

# ***International Congress Hot Topics in Cardiology ZURICH (CH), October 05<sup>th</sup>-07<sup>th</sup>, 2017 Highlights***

## **Introduction**



Prof. Lüscher, chairman of the symposium, opened the congress, by highlighting the high scientific level of this meeting, focusing on the main hot topics in Cardiology like prevention, diagnosis, acute care, intervention and secondary prevention. More in particular the speaker highlighted that this meeting has been dedicated to an update on hypertension, diabetes, acute myocardial infarction, acute coronary

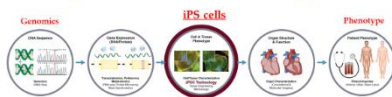
syndromes, the novelties in the interventional techniques and the ones in secondary prevention like the association between rivaroxaban and aspirin in patients affected by CVDs and finally on heart failure and SCD. The congress has been attended by many of the top researchers of this field coming from all the world and by many cardiologists and students attending the University of Zurich.

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# Stem Cells and Genomics for Precision Medicine

## Missing Link of Genomics → Phenotype Studies



“For most common diseases, there are hundreds of genetic risk variants with small effects, thus *difficult* to develop a clear picture of who is really at risk for what.

“This is b/c of complex world of epigenomics, transcriptomics, metabolomics, and environmental omics *not* captured by DNA-seq.

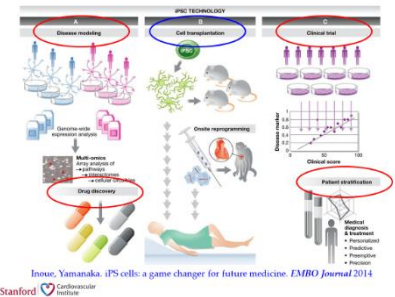
“Ideally, we would like to study patient's *heart* in response to treatment so we can accurately measure tissue specific changes. But we could not in the past b/c we did not have access to these tissues, and hence we use blood as *indirect* biomarkers. *This has now changed with human induced pluripotent stem cells.*

Stanford Cardiovascular Institute

“Stem Cells and Genomics for Precision Medicine”, was the topic discussed by Prof. Wu in his lecture. The speaker, coming from Stanford (USA), went deeper in his talk and presented very interesting data on the main phenotype studies running in his clinical center. In the main part of his lecture, Prof. Wu talked about the tight relationship between genomics and phenotyping and highlighted that physicians use blood biomarkers for treating diseases despite they are only indirect biomarkers of diseases. The

speaker presented very interesting and impressive data on the main experiments running in his center on the generation of human heart cells de novo, with a 90% efficiency obtained in 2017.

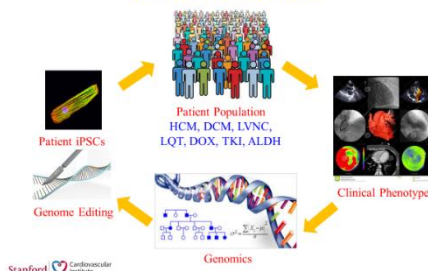
Prof. Wu pointed out that his team is able to develop new disease models to be applied in many fields like new drug discovery, cell transplantation and clinical trials based on precise patient stratification, through the application of the iPSC technology. In the second part of his lecture, Prof. Wu talked about the main clinical applications of this technique developed in his center and presented very impressive data on patients affected by familial hypertrophic cardiomyopathy, familial dilated cardiomyopathy, left ventricular non-compaction, long QT syndrome and on cardio-oncology. Finally, Prof. Wu talked about the IPCS platform application in the project called “clinical trial in a dish” and highlighted that one of the major



Inoue, Yamataka. iPSC cells: a game changer for future medicine. *EMBO Journal* 2014  
Stanford Cardiovascular Institute

causes of the new drugs withdrawal is due to their cardiac toxicity and the IPCS platform application can reduce this problem. More in particular the speaker presented very impressive data on the three phases of the IPCS clinical trial model, starting from the phase 0.5 characterized by the performing of toxicity tests, through the phase 1.5 constituted by the selection of the responders, till the phase 2 characterized by trials running only on responders. In conclusion, Prof. Wu pointed out that Stanford in the past has created a biobank of 1,00 iPSC lines to enable CV research.

