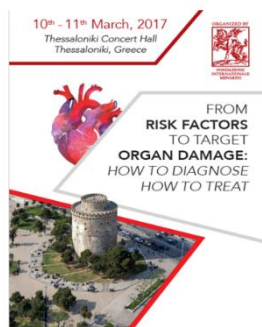


FROM RISK FACTORS TO TARGET ORGAN DAMAGE: HOW TO DIAGNOSE HOW TO TREAT Highlights

Thessaloniki (Greece), March 10-11, 2017

Introduction



Prof. Manolis, chairman of the symposium, opened the congress, by highlighting the high scientific level of the University of Thessaloniki in full compliance with the scientific level of this congress focused on the risk factors and the target organ damage of CVD patients. Many top researchers in cardiology focused on CVD epidemiology, diagnosis, prevention and treatment, coming from all the world attended this symposium together with young physicians and cardiologists. This

congress represented a very unique occasion for a full update on CVDs diagnosis, prevention and treatment with a particular focus on the residual risk and the new ways for its reduction.

To follow the presentations of this congress, click on the link below:

<http://www.fondazione-menarini.it/Archivio-Eventi/2017/From-Risk-Factors-to-Target-Organ-Damage-How-to-diagnose-how-to-treat/Materiale-Multimediale> ... and, after having logged in, enter in the multimedia area.

BP measurement: office, home or ABPM?

When measuring BP in the office, care should be taken:

- Allow the pts to sit for 3–5 minutes before beginning BP measurements.
- At least two BP measurements, in the sitting position, spaced 1–2 min apart, and additional measurements if the first two are quite different. Consider the average BP if deemed appropriate.
- Repeated measurements of BP in pts with arrhythmias, such as AFib.
- Use a standard bladder (12–13 cm wide and 35 cm long), but have a larger and a smaller bladder available for large (arm circumference >32 cm) and thin arms, respectively.
- Have the cuff at the heart level, whatever the position of the patient.
- Measure BP (simultaneously) in both arms at first visit to detect possible differences. In this instance (higher risk), take the arm with the higher value as the reference.
- Measure at first visit BP 1 and 3 min in standing position in Elderly, Diabetics, and in other suspected conditions for Orthostatic Hypotension Δ SBP>20mmHg & Δ DBP>10mmHg.
- Measure, in case of conventional BP measurement, heart rate by pulse palpation after the second measurement in the sitting position (independent predictor of CV Risk).

Prof. Pittaras from Athens (GR), spoke about the choice of the right BP measurement between office, home and ABPM. The speaker went deeper in his talk, by presenting very interesting data on the devices used for the BP measurement, by highlighting that the three types of methods have to be unified for a better BP control. Going

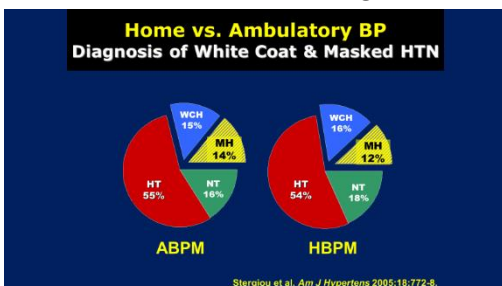
deeper in his lecture, Prof. Pittaras presented the main rules to be respected for a valid and reproducible BP measurement. More in particular the speaker pointed out that the home and the ABPM do not present the white coat phenomenon and that it is time for taking seriously care of the home blood pressure measurement for its prognostic value, the diagnostic ability and for its potentiality in the treatment' adjustments and the long-term follow-up. In the main part of his lecture, Prof. Pittaras

AOBP Eliminates the White Coat Response

Blood pressure (mmHg)

	n	Population	Routine Office	AOBP	Awake ABP
Godwin	481	community HT	153/83	140/79	142/80
Myers	309	ABPM unit	152/81	132/75	134/77
Myers	254	ABPM unit (untreated)	150/89	133/80	135/81
Godwin	654	community HT (treated)	149/83	139/80	141/80
Myers	299	community HT	150/81	135/77	133/74
		Mean	151/83	136/78	137/78

presented very interesting data given by clinical trials running in hypertensive patients with office, or home or ABPM measurements and discussed about special findings like “white coat hypertension”, “masked hypertension” “dipping and not dipping” pattern. In conclusion, the speaker pointed out that ABPM may be the best method for the BP measurement.



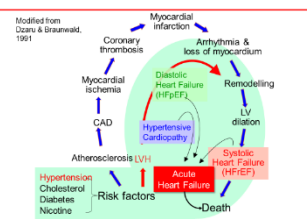
- How many measurements are needed for a correct BP variability estimation from the speaker point of view?
- What is the risk of CV events in patients with the isolated systolic hypertension?
- What is the nocturnal/daytime definition of dipping?
- Why is ABPM a better predictor than OBP for predicting risks from the speaker point of view?
- What are the main specific indication for ABPM?
- What are the main clinical indications for HBPM?

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Subclinical organ damage: diagnostic approach

The cardiovascular continuum



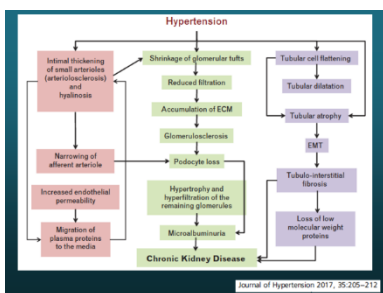
The diagnostic approach of the subclinical organ damage was the topic Prof. Narkiewicz spoke about in his lecture. The speaker coming from Gdansk (PL), started his talk, by presenting very interesting data on the evolution of hypertension and of the tools for its management, pointing to the complex interactions between heart, large vessels and small vessels, the so called “cardiovascular continuum”.

Going deeper in his lecture Prof. Narkiewicz spoke about guidelines, the recent developments and the implementation challenges on the Target Organ Damage. Talking about guidelines, the speaker presented data given by the 2013 ESH/ESC guidelines for the management of arterial hypertension and the 2016 European Guidelines on cardiovascular disease prevention in clinical practice, by highlighting that these documents have introduced contradictories recommendations for the improvement of the CV risk prediction, more in particular on the use of echocardiography. Talking about the recent developments, Prof. Narkiewicz presented very interesting data on the role played by the central pulse pressure as an independent determinant of vascular remodeling, on the hypertensive nephropathy and its merging pathogenetic mechanisms and finally on the brain structural changes in hypertensive patients, detected by MRI. Finally, the speaker talked about the new challenges and more in particular on the recommendations about the treatment for patients at low and moderate total CV risk level.

2013 ESH/ESC Hypertension Guidelines

Factors - other than office BP - influencing prognosis; used for stratification of total CV risk

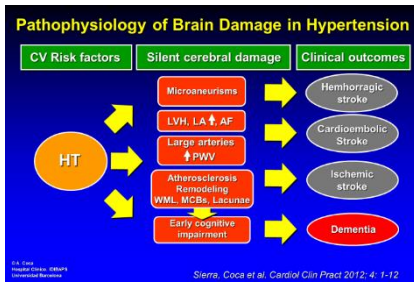
Risk factors	Recommendations
Age	Age > 65 years (men) or > 60 years (women)
Smoking	Current or former smoker
Cholesterol	LDL cholesterol > 190 mg/dL, or HDL cholesterol < 40 mg/dL (men) or < 50 mg/dL (women)
Diabetes	Diabetes mellitus
Family history of premature CVD	Family history of premature CVD (men aged < 55 years, women aged < 65 years)
Albuminuria	Albuminuria (UAE > 30 mg/day)
Left ventricular hypertrophy	Left ventricular hypertrophy (LVH) (LV mass index > 125 g/m ^{2.7} in men and > 110 g/m ^{2.7} in women)
Left atrial enlargement	Left atrial enlargement (LA diameter > 40 mm)
Carotid intima-media thickness	Carotid intima-media thickness (IMT) > 0.7 mm
Coronary artery disease	Coronary artery disease (CAD)
Stroke	Stroke
Peripheral artery disease	Peripheral artery disease (PAD)
Chronic kidney disease	Chronic kidney disease (CKD) (eGFR < 60 mL/min/1.73 m ²)
Target organ damage	Target organ damage (TOD) (LVH, LV hypertrophy, LV dilation, LV remodeling, LVH, LV hypertrophy, LV dilation, LV remodeling, LVH, LV hypertrophy, LV dilation, LV remodeling)



- What's about the evolution of the hypertension from the speaker point of view?
- What's about the total cardiovascular risk assessment from the guideline point of view?
- What are the main limitations in the total risk assessment?
- What's about the night-time hypertension compared to the daytime hypertension from the cardiovascular risk assessment point of view?
- What are the emerging pathogenetic mechanisms of the hypertensive nephropathy?
- What's about the brain structural changes in hypertensive patients presented by the speaker?

