her presentation in order to explain the meaning of these differences, by highlighting that hypertension is more common in women than in man, more in particular in the elderly and that women have different cardiac adaptation mechanisms



compared to men, have higher aortic and local stiffness in large arteries than man and have an higher prevalence in reduced eGFR than man with the increasing of age. Finally, the speaker pointed out that even before the onset of cardiovascular disease, the women patients receive less satisfactory preventive management than men do and these differences are even more marked when the physician is a man.

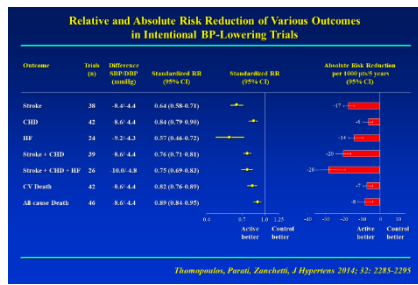


- What's about the BP & lifetime risk for CV disease referred to the Cardiovascular Lifetime Risk Pooling Project?
- What's about the cardiac remodelling in women and men?
- What is the impact of age and sex on LV function?
- What are the CV events in pts with LVH in the Brescia cohort?
- What are the gender differences in regression of electrocardiographic LVH during antihypertensive therapy?
- What are the gender differences in Left Ventricular structure and function during antihypertensive treatment in the LIFE study?

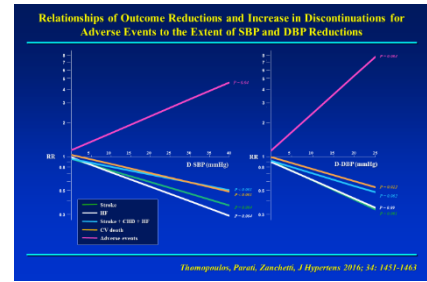
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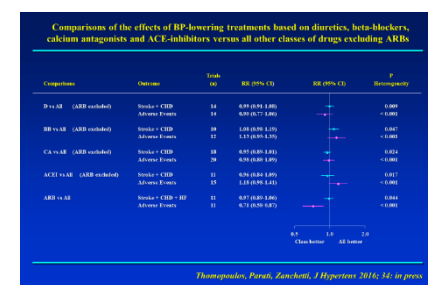
Recent meta-analyses of randomized trials



Recent meta-analyses of randomized trials running in patients affected by hypertension. was the topic Prof. Zanchetti spoke about. The speaker, coming from Milan (IT), presented very interesting data on the comparison of meta-analyses of BP-lowering trials with a particular attention to the relationship between outcome



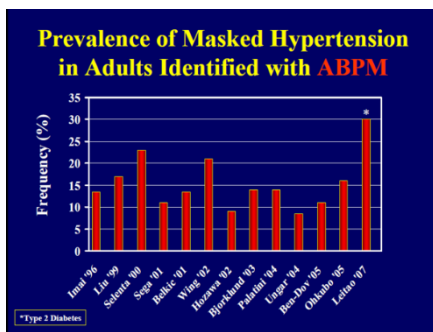
reductions and the extent of blood pressure reductions. The speaker went deeper in his lecture, by presenting some data on the benefits and the burdens of the antihypertensive treatment at different SBP targets. More in particular Prof. Zanchetti highlighted that the benefits of any treatment below the level of 130 mmHg become lower and at the same time there is a significant rise in adverse event rate. In the last part of his talk, the speaker presented other data given by a new meta-analysis conducted on the head-to-head comparison of BP-lowering drug classes, with the evidence of a higher burden of adverse event incidence with any drug class other than ARB. In conclusion, Prof. Zanchetti pointed out that any physician before deciding to intensify BP control should carefully evaluate the characteristics of the individual patient and the structure of the physician-patient relationship.



- What are the relationships of Outcome reductions to the extent of Blood Pressure reductions?
- What are the Relationships of Outcome reductions and increase in Discontinuations for adverse events to the extent of SBP and DBP reductions?
- What are the benefits and the burden of the Antihypertensive treatment at different SBP targets?
- What are the benefits and the burdens of various classes of antihypertensive treatments?
- What to decide about the benefits and the burdens of the antihypertensive treatment? For individual patients?

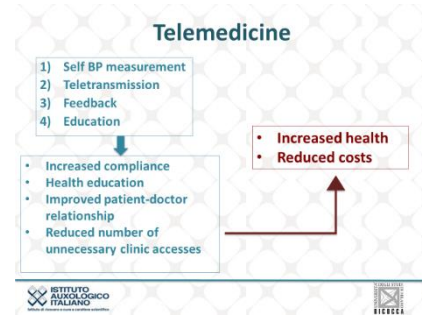
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BP measurement and control

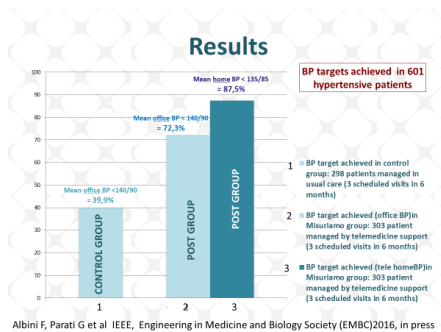


BP measurement and control was at the core of Prof. Parati presentation. The speaker, coming from Milan (IT), presented very interesting data, starting from unmet needs in hypertension management. More in particular the speaker talked about the importance of controlling out-of-office blood pressure and about the contributions from developments in

information and communication technology. Concerning on the control of out-of-office BP, the speaker presented very interesting data on masked hypertension, by pointing to its definition, prevalence, target organ damage, adverse event rate, diagnosis and treatment. In the second part of his lecture, Prof. Parati spoke about



telemedicine as a technology able to improve blood pressure control, patient compliance, patient-doctor relationship and at the same time to reduce costs. The speaker presented very interesting data given by the so called TeleBPCare study, a project on the home BP telemonitoring with the aim to improve hypertension control. Finally, the speaker spoke about another project the “patient Optimal Strategy for Treatment pilot study with the aim to an improvement in hypertension control and cardiovascular risk reduction.