## Human iPSCs: From Precision Medicine to Clinical Trial in a Dish



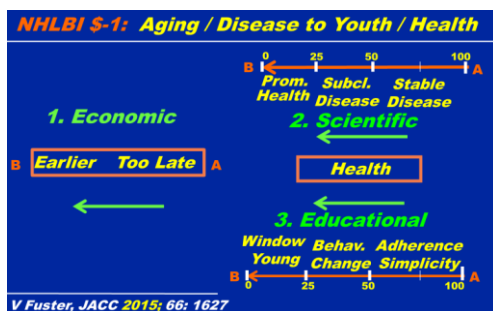
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- What's about the precision medicine meaning from the speaker point of view?
- What's about the missing link of Genomics, from the speaker point of view?
- How does the MYH7 Arg663His mutation cause hypertrophic heart and cardiac arrhythmias in patients, based on the data presented by the speaker?
- How does the TNNT2 (Arg173Trp) mutation cause dilated cardiomyopathy in patients, based on the data presented by the speaker?
- How does the TBX20 mutation cause left ventricular non-compaction in patients, based on the data presented by the speaker?

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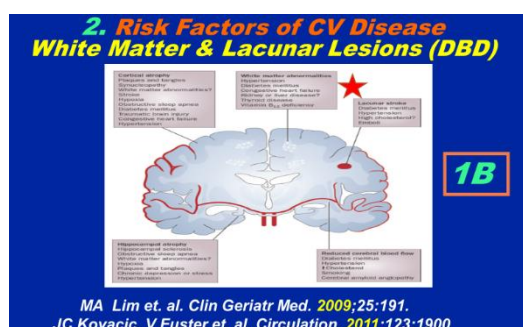
# Prevention or intervention?



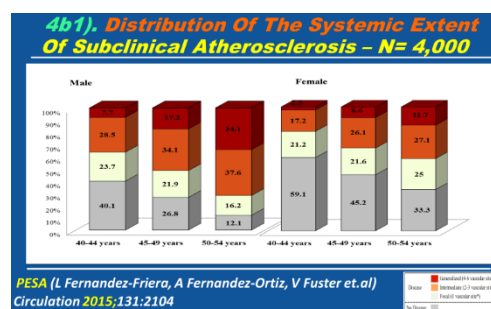
Prof. Fuster from New York (USA), spoke about “Prevention or intervention?”. Going deeper in his lecture, the speaker presented very interesting and impressive data on the main problems linked with the actual standard of care. Going deeper in his lecture, Prof. Fuster talked about scientific and educational topics for people from 25 to 50 years old. In the main part of his lecture, the speaker presented very interesting and impressive data given from clinical trials,

like the bioimage study designed for the detection of the subclinical atherosclerotic burden and the PESA study aiming to the detection of the atherosclerosis assessment. Prof. Fuster talked about new strategies available for identifying patients at high CV risk and presented very interesting data on new applications of the imaging techniques, on the tight relationship between the atherosclerosis risk and the type of breakfast consumed or the social eating. In the second

part of his lecture, the speaker talked about two projects, the first one running in AMPATH centers in Kenia, where people has been involved in an educational model aiming to a better



control of BP. The second one project was about the seven-community study running in Spain. Finally, Prof. Fuster talked about the correlation between brain lacunar lesions and the presence of cardiovascular risk factors in people and highlighted that this correlation is very impressive. In conclusion, the speaker pointed out that the evolution of CVD worldwide knowledge and prevention is dealing with health, but also with science and education.

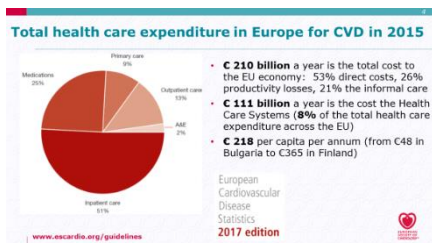


- What's about the role of inflammation in ischemic CVD, based on the data presented by the speaker?
- What's about the Subclinical Atherosclerotic Burden presented by the speaker?
- What are the key topics of the Bioimage Study, based on the data presented by the speaker?
- What are the temporal sequence and functions of leukocytes in the coronary arteries presented by the speaker?
- What's about the atherosclerosis assessment, based on the PESA study presented by the speaker?
- Is there any correlation between the CV risk factors and the lacunar lesions in the white matter, based on the data presented by the speaker?
- What are the key points of the children program presented by the speaker?