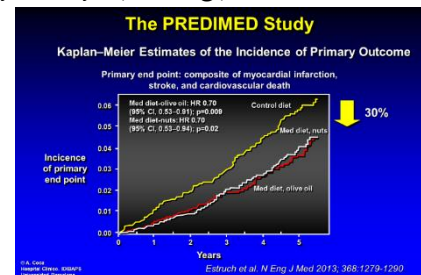
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Hypertension and stroke

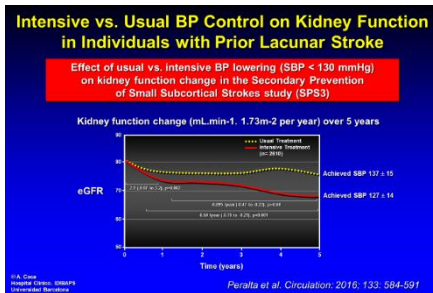


Hypertension and stroke was the topic discussed by Prof. Coca. At the beginning of his lecture the speaker, coming from Barcelona (ES) presented very interesting data on the risks factors for different stroke subtypes, by highlighting that hypertension as well as smoking and alcohol excess but not diabetes are very important risk factors for the onset of the lacunar ischaemic stroke. Going deeper in his presentation, Prof. Coca spoke about the pathophysiology of the brain

damage in hypertension, by highlighting the role played by HT from all point of view, also including the onset of dementia. In the main part of his lecture, the speaker presented data on the BP target in a primary prevention setting and on the role played by the Mediterranean diet in the stroke risk reduction. Prof. Coca, presented also very interesting data on the BP management in the acute phase of an ischaemic stroke, by highlighting that not in all stroke patients BP has to be reduced in the first week after the event. The speaker talked also about the need for a very effective statin therapy to be implemented as soon as possible for a better



patients' protection. Finally, Prof. Coca presented very interesting data on the secondary stroke prevention and the related BP targets, by highlighting that a very important reduction of BP levels is associated with a poor survival in patients with stroke. In conclusion, the speaker pointed out that the BP control is the corner stone of the primary stroke prevention and that the BP levels should be maintained below 140/90 mmHg in patients with an acute ischaemic stroke to prevent recurrences.



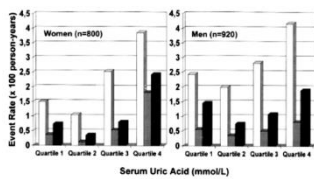
- What are the main risk factors for the different stroke subtypes?
- What's about the pathophysiology of the brain damage in hypertension?
- What is the correct BP target in primary stroke prevention from the speaker point of view?
- What's about the AHA/ASA guidelines for the primary prevention of stroke?
- What's about the high blood pressure management in the acute phase of the ischaemic stroke?
- What's about the strategies to be applied for the stroke recurrence prevention?
- What are the blood pressure targets for the stroke secondary prevention?
- What's about statins in ischaemic stroke secondary prevention?

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Uric Acid: risk factor or marker?

Unadjusted rate of total CV events, cardiovascular deaths, and all-cause deaths per quartiles of serum uric acid in hypertensives (PIUMA)

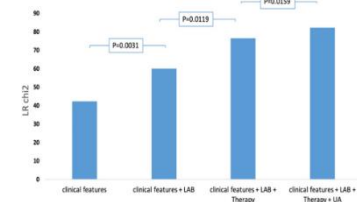


Verdecchia P et al, Hypertension 2000

Uric Acid: risk factor or marker was the topic of the lecture discussed by Prof. Ambrosio. The speaker, coming from Perugia (IT), introduced his talk by presenting very interesting data given by a clinical trial running in his clinical center on hyperuricemic patients affected by CVD, on the role played by uric acid in the onset of the cardiovascular disease events. Going deeper in his talk, Prof. Ambrosio presented very interesting data on the relationship between hyperuricemia and the onset of hypertension in adults and in

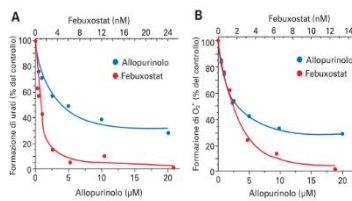
children. The speaker discussed also other data on the relationship between uric acid and HF with reduced EF and presented very interesting unpublished data on the role of uric acid as an independent risk factor for a better prognostic stratification of hospitalized HFrEF patients. In the main part of his lecture, Prof. Ambrosio spoke about the inflammatory effects of the uric acid crystals and about the aggravation of the oxidative stress due to the simple production of uric acid, by highlighting that the more xanthine oxidase pathway is activated the more uric acid effects on oxidative stress are evident. In the second part of his lecture, Prof. Ambrosio presented very interesting data on the effects of the xanthine oxidase inhibitors on blood pressure, CV event and stroke risk reduction. More in particular, the speaker discussed the data given by clinical trials running in hyperuricemic patients affected by HF, Hypertension, Coronary endothelial Dysfunction and stable Angina. In conclusion, Prof. Ambrosio pointed out that Hyperuricemia is an important risk factor for cardiovascular disease and that the selectivity of the XO-inhibition can play a primary role in the management of hyperuricemia and of the other inflammatory effects leading to the oxidative stress activation.

Additive Prognostic Stratification by Uric Acid in hospitalized HFrEF



Carluccio et al, unpublished

Allopurinol, febuxostat and XO-inhibition



Malik Uk et al, Free Radical Biology & Medicine 2011

- What are the ongoing febuxostat rCTs with CV outcomes presented by the speaker?
- What's about allopurinol and the cardiovascular outcomes in adults with hypertension?
- What are the molecular mechanisms of the crystal-related necroinflammation due to the presence of the uric acid crystals in the tissues?
- What's about the relationship between uric acid and the presence of chronic inflammation in HF patients?
- What's about the prognostic value of uric acid in HFrEF patients?

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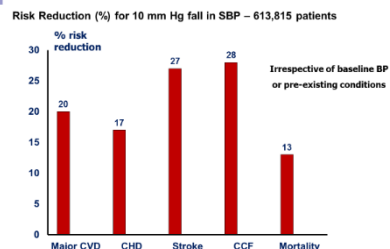
Are all antihypertensive drugs equally effective?

BP targets in 2017

- 2013 ESH/ESC GDLs: O.BP<140/90 mmHg for all
- 2014 JNC 8:
 - If age<60 yrs: O.BP<140/90 mmHg
 - If age≥60 yrs: O.BP<150/90 mmHg
- 2015 SPRINT: O.BP<120mmHg for selected individuals >50 yrs old with increased CV risk and BP >130mmHg
- 2016 Meta-analysis: O.BP<130 mmHg

Prof. Tsioufis spoke about the antihypertensive treatment and more in particular on the real effectiveness of the available drugs. The speaker, coming from Athens (GR), started his lecture, by presenting data on the effects of the BP lowering drugs, the TOD protection and the cardiovascular protection. Going deeper in his lecture Prof. Tsioufis highlighted that the choice

of any specific drug should be driven by the presence of specific conditions like subclinical TOD, metabolic syndrome or post MI status. In the main part of his lecture, the speaker presented very interesting data given by a recent meta-analysis on the correlation between the antihypertensive drug choice and the CV outcome. More in particular Prof. Tsioufis presented very interesting data on the effects of the main five drug categories on seven predetermined outcomes like stroke, CHD, HF hospitalization, Stroke +CHD, stroke + CHD and HF and finally death for CV events and death for all causes. In the second part of his lecture, the speaker talked about the methods to be applied for the selection of the best antihypertensive class and of the more profitable drug combinations. In conclusion, Prof. Tsioufis pointed out that the combination therapy can lead to a complementary effectiveness on different cardiovascular events.



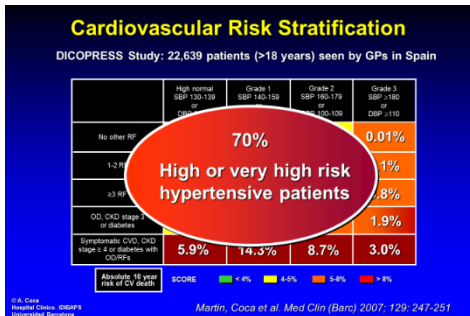
Will future antihypertensive drugs contribute in the better management of HTN?

M. Kladis, et al. | Efficacy, Safety, and Mechanisms of Interventional Therapies for Essential and Secondary Hypertension, Springer 2016

- What are the strengths of the meta-analysis presented by the speaker?
- What's about the selection of a class vs the selection of a single antihypertensive drug?
- How to select the right antihypertensive drug from the speaker point of view?
- What are the main messages of the meta-analysis presented by the speaker on the choice of the antihypertensive drugs?
- What's about the seven predetermined outcomes presented by the speaker?