- What are the unmet needs in hypertension management?
- What are the main inadequacies of traditional BP measurements?
- What are the clinical indications for out-of-office blood pressure measurement for diagnostic purposes?
- What’s about the definition of masked hypertension?
- What is the prevalence of masked hypertension in adult patients identified with ABPM?
- What’s about MASTER project?
- What is the aim of the TeleBPCare study?
- What is the current contribution from information technology?
- What’s about the Patient Optimal Strategy for Treatment (POST) – Pilot Study?

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Heart structure and function assessment

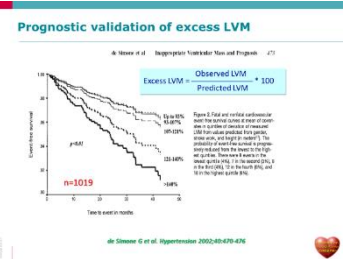
Imaging techniques for LV quantification.

We recommend concurrent measurement of blood pressure for estimating functional parameters

Scoring utility...

CRITICAL	USEFUL	USEFULNESS
LV geometry	LV performance	Do not want to say...
LA size	Output impedance	
LV chamber function	Aortic size	
LV chamber size	LV filling pressure	

Heart structure and function assessment was the topic discussed by Prof. de Simone. The speaker, coming from Naples (IT), presented very interesting data about target organ damages and the Imaging techniques available for their detection at the LV level. At the beginning of his presentation Prof. De Simone highlighted that 2D echocardiography is still the method of reference for arterial hypertension and presented a huge amount of data on the structural and functional parameters of any potential clinical utility like LV geometry, LV chamber function, LV wall mechanisms, LV pump performance, myocardial afterload and contractility, LA size, La function and Aortic size. In conclusion, the speaker pointed out that among these parameters the more useful are LV performance, Output impedance, Aortic size and LV filling pressure.

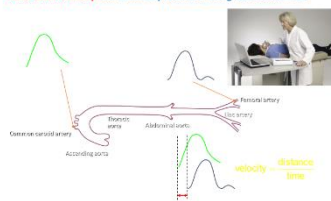


- What are the reasons for which 2D echocardiography is still the method of reference for arterial hypertension?
- What are the structural and functional parameters of potential clinical utility?
- 2-tiered or 4-tiered patterns of LVH?
- What are the different hemodynamic patterns in relation to LV geometry?
- What's about the prognostic validation of excess LVM?

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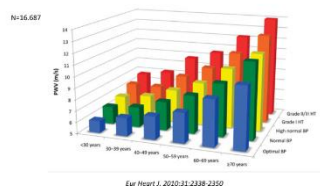
Large arteries and central BP evaluation

Pulse Wave Velocity Non-invasively recorded Along the Arterial Tree

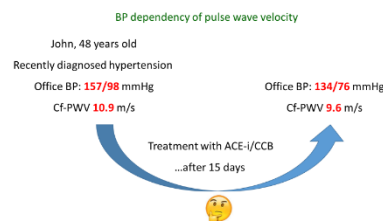


The speaker went deeper in his talk, by highlighting the associations of carotid systolic stiffening and aortic PWV with LV mass index. Dr. Pucci presented some data, all of them produced by his group of research, with the aim to illustrate the correlation of the stiffness constant with the estimated coronary risk. In

Establishing reference values for carotid-femoral pulse wave velocity in healthy people



Dr. Pucci from Perugia (IT), spoke about large arteries and central BP evaluation. More in particular the speaker presented very interesting data on the Pulse Wave velocity as a measure of arterial stiffness, starting from the concept that BP values are highly dependent by pulse



the second part of his presentation, spoke about the now perspectives in the measurements of central pressure and its correlation with pulse pressure amplification. In conclusion, the speaker pointed out that arterial stiffness and Central BP are relevant from a pathophysiological point of view, associated with major CV risk factors and TOD, but not yet standardized measurements.

- What's about Pulse Wave Velocity as a Measure of Arterial Stiffness?
- What is the prognostic value of carotid-femoral PWV?
- What's about the novel perspectives of the measurement of the Central Pressure?
- What's about the relationship between organ target damage and office central vs brachial BP measurements?
- What's about the relationship between left ventricular mass and 24 hours Central vs brachial BP measurement?

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Retinal arterioles to address the microcirculation

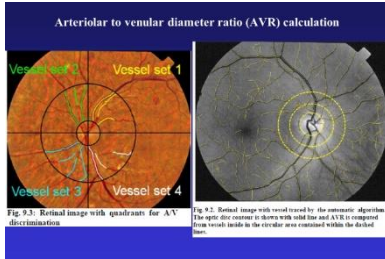


Fig. 9.3. Retinal image with quadrant for AVR discrimination.