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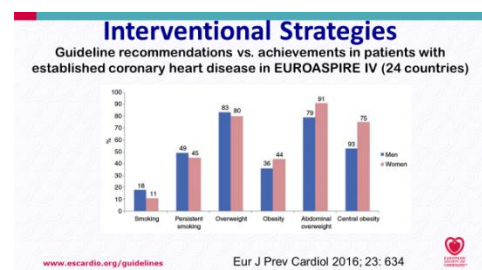
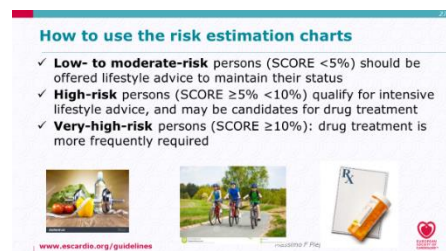
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# What can we learn from the new ESC Guidelines on CVD prevention?



“What can we learn from the new ESC Guidelines on CVD prevention?”, was the topic Prof. Piepoli spoke about in his lecture. The speaker coming from Piacenza (IT), presented very interesting data on the novelties and the controversial issues related to the European 2017 guidelines on CVD prevention. Going deeper in his lecture, Prof. Piepoli pointed out that the CVD burden in Europe has been more than 210 billion euro a

year in the 2015. In the main part of his lecture, the speaker presented very interesting data on key points of these new guidelines compared to the ones published in 2012. More in particular Prof. Piepoli highlighted that new recommendations have been published on prevention at population level and on disease-specific prevention. Speaking about the promotion of the healthy lifestyle and environmental in non-communicable diseases, Prof. Piepoli highlighted that NCDs are often caused by behavioural risk factor like, tobacco use, unhealthy diet and insufficient physical activity. Prof. Piepoli talked about all the key points of the new guidelines like cost-effective prevention of CVD, population-based approaches to physical activity, the identification of relevant groups from the risk level point of view, like the youngs or people over 60 years old



or people treated for cancer. In the second part of his lecture, the speaker talked about the risk tools and more in particular on their key characteristics. Finally, Prof. Piepoli presented very interesting data on the risk factors goals and target levels and on the interventional strategies. In conclusion, the speaker pointed out that in order to improve patient adherence it is of high importance to give clear messages simple to be read and understood by

patients.

- What are the major new key messages since 2012, from the speaker point of view?
- What's about the cost-effective prevention of cardiovascular disease, based on the data presented by the speaker?
- What are the population-based approaches to physical activity, based on the data presented by the speaker?
- What's about patients treated for cancer, based on the data presented by the speaker?
- How to use the risk estimation charts?
- What are the characteristics of the SCORE-guided European guidelines on CVD prevention, based on the data presented by the speaker?

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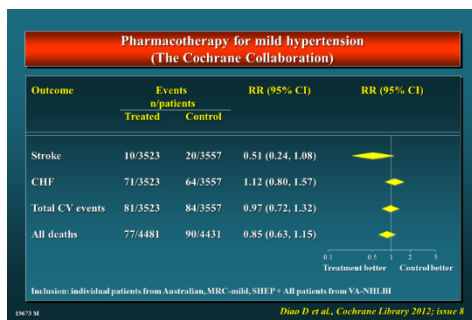
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significant way. In conclusion, the speaker pointed out that the true meaning of prevention is about “giving your best to protect your loved ones”.

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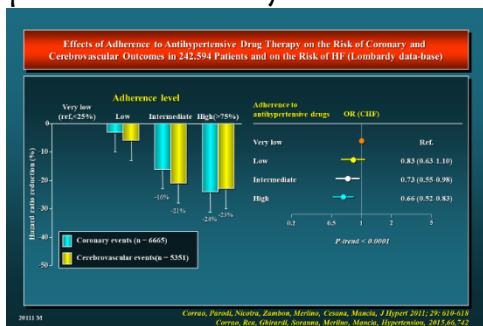
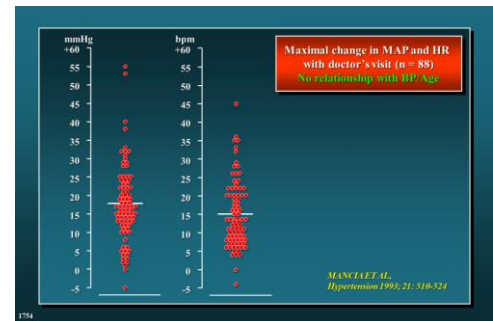
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# Hot topics in the management of hypertension



“Hot topics in the management of hypertension”, was the topic discussed by Prof. Mancia in his lecture. The speaker, coming from Milan (IT), talked about the way to start drug treatment in hypertension. Going deeper in his lecture, Prof. Mancia pointed out that in the 2013 ESH/ESC hypertension guidelines, patients at grade 1/low CV risk were recommended to start drug therapy only after lifestyle changes, but with poor results in CVD events reduction. In the main part of his

lecture, Prof. Mancia presented other very interesting data also in elderly patients, defined as patients below and above 80 years, pointing to the messages driven by SPRINT study, where through the SBP reduction below 140 mmHg, great benefits have been achieved in normal, but also in frail elderly patients. The speaker talked also about other patient populations like the diabetic ones and the patients affected by stable coronary angina and presented