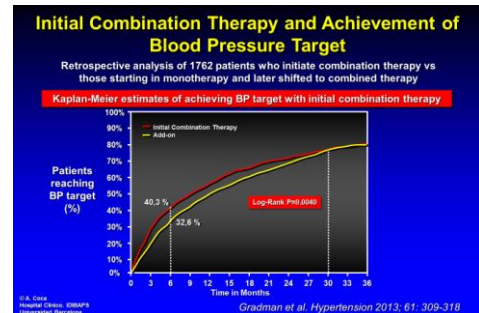
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Resistant hypertension: which combination?

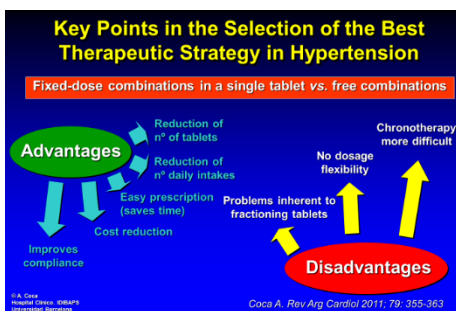


The right combination therapy for the management of the resistant hypertension was the topic of Prof. Coca presentation. The speaker, coming from Barcelona (ES), talked about the therapeutic decisions to be taken in essential Hypertensive patients related to the specific total cardiovascular risk assessment. Going deeper in his lecture, Prof. Coca presented very interesting data on the prevalence of hypertension and

other associated CV risk factors in Spain, by highlighting that obesity is an emerging problem and that thanks to the interaction between the different risk factors, in Spain there are more than 70% of hypertensive patients at high risk for CV disease. In the main part of his lecture, the speaker presented very interesting data given by rCTs on the effects of the combination therapy in high risk patients, compared to monotherapy and on the effects of the combination therapy in the early blood pressure control. In the last part of his lecture, Prof. Coca spoke about the drugs to be included in the first combination therapy strategy, by highlighting that the best choice



may be the combination between ARB and CCB or diuretic in particular conditions. The speaker went deeper in this topic and presented very interesting data on the adherence to treatment and on the comparison between fixed-dose and free-dose combination therapy. In conclusion, Prof. Coca pointed out that fixed-dose combination improves the treatment compliance and reduces mortality.

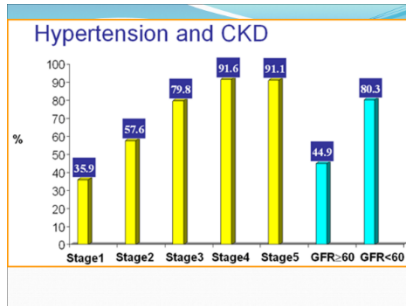


- What are the treatment goals for an effective BP lowering and total cardiovascular risk reduction?
- What's about the total cardiovascular risk assessment?
- What's about the initial combination therapy and the achievement of the blood pressure target based on the data presented by the speaker?
- Which drugs should be included in the first combination therapy?
- What are the main arterial structural changes induced by any specific antihypertensive treatment?
- What's about the prevention of the new onset diabetes by any antihypertensive treatment?

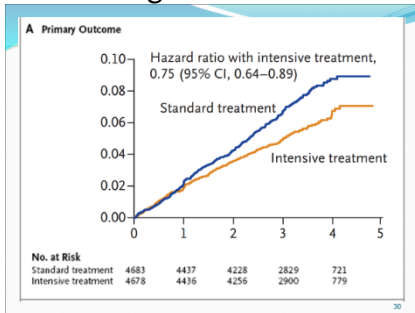
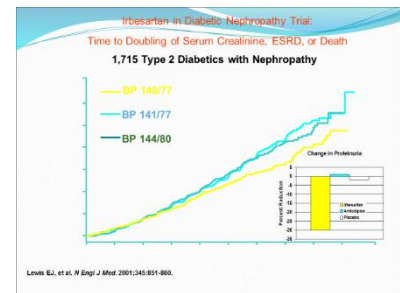
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How to manage high blood pressure in chronic kidney disease?



Prof. Vlahakos, coming from Athens (GR) spoke about how to manage HT in patients affected by chronic kidney disease. At the beginning of his lecture, the speaker highlighted that more than 90% of CKD advanced patients suffer from high blood pressure. Going deeper in his talk Prof. Vlahakos spoke about the intrarenal effects of ACEi and of ARBs, by highlighting that these drugs are more effective than others in hypertensive, CKD diabetic patients. In the main part of his lecture, the speaker presented data given by guideline recommendations on the antihypertensive treatment in CKD patients and more in particular he talked about the RAS inhibition in CKD patients. Finally, Prof. Vlahakos presented very interesting data on the SPRINT trial and on the EMPA-REG Outcome trial, pointing to the drugs' effects at the glomerular level.



- What 's about the antihypertensive treatment for people with nephropathy?
- What 's about the preferred hypertension treatment in specific conditions?
- What's about the effect of the Dual SGLT2 and RAS inhibition combination therapy at the glomerular level?
- What is the effect of empagliflozin on the incidence of worsening nephropathy?
- What's about the RAS inhibition in CKD patients based on the data presented by the speaker?

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Alexander the Great



Prof. Stamatopoulou, coming from Oxford (UK) spoke about Alexandre the Great, by presenting very interesting data given by archaeological studies running on many sites located in Macedonia as well as in other African and Asian countries all involved in the great Empire born by the incredible war campaigns held by Alexander the Great. Going deeper in her lecture, the speaker presented very impressive data on the Macedonia archaeological sites, more in particular on the Philipp II' Royal Palace located

in Aigai, with the intention to describe the Alexander personality starting from his origins, the time he lived together with his father the powerful King Philipp II. In the main part of her lecture, Prof. Stamatopoulou spoke about the innovations in many fields like art, architecture and culture, driven by Alexander thanks to his military conquests. The speaker pointed out that Alexander had the great intuition to go deeper in the culture of the conquered people with the aim to integrate these cultures with the greek one, probably the first example in the ancient world of an intercultural model.



Prof. Stamatopoulou presented a huge amount of data on the archaeological finds showing the results of this intercultural process: mosaics, bas-reliefs, sculptures, all of them representing Alexander in many different situations and also archaeological plants of cities located in several countries, powerful witnesses of the greatness of this unique man. In conclusion, Prof. Stamatopoulou pointed out that Alexander the Great remains in the history as a unique example of how a single person can lead to the onset of a multicultural society, composed by different people and cultures, based on the continuing negotiation from a political, administrative and justice point of view.

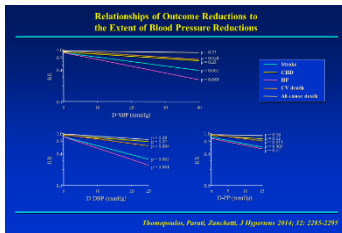


- What's about King Philipp II, Aigai and the expansion of the Macedonia power?
- What's about the Macedonia Kingship and the elite ideology based on the data presented by the speaker?
- What' about the first actions of Alexander as a new King from the speaker point of view?
- What's about Alexander and the East between Kingship and Conquest?
- What's about Priene as a typical Greek city located in Asia Minor?
- What's about the Museum and the Library of Alexandria, based on the data presented by the speaker?
- What's about the diffusion of Education, Culture and Training in the Alexander Empire?

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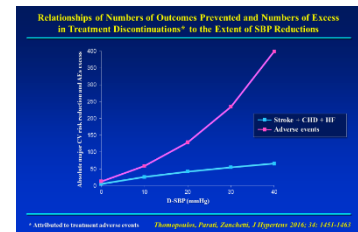
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Upcoming hypertension guidelines: how far should BP be lowered?

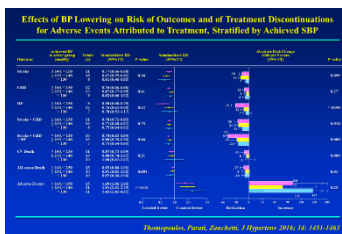


The upcoming hypertension guidelines: how far should BP be lowered? was the topic discussed by Prof. Zanchetti. The speaker, coming from Milan (IT), presented very interesting data on the relative and the absolute risk reduction of the main outcomes in BP lowering trials with the aim to correlate the outcomes reduction with the amount of BP reduction. Going deeper in his lecture, Prof. Zanchetti pointed out that the BP-

lowering treatment is also associated with untoward effects of variable severity, in particular in the case of therapy discontinuation and presented very impressive data given by a meta-analysis pulling 50 RCTs on 179949 patients followed by 4 years. In the main part of his lecture, the speaker talked about the optimal medical treatment for hypertensive patients and the so called J-shaped curve hypothesis. Prof. Zanchetti presented very interesting data given by his



meta-analysis on the benefits and the burdens of the antihypertensive treatment, by highlighting that the absolute benefit is going down when SBP is reduced under 140 mmHg or more. In conclusion, Prof. Zanchetti pointed out that the question “how much and how far is to lower the BP” has not a fixed answer, but it is necessary to evaluate the characteristics of any individual patient and also the physician-patient relationship.