The Retinal arterioles for addressing the microcirculation, was the topic discussed by Prof. Rizzoni from Brescia (IT). The speaker started his talk by highlighting that there is a tight association between advanced retinopathy and LVH and in order to find a relationship

between early retinal changes and target organ damage, he presented very interesting data given by some clinical studies running in hypertensive patients with specific retinal vascular alterations. In the main part of his lecture, Prof. Rizzoni presented very interesting data on the evaluation of the retinal

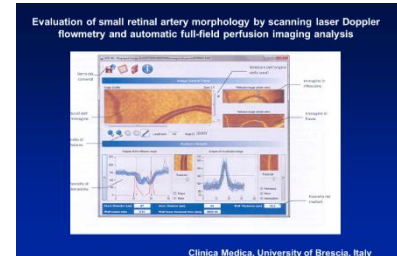
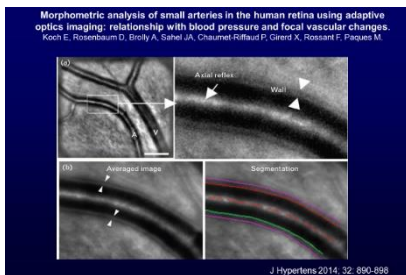


Fig. 9.2. Retinal image with overlaid algorithm. The optic disc contour is shown with solid line and AVR is computed from vessels inside the circle area contained within the dashed line.

changes in hypertension, by applying new techniques like the adaptive optics imaging, in order to demonstrate the relationship between retinal microvascular tree and target organ damage in hypertensive patients. In conclusion, Prof. Rizzoni pointed out that these new technologies can help physicians for a better stratification of the cardiovascular risk of patients affected by hypertension.



Morphometric analysis of small arteries in the human retina using adaptive optics imaging: relationship with blood pressure and focal vascular changes. Koort E, Rosenbaum D, Brody A, Sahel JH, Chaumet-Riffaud F, Girard A, Rossant F, Pasques M. J Hypertens 2014; 32: 890-898

- What's about the classification of hypertensive changes in the retina in a severity scale?
- What's about fundoscopy as a methodology for searching for subclinical organ damage?
- What's about the arteriolar to venular diameter ratio (AVR) calculation?
- What is the relationship between the quantification of topological changes in retinal vascular architecture and essential and malignant hypertension?
- What is the effect of the antihypertensive treatment on retinal microvascular changes in hypertension?
- What's about adaptive optics imaging system for the morphometric analysis of small arteries in the human retina?

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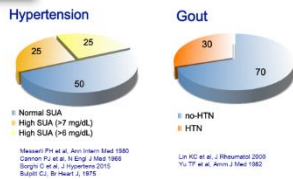
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Uric acid and hypertension



Prevalence (%) of high BP and hyperuricemia in patients with HTN and gout



Prof. Borghi from Bologna (IT), spoke about uric acid and hypertension. The speaker started his talk, by highlighting that the 50% of hypertensive patients present high serum uric acid levels. Prof. Borghi went deeper in his talk, by presenting very interesting data on the correlation between hyperuricemia, blood pressure levels and CV risk factors, both in animals and in humans. More in particular, the

speaker discussed very interesting data, like a multivariate analysis of factors associated with apparent resistant hypertension taken by the EURIKA study, where serum uric acid is one of main factors. In the second part of his lecture, Prof. Borghi talked about the possible mechanisms of interaction between elevated uric acid levels and Hypertension with a particular focus on the xanthine oxidase gene variants, the renal involvement and the associated oxidative stress.

Association of genetic urate score with CVD risk factors and CHD in 22,054 individuals

phenotype*	Genetic Urate Score, per 1SD (mmHg)					
	Age-sex Adjusted			Multivariable Adjusted		
	Beta (95% CI)	95% CI	P-value	Beta (95% CI)	95% CI	P-value
Hyperuricemia prevalence	-0.09	(-0.10, -0.08)	0.43	-0.07	(-0.08, -0.06)	0.24
SBP (mm Hg)	-0.15	(-0.14, -0.17)	0.30	-0.13	(-0.14, -0.12)	0.54
DBP (mm Hg)	-0.04	(-0.10, 0.02)	0.22	-0.07	(-0.14, -0.03)	0.39
SBP (not treated, mmHg)**	-0.21	(-0.16, -0.24)	0.14	-0.19	(-0.20, -0.18)	0.2
DBP (not treated, mmHg)**	-0.12	(-0.19, -0.05)	0.04	-0.12	(-0.15, -0.09)	0.06
prevalence diabetes	-0.03	(-0.03, 0.00)	0.07	-0.4	(-0.40, -0.39)	0.07
log eGFR-Creatinine (ml/min/1.73m ²)	-0.0009	(-0.001, 0.0009)	0.3	-0.0004	(-0.001, 0.0007)	0.32
CKD	-0.01	(-0.01, 0.00)	0.11	-0.01	(-0.01, 0.00)	0.17
incident CHD	-0.05	(-0.10, 0.00)	0.02	-0.03	(-0.05, -0.01)	0.01

*includes 5407 cases of incident hypertension, 557 cases of prevalent diabetes, 1333 cases of CKD, and 411 cases of CHD.
 **genetic blood pressure (<10 mm Hg if treated), diastolic blood pressure (<5 mm Hg if treated).
 **Individuals taking anti-hypertensive treatment were excluded from this analysis.

Yang Q et al. Circ Cardiovasc Genet 2010;3:523-530

Finally, the speaker presented some data on the therapeutic evidence of this relationship between SUA and hypertension, by presenting data on the effects of the xanthine-oxidase inhibitors on hypertension and cardiovascular outcomes. In conclusion, Prof. Borghi pointed out that for the evidence of the role of SUA in hypertension it is also necessary to investigate the role of SUA/XO relationship as a functional marker in Hypertension and the efficacy of ULT.