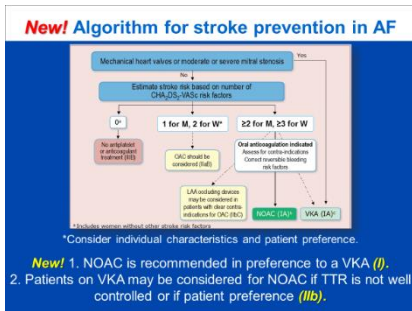
- How far should BP be lowered?
- What’s about the J-curve dilemma presented by the speaker?
- What are the main limitations of a post-hoc analysis of the J-curve?
- What’s about the benefits and the burdens of the antihypertensive treatment from the speaker point of view?

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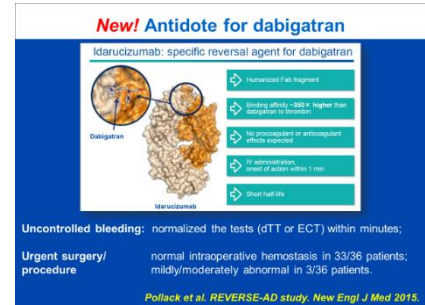
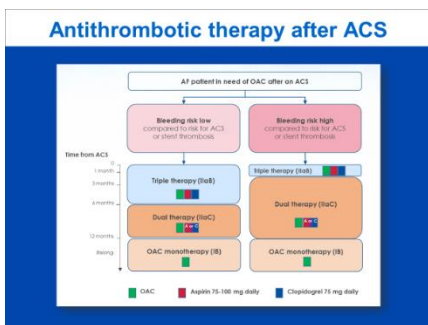
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Atrial fibrillation: key messages from recently published guidelines



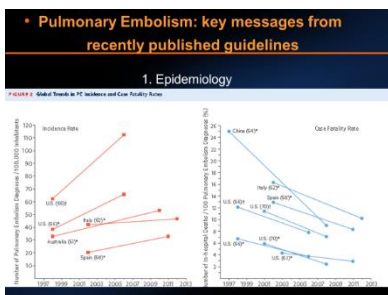
Prof. Vinereanu, talked about Atrial fibrillation: key messages from recently published guidelines. The speaker coming from Bucharest (RO), at the beginning of his lecture talked about stroke prevention in AF patients, by highlighting that NOAC is recommended in preference to Vit. K antagonists and that patients treated with Vit. K antagonists may be considered for NOAC if TTR is not well controlled. Going deeper in his lecture, Prof. Vinereanu presented very interesting data on the effects of NOAC compared to VKA and discussed about the precautions to be taken in patients treated with NOAC. In the main part of his presentation, the speaker talked about the management of bleeding by presenting data given by the specific guideline recommendations, about the initiation of OAC after a stroke/TIA event, by highlighting that also in these patients NOAC is preferred to VKA. Speaking about antithrombotic therapy in AF+CAD patients, Prof. Vinereanu pointed out that OAC monotherapy is sufficient and that neither aspirin nor clopidogrel are needed. Finally, the speaker talked about the rhythm control therapy and about the still unanswered questions, by highlighting that despite the old and the new guidelines many questions are also opened to more suitable solutions.

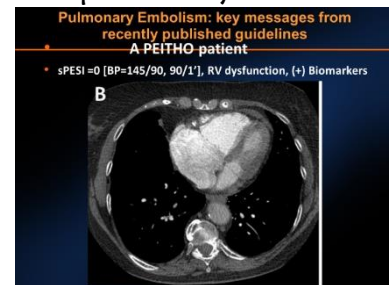
- What's about the new antidote for dabigatran presented by the speaker?
- What is the role of NOAC from the speaker point of view?
- How to use bleeding risk in practice?
- What is the algorithm for stroke prevention in AF patients?
- What's about the NOAC efficiency and safety compared to VKA?
- What is the antidote for dabigatran presented by the speaker?
- What are the main topics of the rhythm control therapy?

To follow the presentations of this congress, click on the link below:
<http://www.fondazione-menarini.it/Archivio-Eventi/2017/From-Risk-Factors-to-Target-Organ-Damage-How-to-diagnose-how-to-treat/Materiale-Multimediale...> and, after having logged in, enter in the multimedia area.

Pulmonary embolism: key messages from recently published guidelines



Prof. Olympios highlighted that diagnosis and treatment of patients with PE are significantly improved leading to the reduction in mortality. Talking about examinations, the speaker presented very interesting imaging data in PE patients and talked about the D-Dimer. From a classification point of view, Prof. Olympios presented very interesting data given by clinical trials like the



PEITHO trial. The speaker talked also about treatment, by presenting data on the treatment of the acute PE phase and on the duration of the treatment. In the last part of his presentation, Prof. Olympkos talked about the reperfusion therapy and more in particular about the thrombolytic treatment of the PE patients. Finally, the speaker pointed to some unanswered questions like the early discharge and the out-patients care for low risk subjects, the use of NOAC in patients affected by Cancer, the diagnosis of acute PE in

Pulmonary Embolism: key messages from recently published guidelines

Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis

Table 3 Safety outcomes, subgroup analysis

All studies	Atypical		Tetrasyllabic		Other streptolydigin		Group difference
	OR (95% CI)	P-value	OR (95% CI)	OR (95% CI)	OR (95% CI)	P-value	
Major bleeding	2.91 (1.95 to 4.36)	<0.001	2.57 (1.71 to 3.87)	3.02 (2.11 to 4.36)	2.16 (1.52 to 3.07)	0.02	
Haemorrhagic death	3.12 (1.25 to 8.17)	<0.001	1.92 (1.07 to 3.46)	7.22 (3.11 to 16.24)	NA	0.07	

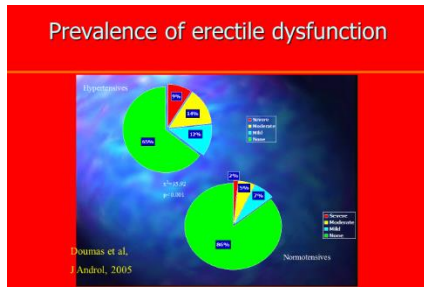
pregnancy and the subsegmental PE.

- What's about the antithrombotic treatment from the speaker point of view?
- What is the choice of an initial parenteral anticoagulant regimen in PE patients?
- What's about the PE classification?
- What are the main characteristics of the original and simplified PE severity index (PESI) presented by the speaker?
- What's about the key messages on the pulmonary embolisms given by recent published guidelines?

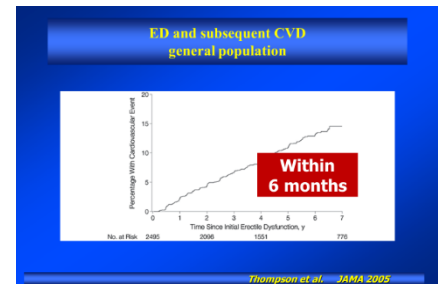
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Sexual dysfunction in daily practice



Sexual dysfunction in daily practice was the topic discussed by Prof. Doumas in his lecture. The speaker coming from Thessaloniki (GR), talked about the vascular origin of the sexual dysfunction and the rationale for the ED inquiry in cardiology, internal medicine and primary care settings. Going deeper in his lecture, the speaker



presented very interesting data on the increased ED prevalence and its effects on the quality of life. In the main part of his talk Prof. Doumas spoke about the adherence to therapy and about the drugs actions and interactions and highlighted that thanks to the introduction of the PDE-5 inhibitors the rate of patients compliant to therapy significantly raised. Finally, Prof. Doumas presented very interesting

Frequency of sexual activity and CV events

Model	Cardiovascular Disease	
	Measured by Self-Report, Medical Record, or ICD	Measured by Medical Record or ICD
	HR (95% CI)	p Value
Frequency of sexual desire		
Phosphodiesterase and cardiovascular adjustment	1.05 (0.88-1.27)	0.72
Monthly or less vs >2-3 times weekly	1.28 (0.85-1.97)	0.25
Frequency of sexual activity		
Phosphodiesterase and cardiovascular adjustment	1.09 (0.76-1.57)	0.66
Monthly or less vs >2-3 times weekly	1.88 (0.68-5.19)	0.25
Frequency of sexual activity		
Phosphodiesterase and cardiovascular adjustment	1.14	1.01 (0.72-1.42)
Monthly or less vs >2-3 times weekly	1.44	1.24 (0.87-1.77)
Phosphodiesterase and cardiovascular adjustment	1.44 (1.02-2.04)	0.04
Monthly or less vs >2-3 times weekly	1.45 (1.02-2.04)	0.04

Hall et al. Am J Cardiol 2010

data on the early identification of ED patients, by highlighting that ED usually precedes the onset of CAD. The speaker discussed also other data on the necessity for a very effective sexual counselling for hypertensive patients. In conclusion Prof. Doumas pointed out that, thanks to his working group on sexual dysfunction in hypertension, he has the dream to rise the rate of interviewed hypertensive patients for the ED prevention to more than 40% in 2020

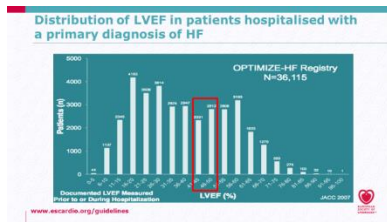
and to more than 80% in 2025.

- What's about the increased prevalence of ED based on the data presented by the speaker?
- What are the main drug actions and interactions?
- How to identify the asymptomatic CAD patients?
- What is the correlation between sexual activity and the cardiac risk assessment?
- What are the main topics of the working group on sexual dysfunction in hypertension?

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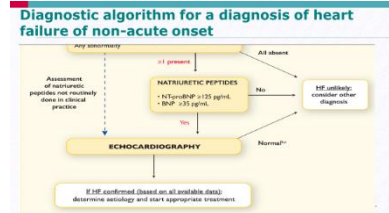
<http://www.fondazione-menarini.it/Archivio-Eventi/2017/From-Risk-Factors-to-Target-Organ-Damage-How-to-diagnose-how-to-treat/Materiale-Multimediale> ... and, after having logged in, enter in the multimedia area.

Diagnostic approach

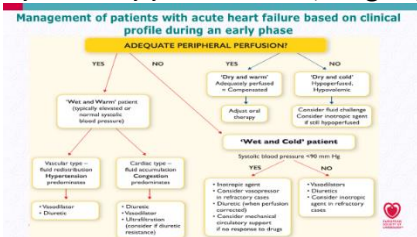


Prof. Rosano from London (UK), presented very interesting data on the diagnostic approach of patients with HF and more in particular on HF definition, the new classification according to the left ventricular heart failure and finally on the diagnosis of HF with preserved ejection fraction. Speaking about definition, Prof. Rosano

presented the guidelines definitions of the new three types of HF, divided in HF with preserved, reduced and mid-range ejection fraction and discussed about the real patients with the same EF at admission but with very different outcomes and different underlying factors. Speaking about diagnosis, Prof. Rosano presented the guidelines position on the Natriuretic Peptides application, by highlighting that NPs are useful for ruling-out HF, but not for the



diagnosis establishment. Finally, Prof. Rosano spoke about acute heart failure, by presenting the flow-chart for diagnosis and treatment of AHF patients. In conclusion, the speaker pointed out that in order to manage at the best HF patients is fundamental to be excellent trained, well experienced and superb judgment endowed doctors.



- Which are the LVEF cut-off to use for the HF with preserved EF and with reduced EF, based on the data presented by the speaker?
- What are the main differences between HFpEF, HFmrEF and HFrEF, from the guidelines point of view?
- When is it the right time for the LV function measurement?
- What are the main topics of the diagnostic algorithm for a diagnosis of heart failure of non-acute onset?
- What's about natriuretic peptides from the speaker point of view?
- What are the main characteristics of the acute heart failure presented by the speaker?

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Treatment of acute and chronic heart failure

Guidelines: implications for clinical practice

Type of HF	HFrEF	HFmrEF	HFpEF
1	Symptoms + Sign ^a	Symptoms + Sign ^a	Symptoms + Sign ^a
2	LVEF <40%	LVEF 40-49%	LVEF ≥50%
3	–	1. Elevated levels of natriuretic peptide ^b 2. At least one additional criterion: a. relevant structural heart disease (LPH and/or LAE) b. diastolic dysfunction (for details see Section 4.3.2)	1. Elevated levels of natriuretic peptide ^b 2. At least one additional criterion: a. relevant structural heart disease (LPH and/or LAE) b. diastolic dysfunction (for details see Section 4.3.2)

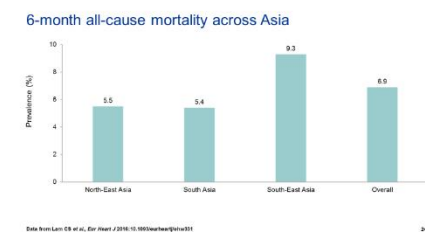
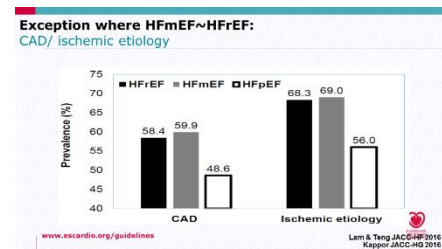
^aSigns may not be present in the early stages of HF (especially in HFpEF) and in patients treated with diuretics.
^bBNP > 35 pg/ml and/or NT-proBNP > 125 pg/ml

Identifying HF with mid-range ejection fraction (HFmrEF) as a separate group will stimulate research into underlying characteristics, pathophysiology and treatment of this population

www.escardio.org/guidelines

The main topic at the core of Prof. Lam presentation, was the treatment of acute and chronic heart failure. The speaker, coming from Singapore (SGP), presented very interesting data on the guideline recommendations for the treatment of acute HF patients, starting from the algorithm of their therapeutic approach. Speaking

about HF mrEF, Prof. Lam pointed out that this new entity aims to cover the lack of indications between the other two forms typical of the old guidelines, with the exception of only one characteristic: the ischemic origin, more similar to the reduced EF than the preserved EF type. In the main part of her presentation, the speaker spoke about the important effects of the comorbidities in patients with HF and presented very interesting data on an Asian study running in HF patients, characterized by the very younger age of the patients linked with the presence of a lot of comorbidities. Prof. Lam spoke also about the correlation between regional income levels, the prevalence of comorbidities and the related outcomes, by presenting very impressive data on the differences in the death events rate between India and Singapore. Finally, the speaker talked about diabetes, CKD and Iron deficiency, their prevalence in Asia, and the new drugs to be used for. In conclusion, Prof. Lam pointed out that the management of the comorbidities it is fundamental for a better control of



the HF evolution.

- What is the mean age of Asian HF patients?
- What's about diabetes in Asian people, based on the data presented by the speaker?
- What is the prevalence of the iron deficiency in Asia based on the data presented by the speaker?
- What is the effect of the black tea on the iron absorption rate?
- What about sleep apnea and the related CV mortality in HF patients?

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Key messages from recently published guidelines

ESC Levels of Evidence

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

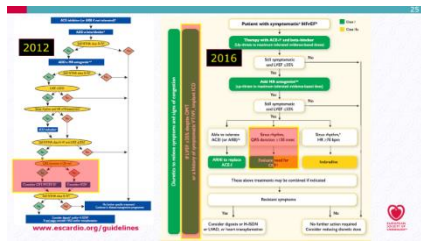
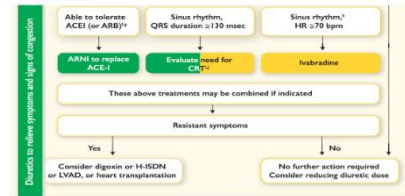
www.escardio.org/1073



The main topics at the core of Prof. Filippatos presentation, were the key messages from recently published guidelines. The speaker, coming from Athens (GR), presented very interesting data, starting from the main changes from the 2012 guidelines. Going deeper in his presentation, the speaker talked about the new HF definition and about the new diagnostic and

treatment algorithm, characterized by the presence of the so called mid-range patients. In the main part of his lecture, Prof. Filippatos spoke about the differences in beta-blockers use recommendations between the USA and the European guidelines and about the differences in the treatment

Therapeutic algorithm for a patient with symptomatic HF with reduced ejection fraction



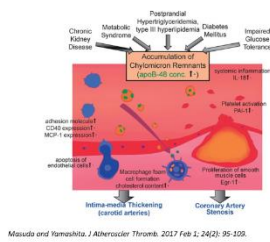
algorithm between these two guidelines. The speaker talked also about HF with preserved EF and the ICDs implantation, by highlighting the huge amount of publications since the 2012 that have determined the radical change in ICDs implantation recommendations. Finally, Prof. Filippatos talked about the new device like those ones delivered for the measurement of the pulmonary pressure.

- What's about the new definition of the HF syndrome presented by the speaker?
- What are the main limitations of the HFmrEF patient definitions?
- What are the main differences between the 2012 and the 2016 guidelines on the ICDs implantation?
- What's about the new meta-analyses published since the 2012 on the ICDs implantation?
- What's about the exercise prescription in HF patients from the speaker point of view?