Possible mechanisms of interaction between elevated SUA and HTN

- Play of chance -
- Vascular urate deposition ±
- Genetic predisposition(s) +
- Renal involvement +
- Associated/generated oxidative stress ++

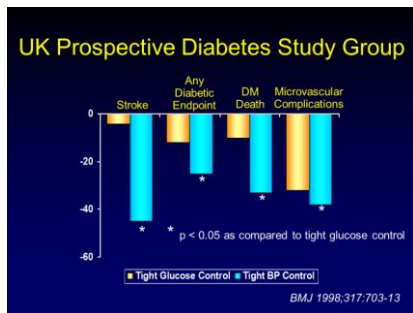
- What are the determinants of Serum Uric Acid levels?
- What is the prevalence (%) of high BP and hyperuricemia in patients with HTN and gout?
- What's about Febuxostat and systemic and glomerular hypertension in rats?
- There is a correlation between Serum Uric Acid and Arterial Stiffness?
- What are the possible mechanisms of interaction between elevated SUA and HTN?
- What's about the relationship between Allopurinol and blood pressure?
- What are the possible limitations about the relationship between SUA and Hypertension?

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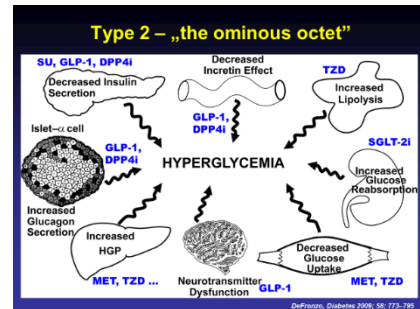
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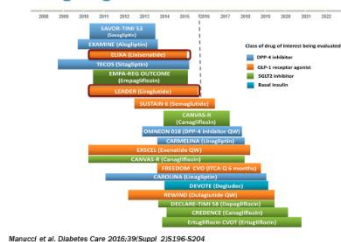
New antidiabetic drugs and the effects on blood pressure



In the main part of his presentation the speaker presented very interesting data on the CV outcomes trials running with glucose-lowering drugs in patients affected by type 2 diabetes and more in particular, on the present and future DPP-4 studies like CAROLINA, CARMELINA and others. DPP-4 inhibitors were not the only drugs discussed by Prof. Narkiewicz, he spoke also about trials conducted with GLP-1 receptor agonists, SGLT2 inhibitors and basal insulin. Prof. Narkiewicz presented a huge amount of data on these new drugs and more in particular he highlighted the potential pathways linking the SGLT2 inhibition with a lower risk for heart failure.



Timing of CV safety trials with glucose-lowering drugs for T2DM

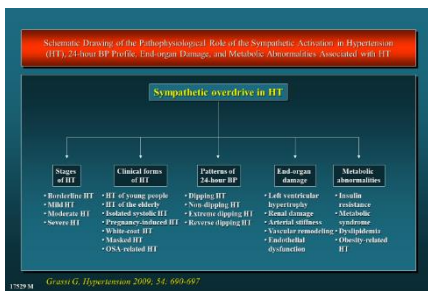


- What's about the ongoing CVOTs in patients with T2DM?
- What is the timing of CV safety trials with glucose-lowering drugs for T2DM?
- What are the primary endpoints of the main DPP-4 CV outcome trials?
- What are the main CV outcomes trials of glucose-lowering drugs in T2DM?
- What is the effect of diabetes and SGLT2 inhibition?
- What are the potential pathways linking empaglifozine with lower risk for heart failure?

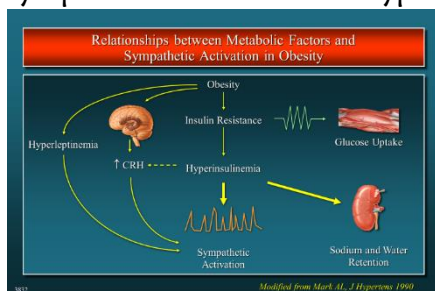
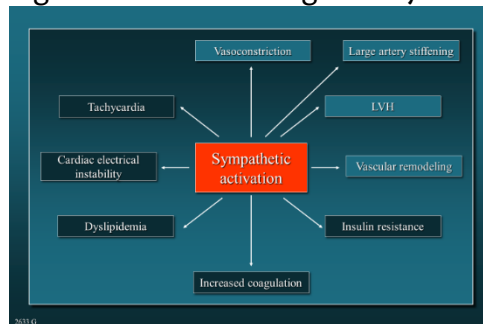
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The SNS in hypertension



Prof. Grassi from Milan (IT), spoke about the SNS in hypertension. The speaker started his talk, by highlighting the role played by sympathetic nervous system on hypertension control, by presenting a huge amount of data given by some studies conducted by his team of researchers. In the main part of his lecture, Prof. Grassi talked about the relationship between sympathetic activation and target organ damage, the Sympathomodulatory effects of anti-HT drugs and finally about the residual risk and the persistence of sympathetic activation in hypertensive treated patients.



Finally, Prof. Grassi pointed out that among the priorities for SNS research in Hypertension, a particular role could be played by the implementation of new techniques, the dynamic assessment of SNS during sleep, the evaluation of Genetic/SNS interactions, the assessment of the link between SNS activation and HT prognosis and the deeper assessment of new therapeutic procedures.

- What's about the evidence of sympathetic activation in essential hypertension?
- What is the relationship between BP and adrenergic drive in HT?
- What is the effect of sympathetic activity in patients with complicated hypertension?
- What's about Blood Pressure Variability and Its modulation?
- What are the relationships between metabolic factors and Sympathetic Activation in obesity?
- What are the possible favourable effects of antihypertensive drugs-induced sympathoinhibition?
- What are the effects of different antihypertensive drugs on Central, Peripheral and Cardiac Sympathetic Drive?

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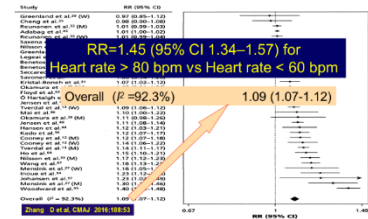
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Hypertension and heart rate

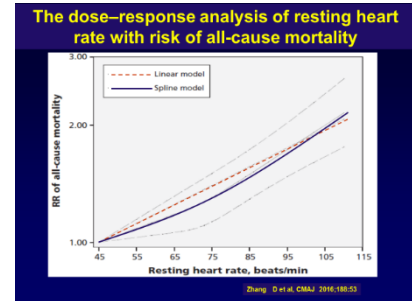
Resting heart rate and all-cause mortality in general populations: a meta-analysis

46 studies, N=1 246 203

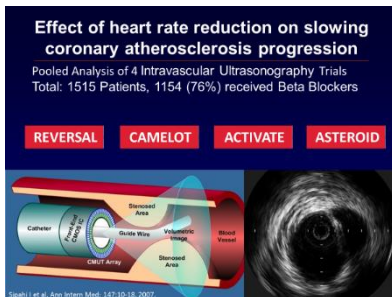


demonstrating a strict correlation between heart rate and mortality. In the main part of his presentation the speaker talked about the upper normal limits for office heart rate in hypertension, by highlighting that a very upper limit does not exist, but this correlation is j-shaped. Prof. Palatini talked also about the criteria for defining high heart rate a CV risk factor, by presenting a huge amount of data on heart rate as an

Hypertension and heart rate was the topic Prof. Palatini spoke about. The speaker, coming from Padua (IT) started his lecture by presenting very interesting data on a meta-analysis about resting heart rate and all-cause mortality in general populations, showing a 46% increase in mortality rate in patients with heart rate more than 80 bpm compared to patients with an heart rate less than 60 bpm. Prof. Palatini presented other data



independent risk factor. Finally, the speaker talked about tachycardia as a therapeutic target in hypertensive patients, by presenting very interesting data on the effects of heart rate reduction on the progression of coronary atherosclerosis. In conclusion, Prof. Palatini pointed out that despite these results, data on mortality reduction are lacking and it is necessary to implement a randomized clinical trial aiming at the evaluation of the effects of HR reduction in hypertensive patients with high HR.



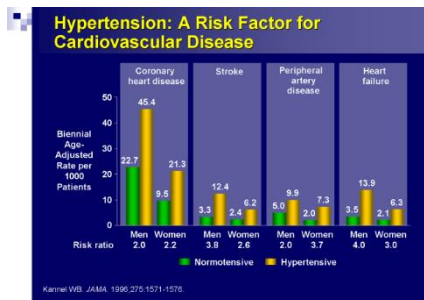
- What are the upper normal limits for office heart rate in Hypertension?
- Can high heart rate be a CV risk factor?
- What is the association Between Heart Rate and Other Risk Factors for Atherosclerosis?
- What's about Heart Rate as Independent Risk Factor?
- Should tachycardia be a target for treatment in hypertension or influence drug choice?
- What is the effect of heart rate reduction on slowing coronary atherosclerosis progression?
- What is the relationship between paced Heart Rate and PWV in Human Beings?

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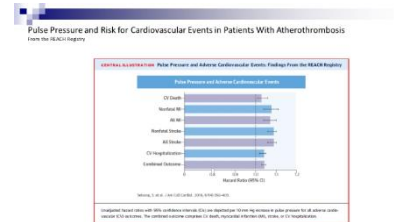
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Hypertension and coronary artery disease



Hypertension and coronary artery disease was the topic Prof. Tsioufis spoke about. The speaker, coming from Athens (GR) started his lecture by presenting very interesting data on epidemiology, diagnosis of CAD and therapy. At the beginning of his talk, Prof. Tsioufis spoke about CAD risk factors like smoking, obesity and physical activity, then went deeper in his



Sevaraj et al, JACC 2016

lecture, by presenting data on the relationship between BP and CAD, more in particular he spoke about pulse pressure and morning home blood pressure as strong predictors of coronary artery disease. Speaking about diagnosis, Prof. Tsioufis presented data on the total cardiovascular risk assessment as the first step for an effective diagnostic process, on microalbuminuria as an independent risk factor for cardiovascular disease and on the preferable stress tests to be performed. In the second part of his talk the speaker presented data on treatment and, more in particular on the BP targets to be achieved in hypertensive patients affected by chronic CAD, starting from the SPRINT data. Finally, Prof. Tsioufis spoke about drugs and more in particular, about the effects of ACEi, Beta-blockers, ARB. In conclusion, the speaker highlighted that it is important not to treat but to prevent the disease as well as not merely reduce BP levels but treat the patient.

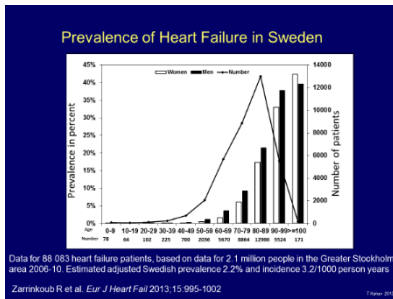


- What are the relative contributors of risk factors to risk of AMI in the INTERHEART study?
- What's about Pulse Pressure and Risk for Cardiovascular Events in Patients with Atherothrombosis?
- What is the first step in the diagnostic process from the speaker point of view?
- What's about the structural components and pathophysiological impact of myocardial remodelling in hypertensive heart disease?
- What are the goals in treating pts with chronic stable CAD?
- What's about the results of EUROASPIRE III?