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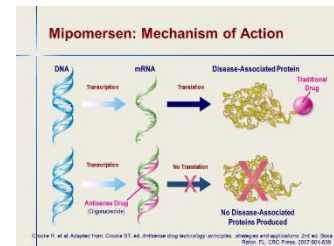
An update in the treatment of dyslipidaemia



Masuda and Yamashita, J Atheroscler Thromb. 2017 Feb 1; 24(2): 95-109.

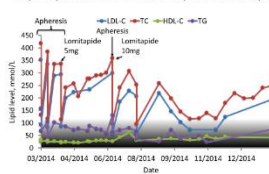
Prof. Kolovou, coming from Athens (GR), spoke about the update in dyslipidaemia treatment. At the beginning of her presentation the speaker pointed out that the more important change is not about drugs but about the mental approach to these diseases. Going deeper in her lecture, Prof. Kolovou talked about Tgs and the drugs used for hypertriglyceridemia and for diabetic hypertriglyceridemic patients like

DPP-4 inhibitors and GLP-1 analogues. In the main part of her talk, the speaker presented data on statins therapy for LDL lowering and CVD reduction and on CEPT inhibitors able to reduce the LDL cholesterol and to rise the HDL-cholesterol levels of about the 90%. Speaking about other LDL lowering drugs, Prof. Kolovou presented very interesting data on the PCSK9 inhibitors, on Mipomersen, that is an apoB-100



inhibitor for HFH patients and on Lomitapide, an MTP inhibitor able to reduce the LDL-C of about 30%. Finally, the speaker presented also data on new developing drugs and more in particular on the Bempedoic acid, Gemcabene and on the CEPT inhibitors. In conclusion, Prof. Kolovou pointed out that statins will remain the backbone of LL-therapy, but several novel agents are in development with very interesting but preliminary results.

Lipid profiles on lomitapide therapy

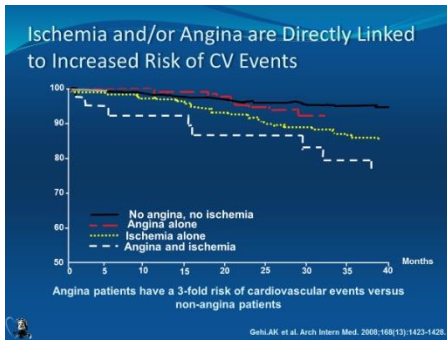


- Why are we looking for new LDL lowering drugs?
- What's about the clinical events related to lomitapide?
- What is the main mechanism of action of Mipomersen?
- What is the main mechanism of action of Ezetimibe based on the data presented by the speaker?

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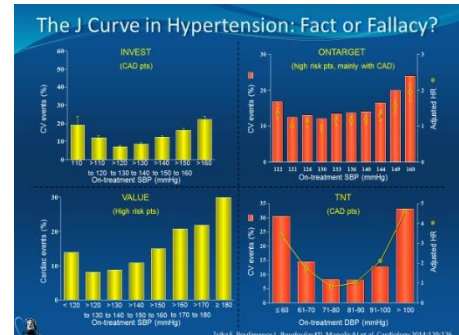
<http://www.fondazione-menarini.it/Archivio-Eventi/2017/From-Risk-Factors-to-Target-Organ-Damage-How-to-diagnose-how-to-treat/Materiale-Multimediale...> and, after having logged in, enter in the multimedia area.

Pathophysiology and diagnostic approach of SCHD

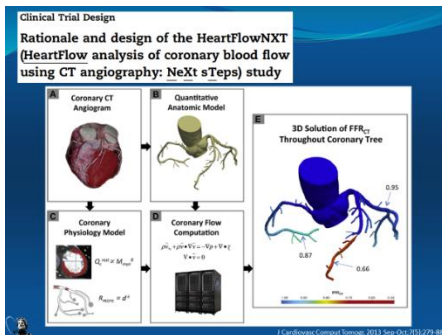


The Pathophysiology and the diagnostic approach of SCHD, was the topic at the core of Prof. Poulimenos presentation. The speaker coming from Athens (GR), at the beginning of his presentation talked about the symptoms at the end of the ischemic cascade, by highlighting that many episodes of ischemia never become painful, but this symptomatology is directly linked with an

increased risk of CV events. Going deeper in his presentation, Prof. Poulimenos, spoke about the coronary microvasculature and its cyclic compression and presented very interesting data on the coronary autoregulation mechanisms. In the main part of his lecture, the speaker presented very interesting data given by clinical trials on the event-free survival rate, like the



FAME study and spoke about the presence of the J-curve phenomenon in HT treated patients. Prof. Poulimenos, talked also about the angina pain, the pre-test probability and about the diagnosis of myocardial ischemia in HT patients. In the last part of his talk the speaker presented also data on CT imaging given by the PROMISE, the C MARC2 trial and the HeartFlowNXT study, by highlighting that with these tools it is possible to avoid coronarography and to save at list more than 200 pounds



per patient.

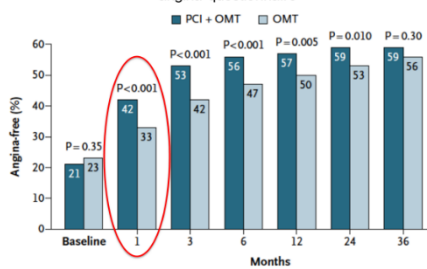
- What's about the primary outcomes in FAME 2 study?
- About the J curve in hypertension: fact or fallacy?
- What are the main indications for the diagnostic tests in patients with suspected CAD and stable symptoms?
- What's about the initial diagnostic management of patients with suspected SCAD?
- What's about the HeartFlowNEXT study presented by the speaker?

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SCHD in women and diabetes

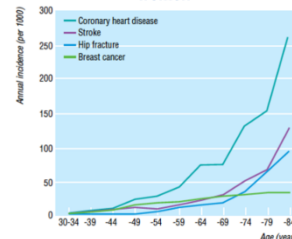
Freedom from angina over time as assessed with the seattle angina questionnaire



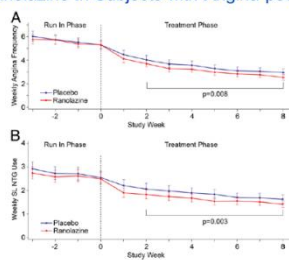
The SCHD in women and diabetes, was the topic at the core of Prof. Collins presentation. The speaker coming from London (UK), presented very interesting data on SCHD, pointing out that it is necessary to apply for a more comprehensive approach with the aim to refocus preventive and therapeutic strategies and to decrease morbidity and mortality. Going deeper in his lecture, Prof. Collins presented very interesting data on two

primary goals for the treatment of patient with instable angina: the survival and the QoL improvement. The speaker talked also about the ESC 2013 guidelines for the angina relief management and presented very interesting data on women and on diabetic patients, all of them at a higher CAD risk, more in particular for women in postmenopausal phase. In the main part of his lecture, Prof. Collins spoke about the microvascular angina and its potential treatment starting from the patient risk stratification till the interventions for refractory angina. Finally, the speaker talked about the SCHD diabetic patients, by presenting very impressive data given by the

Incidence of chronic diseases in relation to age in women



TERISA – Type 2 diabetes Evaluation of Ranolazine In Subjects with Angina pectoris



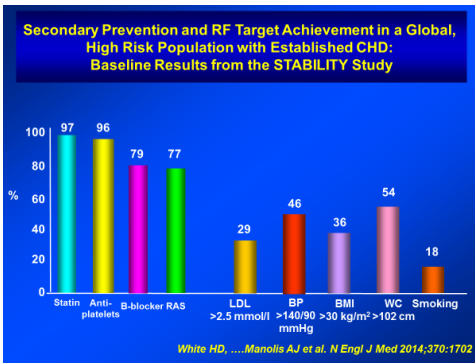
main clinical trials runned in these patients, like ACCORD and EMPA-REG and spoke also about the revascularization procedures. Prof. Collins, presented also very impressive data on the effect of ranolazine in diabetic patients affected by stable angina. In conclusion, Prof. Collins, pointed out that women have more microvascular disease than men and that diabetic patients require more intensive and additional management strategies.

- What's about the solar system of IHD presented by the speaker?
- What's about the difference in CHD death between Men and Women?
- What's about the microvascular spasm in patients with cardiac syndrome X?
- What's about the main therapies for microvascular angina presented by the speaker?
- What's about the effects of ranolazine in diabetic patients with stable angina presented by the speaker?