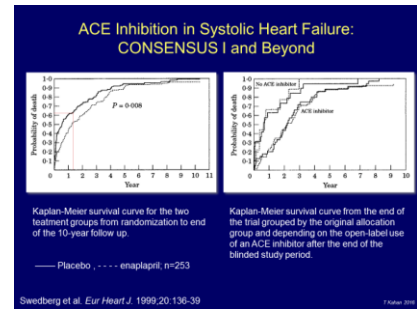
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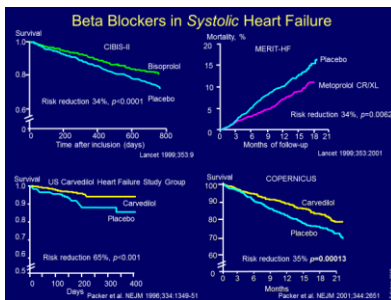
Hypertension and congestive heart failure



Prof. Kahan spoke about Hypertension and congestive heart failure. The speaker, coming from Stockholm (SW) started his talk by presenting very interesting data on the state of the art of Heart Failure in Sweden, its prevalence, risk factors and treatment. More in particular Prof. Kahan spoke about the effect of ACE inhibitors, Beta-blockers, Calcium channel blockers, ARB and MRA in monotherapy and/or in combination therapy. In the second part of his presentation the speaker talked about HF with preserved ejection fraction,



blockers, ARB and MRA in monotherapy and/or in combination therapy. In the second part of his presentation the speaker talked about HF with preserved ejection fraction,



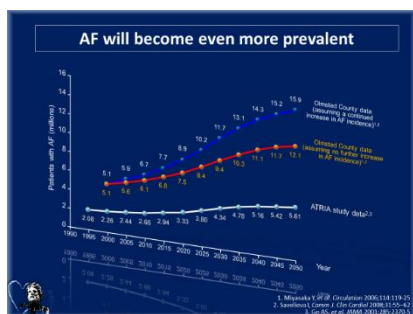
by presenting a huge amount of data given by the main clinical trials designed in this disease. Finally, Prof. Kahan spoke about the relationship between BP reduction and its effect in HF evolution and about the effect on empaglifozin on HF outcomes. In conclusion, the speaker pointed out that a careful blood pressure control is indicated in HFpEF patients and in HFREF patients it is important to reach the target of 130-135/80-85 mmHg.

- What are the standardised Effects of a 10 mm Hg Reduction in SBP?
- What's about the intensive BP lowering and risk of CV outcomes?
- What are the main key points of Beta Blockers in Heart Failure?
- What's about the proposed use of Beta-Blockers for Hypertension from the speaker point of view?
- What's about mortality and HF hospitalisations in CV and HF-PEF Trials?
- What's about the role of the renal angiotensin system in the pathophysiology of Heart Failure?

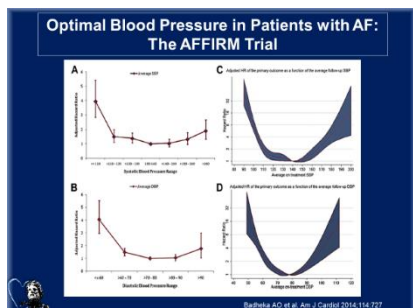
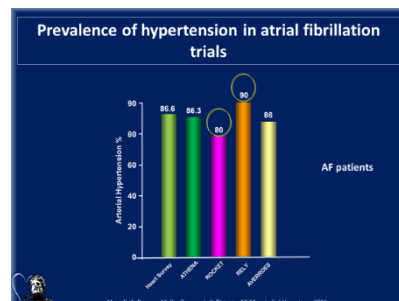
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Hypertension and atrial fibrillation



to be achieved in hypertensive patients with AF. About hypertension measurement, the speaker highlighted the need for repeated BP measurements for the improvement of accuracy in arrhythmic patients such as atrial fibrillation. Talking about atrial fibrillation detection, Prof. Kallistratos presented data on the life time risk for developing AF and on the silent atrial fibrillation. Finally, Prof. Kallistratos presented very



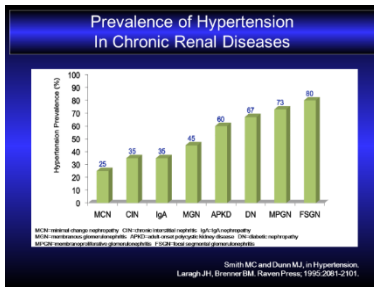
interesting data on the management of arterial hypertension and the atrial fibrillation treatment, with the use of ACE inhibitors, ARB, Beta-blockers and Calcium channel blockers, by highlighting that the goal is to control hypertension and to reduce hypertrophy as a key element for the AF control and prevention. In conclusion, Prof. Kallistratos pointed out that the control of blood pressure is mandatory in these patients, but it is necessary to pay attention to the J curve effect present also in AF patients.