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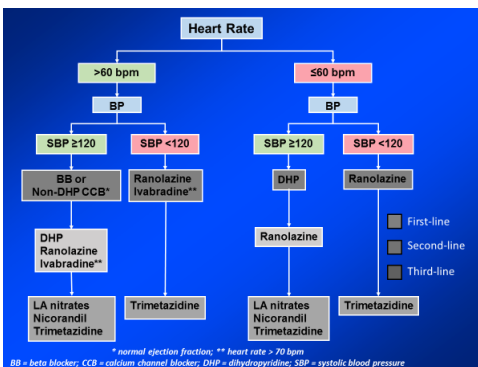
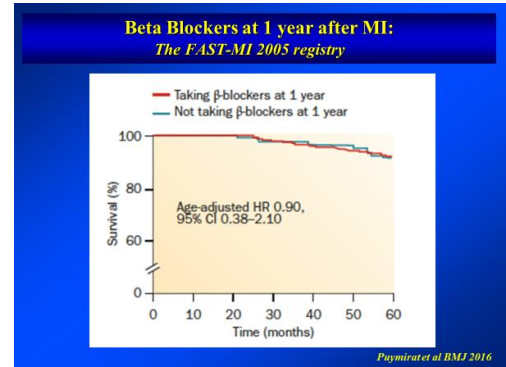
<http://www.fondazione-menarini.it/Archivio-Eventi/2017/From-Risk-Factors-to-Target-Organ-Damage-How-to-diagnose-how-to-treat/Materiale-Multimediale> ... and, after having logged in, enter in the multimedia area.

Medical treatment of SCHD: a new tailored therapeutic approach



The medical treatment of SCHD: a new tailored therapeutic approach was the topic Prof. Manolis talked about. The speaker, chairman of this symposium, at the beginning of his lecture talked about the medical management of patients with SCAD and presented the ESC guideline position for patients with CHD. Going deeper in his lecture, Prof.

Manolis spoke about the effects of beta-blockers and CCBs in SCHD patients, by highlighting that these drugs may not reduce the cardiovascular morbidity and mortality in these patients, particularly after PCI. The



speaker talked also about the combination therapy and more in particular about the addition of CCBs to Beta-blockers or ARB. In the main part of his lecture, Prof. Manolis presented very interesting data on the drugs developed in these last years like ranolazine and ivabradine. Finally, the speaker talked about a new therapeutic algorithm for patients affected by stable angina, primarily based on the heart rate and only after on the basal and on the target BP levels.

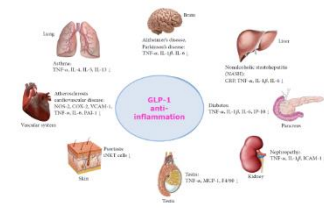
- What's about the combination therapy in SCHD?
- Where is the evidence of the effects of the long acting nitrate therapy based on the data presented by the speaker?
- What are the preferred drugs for the stable angina patients' treatment presented by the speaker?
- What's about diastolic blood pressure, subclinical myocardial damage and cardiac events based on the data presented by the speaker?
- What are the key points of the therapeutic algorithm presented by the speaker?

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What's new in diabetes and CVD

Anti-Inflammatory Effects of GLP-1-Based Therapies beyond Glucose Control

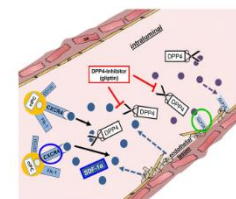


Young-Sun Lee and Hee-Sook Jun
Hindawi Publishing Corporation, Mediators of Inflammation, Vol.2016

What's new in diabetes and CVD, was the topic at the core of Prof. Hatziagelaki presentation. The speaker coming from Athens (GR), at the beginning of her lecture addressed then audience, by pointing out that every 6 seconds 1 person dies for diabetes-related complications. Going deeper in her lecture, Prof. Hatziagelaki talked about the main available drugs for the diabetes control and treatment, by presenting very interesting data on Metformin, DPP-4



Endothelial effects of pharmacological dipeptidyl peptidase 4 inhibition.

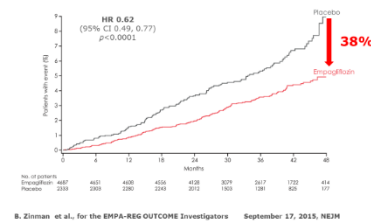


Friderika Ramm et al. Eur Heart J Cardiovasc Pharmacother 2015;5:135-139

1. Activated platelets, smooth muscle and endothelial cells secrete SDF1
2. SDF1 binds to the CXCR4 receptor of circulating progenitor cells and mediates their recruitment to the injured vascular wall
3. GLP1 binds to the GLP-1 receptor on the vascular wall and improves endothelial function
4. Gliptins can inhibit cleavage of SDF1 and GLP1 and thus facilitate improved vascular recovery

inhibitors, GLP-1 receptor agonists and SGLT2 inhibitors. More in particular, Prof. Hatziagelaki spoke about the role of incretins and the enzyme DPP-4 in glucose homeostasis and discussed the role played by GLP-1 in human physiology. In the main part of her lecture, the speaker presented very interesting data on the GLP-1 analogues, given by clinical trials running in diabetes patients treated with these drugs. Prof. Hatziagelaki spoke also about the fixed combination composed by basal insulin and GLP-1

...a marked effect on CV death



B. Zinman et al., for the EMPA-REG OUTCOME Investigators September 17, 2015, NEJM

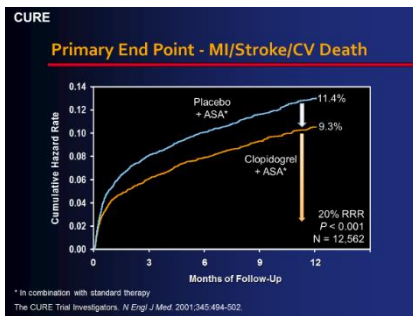
and about other drugs like exanotide, dulaglutide, liraglutide and semaglutide. Finally, the speaker presented very interesting data on the new SGLT2 inhibitors, their mechanism of action, their glycemic effect in monotherapy, the effect on the body weight and on the cardiovascular outcomes characterized by a very important reduction in CV death events. In conclusion, Prof. Hatziagelaki pointed out that a good glycemic control remains the cornerstone of the diabetes care, but the treatment should be individualized for any patient.

- What's about the features of the ideal antidiabetic medication from the speaker point of view?
- What is the role of incretins and the enzyme DPP-4 in glucose homeostasis?
- What's about the cardiovascular safety of the DPP-4 inhibitors from the speaker point of view?
- What are the main effects on fasting and postprandial glucose of the short and long-acting GLP-1R agonists?
- What's about the SGLT2 inhibitors based on the data presented by the speaker?

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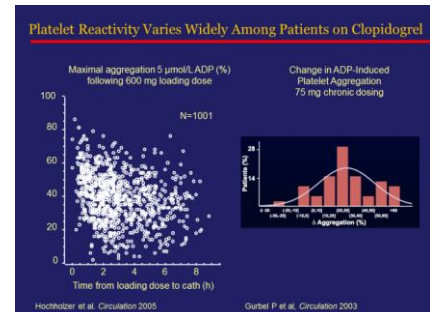
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2017: state of the art approach on DAPT

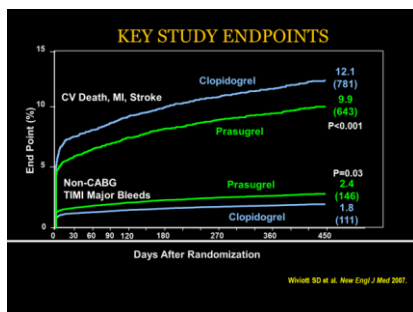


Prof. Ghazzal talked about the state of the art of the approach on DAPT in 2017. The speaker coming from Beirut (LB), presented very interesting data on the double antiplatelet therapy, by highlighting that despite the changes implemented in this type of therapy since the 50s years, the residual cardiovascular risk is already present. Prof. Ghazzal went deeper in his lecture and

presented very interesting and impressive data on the potential role of platelets in inflammation and the role of therapy. In the main part of his lecture, the speaker discussed a huge amount of data, given by interventional clinical trials on DAP therapy, on the effects of prasugrel, ticagrelor and copidogral. Prof. Ghazzal spoke also about the optimal duration of the antiplatelet therapy,



by presenting data given by PEGASUS trial and by the guidelines recommendations. In the last part of his lecture, the speaker talked about the triple therapy and presented very interesting data given by the TRA 2P-TIMI 50 trial, the COLCOT trial, the Cardiovascular Inflammation Reduction trial and the CANTOS trial. In conclusion, Prof. Ghazzal pointed out that we can bridge the gap of the residual risk after ACS, but the way to go is very long.

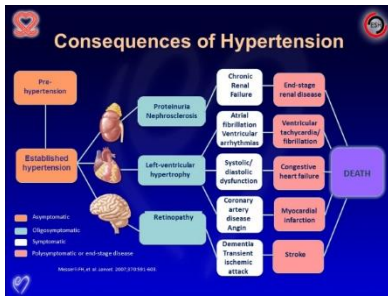


- What is the patient risk of future event after a cardiac catheterization for MI?
- What's about the role of platelets in inflammation?
- How long should DAPT be continued for?
- How about adding anti-inflammatory agents to a double therapy protocol based on the data presented by the speaker?

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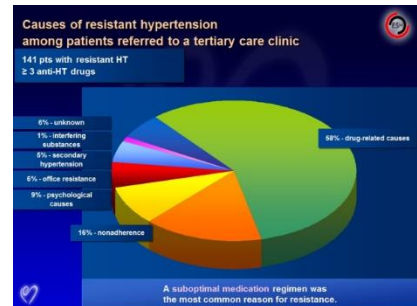
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Resistant hypertension

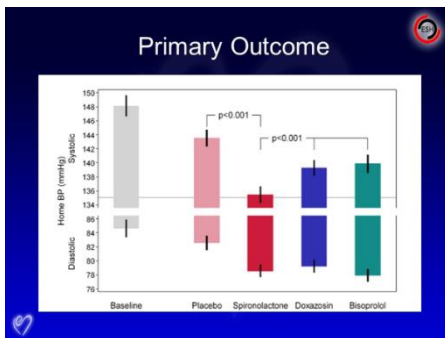


Prof. Erdine talked about resistant hypertension. The speaker coming from Istanbul (TR), at the beginning of her presentation addressed the audience with this question: how to manage a difficult case of resistant hypertension? Going deeper in her lecture, Prof. Erdine presented very interesting data on the consequences of hypertension, the BP control on European and extra European countries, by highlighting that only a few rates of patients are really controlled

even in case of multidrug- regimen therapy. In the main part of her lecture, Prof. Ervine talked about resistant hypertension and uncontrolled hypertension, their definition, causes, prevalence and pharmacological and invasive treatment. The speaker presented a huge amount of data given by clinical trials and registries running in uncontrolled and resistant hypertension patients with the intention to talk about the main important issues of this disease. From the pharmacological point of view, Prof. Ervine, pointed out that the combination therapy represents the best way for a better control of hypertension and presented very interesting data on the aldosterone antagonists, by highlighting that spironolactone is the one among the additional drugs with the largest



amount of evidence. In the last part of her lecture, the speaker presented also data on the invasive treatment of RH patients, speaking about renal denervation, carotid baroreceptor stimulation, A-V fistula, brain stem stimulation and finally about the total sympathectomy splanchnicectomy. In conclusion, Prof. Erdine pointed out that there is the need for future trials with the aim to compare new treatment options against the best drug therapy.

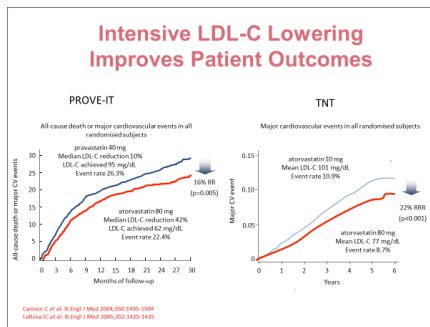


- What are the baseline predictors of increased risk for resistant hypertension?
- What's about the drug addition in RH patients under D/CCBs/RAS blockers?
- What are the main mechanisms of the papillary muscles movements in the functional regurgitation?
- How to measure the tricuspid annulus with 2D technology?
- What's about the dedicated software for TV analysis by transthoracic 3D?
- What are the main mechanisms of functional tricuspid regurgitation?
- What's about the valve tenting in functional regurgitation, based on the data presented by the speaker?

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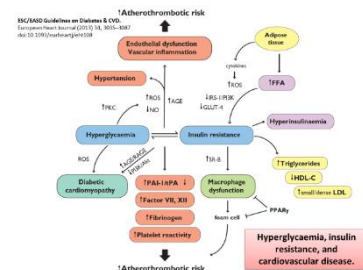
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Stable coronary artery disease and diabetes

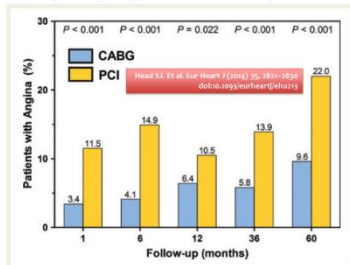


Stable coronary artery disease and diabetes was the topic Prof. Quek talked about. The speaker coming from Kuala Lumpur (MAL), presented very interesting data on the relationship between these two disease and more in particular spoke about diagnosis and the current management of the risk factors for diabetes in the presence of dyslipidaemia in suboptimal control. Prof. Quek presented also very impressive data on the

adverse outcomes in diabetic patients affected by dyslipidaemia and CAD, treated with revascularisation procedures and LDL-C lowering agents. In the main part of his lecture, the speaker talked about the goals to be reached in these type of patients, by highlighting that other than the glycaemic control, these patients are at high atherothrombotic risk and presented the main guidelines recommendations on the optimal glycaemic and blood pressure control in these patients.



Presence of angina during follow-up. CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.



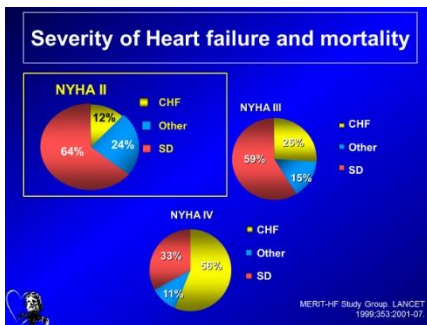
Prof. Quek presented also data on the CV risk and the other evaluations to be implemented in these patients. Finally, the speaker presented very interesting data on the new available drugs for the treatment of these patients like Trimetazidine, Ivabradine, Nicorandil and Ranolazine and spoke about the indications for revascularization.

- What would be your choice of LDL-C lowering agents?
- What would be your preferred diabetic/glycaemic goals in diabetic patients affected by CAD?
- How high is in your opinion the CV risk of such a patient like this?
- What are the best examinations to be performed from a prognostic point of view in a diabetic/dyslipidaemic patient?
- Which are the additional antianginal medications You can consider for the treatment of this type of patients?
- Why PCI revascularization may fail in these patients?

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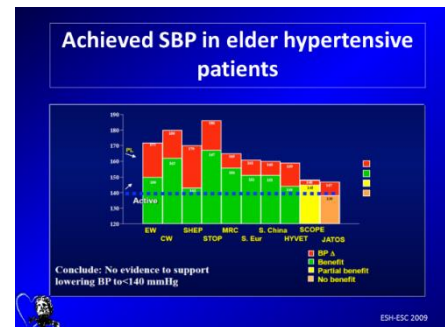
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Heart failure in an elderly patient

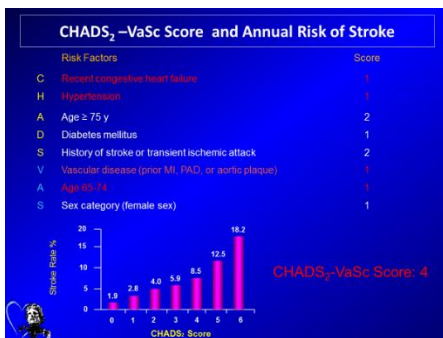


Heart failure in an elderly patient was the topic of Prof. Kallistratos presentation. The speaker coming from Athens (GR), presented very interesting data on prognosis, survival, the natural history, severity and mortality for heart failure in the elderly. Going deeper in his lecture, Prof. Kallistratos spoke about guidelines and addressed the audience with this question: which guidelines should we follow? The

heart failure or the hypertension guidelines? In order to find a comprehensive answer, the speaker presented very interesting data given by the main clinical trials running on these patients. More in particular Prof. Kallistratos spoke about the results of the SPRINT study, by highlighting that the SBP levels reached in this study are not always applicable to elderly HF patients and there is the need for the achievement of a more flexible threshold/target in relation with the total CV risk. In the



second part of his presentation, the speaker talked about some concerns present in these patients like the ones linked with the life style modifications like smoking, diabetes, LVH, hypertension, BMI and alcohol intake and presented very interesting data on the CHADS2-VASc score that calculates the annual risk of stroke. Finally, Prof. Kallistratos spoke about the rate of patients at target therapy and the reasons for its non-achievement in a very high rate of patients.

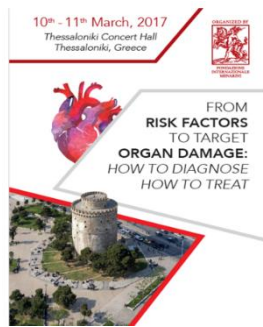


- What are the main concerns about these patients presented by the speaker?
- Is it possible to use B-blockers in COPD HF elderly patients?
- What is the right BP target for HF elderly patients from the speaker point of view?
- Which are the best guidelines to be followed for the treatment of HF elderly patients?
- What's about the relationship between severity of heart failure and mortality, based on the data presented by the speaker?

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These are only some of the topics addressed in the congress's sections

For a deeper knowledge on these topics, please visit the International Menarini Foundation web site where You can find all the speeches in their full version.

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