- What is the prevalence of Atrial Fibrillation?
- What's about the effect of SBP and DBP in the risk of new onset AF?
- What's about blood pressure measurements in patients with AF?
- There is a BP Threshold in patients with atrial Fibrillation?
- What's about Stroke Prevention in Atrial Fibrillation?
-

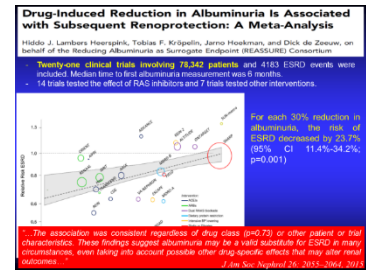
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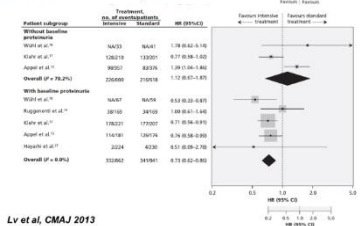
Hypertension and the Kidney



Prof. Salvetti, spoke about Hypertension and its relationship with the kidney. The speaker, coming from Brescia (IT), started his lecture by presenting very interesting data on the prevalence of hypertension in chronic kidney disease and the effects of a eGFR below 75 mL/min. In the main part of his presentation, Prof. Salvetti spoke about the indicators of kidney damage, by highlighting the role played by the left ventricular myocardial mechanoenergetic efficiency and presenting data on the interstitial collagen deposition as one of the typical features of uremic cardiomyopathy and present also in the early phases of CKD. In the second part of his talk Prof. Salvetti presented data on the effect of the antihypertensive treatment in patients affected by CKD, by highlighting the beneficial effect of the intensive blood pressure lowering on the CKD progression and also on the prevention of CV events in the same population. Finally, the speaker talked about the therapeutic strategies in hypertensive patients with nephropathy, by highlighting that there is yet a big work to do in order to obtain satisfactory results.



Effects of intensive blood pressure lowering on the progression of chronic kidney disease: a systematic review and meta-analysis

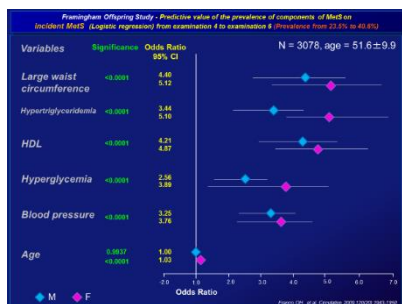


Li et al. CMAJ 2013

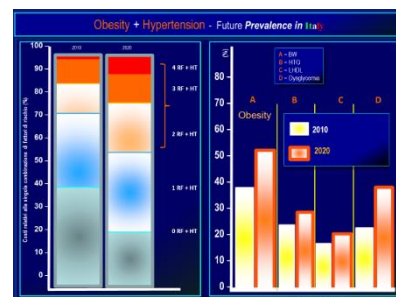
- What is the prevalence of Hypertension in Chronic Renal Diseases?
- What's about the systolic and diastolic left ventricular function according to the presence of kidney damage?
- What are the cardiovascular effects of unilateral nephrectomy in living kidney donors?
- What is the prognostic value of microalbuminuria during an antihypertensive treatment?
- What's about Antihypertensive treatment and CKD?
- What are the effects of an intensive blood pressure lowering on the progression of CKD?

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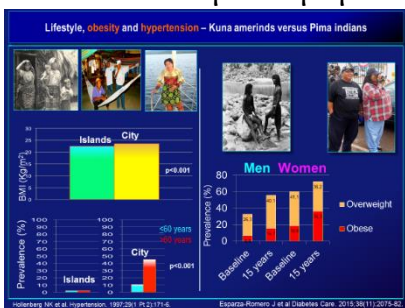
Obesity and hypertension



Obesity and hypertension was the topic at the core of Prof. Ferri presentation. The speaker, coming from L'Aquila (IT) presented very interesting data on the risk factors in hypertension and the relationship between obesity and cardiovascular disease. Prof. Ferri went deeper in his talk by highlighting the highly prevalence of obesity and hypertension in Italian people.



The speaker presented data on the incorrect dietetic abitus and on the sedentary life style that seem to grow in the next years in the all the world. In the main part of his presentation Prof. Ferri talked about the relationship between obesity and hypertension, their prevention and their treatment. Speaking about prevention, Prof. Ferri presented data on the effect of genetic and environmental influences on obesity in a twin model and in special populations like Kuma American Indians and Puma Indians.



The speaker talked also about the problems linked with sedentary life styles like watching TV and prolonged sitting position. From a therapeutic point of view, Prof. Ferri presented a huge amount of data on the effects of metformin also in non-diabetic obese patients and on the effects of SGLT-2 inhibitors. In conclusion, Prof. Ferri pointed out that the reduction of the body weight and the treatment of hypertension are two very important topics for a better and long life.

- What is the prevalence of obesity and hypertension in the general population?
- What's about the relationship between obesity and hypertension?
- What is the effect of genetic and environmental influences on obesity and hypertension?
- What's about lifestyle, obesity and hypertension?
- What's about watching TV and its relationship with abdominal obesity?
- What is the effect of metformin in obese non-diabetic patients?

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Clinical trials in China and the collaboration with ESH



Prof. Zhang spoke about clinical trials running in China and the collaboration with the European Society of Hypertension. The speaker, coming from Beijing (CHINA) started his talk, by presenting data on the trend of the prevalence of hypertension in China and on the RCTs designed for the treatment of Chinese hypertensive patients. More in particular Prof. Zhang spoke about the prevalence of stroke in hypertensive

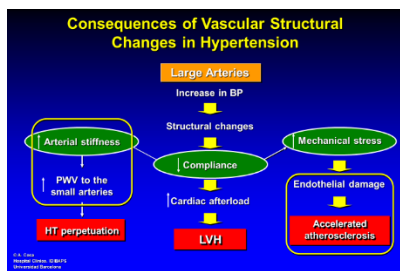
patients and other special issues like low control rate, socioeconomic and lifestyle differences in Chinese hypertensive patients. Speaking about the blood pressure target, Prof. Zhang presented data on the intensive and less intensive treatment given by the FEVER study, showing that the BP lowering produced a very significant reduction in stroke, CV and Cardiac events and death. The speaker presented other data given by studies running in subject with high-normal blood pressure with the aim to understand if a further reduction in blood pressure levels can have a positive impact on the development of new hypertension and CVD events. Finally, Prof. Zhang spoke about ongoing and future trials like ESH-CHL SHOT trial, a study on optimal blood pressure management and other studies like: the Salt restriction study and the J-curve studies.

- What is the prevalence of hypertension in China?
- What's about the incidence and mortality of cerebrovascular disease?
- What are the RCTs on Hypertension performed in China presented by the speaker?
- What's about the special issues for Hypertension control in China?
- What's about intensive or less intensive treatment of hypertension from the speaker point of view?
- Should blood pressure be further reduced in subjects with high normal blood pressure?
- What are the Ongoing and Future Trials presented by the speaker?

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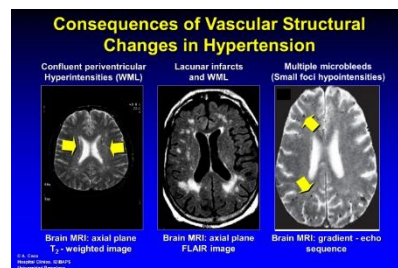
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Hypertension, the brain and cognitive function

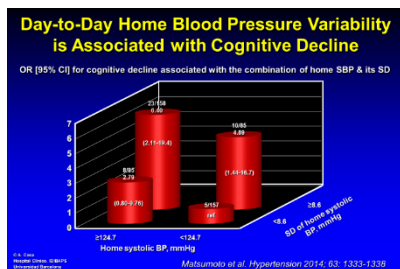


Hypertension and cognitive function was the topic at the core of Prof. Coca presentation. The speaker, coming from Barcelona (ES) started his lecture, by presenting very interesting data on the relationship between HTN and the pathophysiology of the Brain damage. More in particular Prof. Coca highlighted the correlation between HTN and the early cognitive impairment leading to dementia. The speaker went

deeper in his talk, by presenting data on the consequences of the vascular structure changes in hypertension at the brain level, as lacunar infarcts and multiple microbleeding and their correlation with aging. In the main part of his lecture, Prof. Coca pointed out that hypertension leading to dementia is a progressive disease characterized by the progression of atherosclerosis at the arteriolar level in the brain, responsible for the onset of silent cognitive decline and dementia. In the last part of his talk the speaker presented very impressive data



on the effects of the antihypertensive treatment for the prevention of the cognitive decline, pointing out that the antihypertensive treatment and the BP control may delay the progression of cerebral structural and functional damage. In conclusion, the speaker highlighted that, despite the evidence of the close relationship between silent cerebral structural (WML, MBs) and functional damage, further mechanistic and clinical studies are needed to provide insights into this subject.

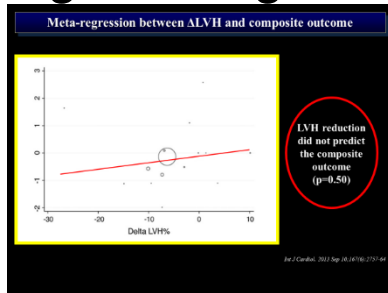


- What's about Pathophysiology of Brain Damage in Hypertension?
- What are the consequences of the vascular structural changes in Hypertension?
- What is the relationship between early silent cerebral damage and Hypertension?
- Is it possible prevent the cognitive decline by reducing the blood pressure levels?
- What's about the effects of the antihypertensive drugs on the risk Alzheimer disease risk reduction?

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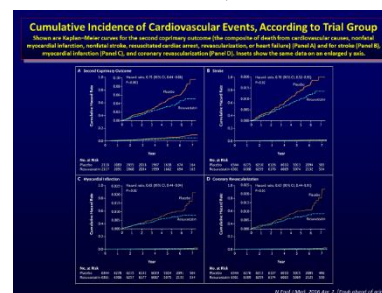
Round Table on Residual risk in hypertension: focus on organ damage and associated risk factors



Prof. Agabiti Rosei, chairman of this symposium opened the round table, by rising this question to the audience” why, despite the progresses in HTN treatment, there is a residual risk in hypertensive patients not yet defeated?” and, in order to

find a possible answer to this very important question, Prof. Franco Veglio, Prof. Pontremoli and Prof. Perroni Filardi spoke

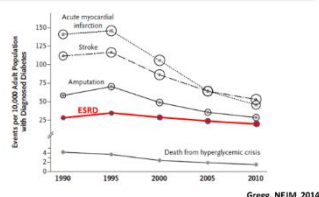
about the main cardiovascular risk factors like LV dysfunction, LDL cholesterol, CKD and diabetes. The speakers went deeper in their talk, by presenting very interesting data given by some



clinical trials running on primary and secondary prevention, showing that despite all the possible interventions and the benefits obtained there is always more or less a residual risk not affected by any type of intervention. In conclusion, Prof. Agabiti Rosei and all the speakers involved in this round table, pointed out that the best strategy for a higher reduction of the risk is linked with an earlier intervention in hypertensive and CKD patients.

Changes in Diabetes-Related Complications in the United States, 1990–2010

Data from the National Health Interview Survey, the National Hospital Discharge Survey, the U.S. Renal Data System, and the U.S. National Vital Statistics System



- Why there is a space for further improvement in CVD risk reduction in patients?
- What is the role played by cardiometabolic syndrome in the maintenance of the residual risk?
- What is necessary to do in CKD patients for a further reduction in residual risk?
- What’s about the improvement of adherence in hypertensive patients, more in particular in the young patients?

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