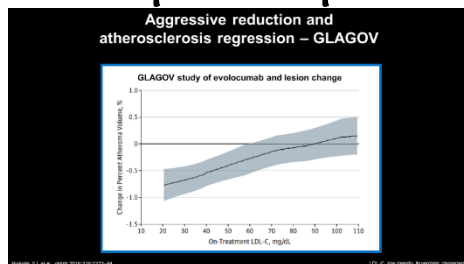
very interesting data supporting the need to reduce SBP in these patients but not below 120 mmHg. for the presence of a J shaped curve for the CV death or non-fatal MI or stroke incidence. Finally, Prof. Mancia presented very interesting data on the comparison between monotherapy and combination strategies for achieving the target BP and highlighted that combination therapy is better from an adherence but also from the CV events incidence point of view.

- What's about the Initiation of drug treatment in hypertension, based on the data presented by the speaker?
- What are the 2013 ESH/ESC hypertension guidelines SBP targets for treatment presented by the speaker?
- What are the final blood pressure values in SPRINT study, presented by the speaker?
- What are the differences between patients with and without diabetes in standardized RR and absolute risk reductions at achieved SBP < 130 mmHg, from the speaker point of view?
- What's about the relationship between risk of discontinuation of antihypertensive treatment and initially prescribed drugs, based on the data presented by the speaker?

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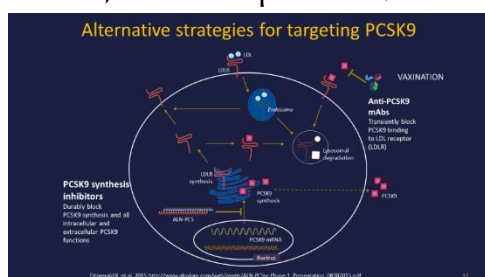
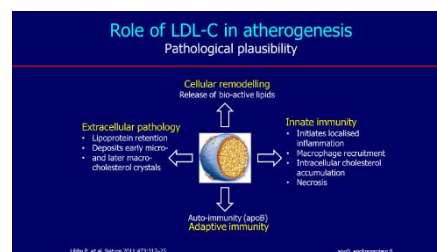
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# Hot topics in lipid management



“Hot topics in lipid management”, was the topic of Prof. Catapano presentation. The speaker, coming from Milan (IT), talked about the goals for LDL cholesterol reduction. Going deeper in his lecture, Prof. Catapano, presented very interesting data on the effect of the LDL reduction in terms of event reduction. More in particular the speaker talked about the PCSK9 inhibitors and their effects on LDL

reduction. In the main part of his lecture, Prof. Catapano pointed out that the LDL reduction seems do not have any J shape curve effect as in the case of lowering BP. The speaker presented a huge amount of data given from clinical studies running also in diabetic patients and treated with the PCK9 inhibitors and highlighted that these drugs have no pro-glycemic effect. In the second part of his lecture, Prof. Catapano talked about the tight relationship between LDL cholesterol reduction and atherosclerosis counteraction through the CV risk reduction.



and atherosclerosis counteraction through the CV risk reduction. In the last part of his lecture, Prof. Catapano presented very interesting data on the risk evaluation, through the score chart but also the genetic risk scores. Finally, the speaker presented very interesting data on the alternative strategies for develop new targets like PCSK9.

- What's about the relationship between treatment goals and CVD risk reduction, based on the data presented by the speaker?
- What is the relationship between aggressive reduction and atherosclerosis regression, based on the data presented by the speaker?
- What's about the effects of the PCSK9 inhibitors in diabetic patients, based on the data presented by the speaker?
- What's about the relationship between time exposure and atherosclerosis development from the speaker point of view?

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# Improving diabetes outcomes: beyond glucose metabolism

## New treatments reducing outcomes

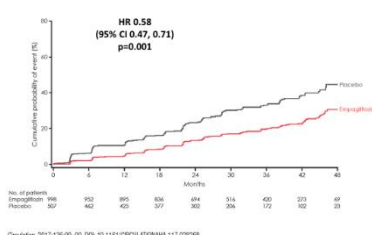
**SGLT2 inhibitors** (EMPA-REG Outcome study & CANVAS programme) are cardio/renoprotective through **multiple effects**  
NEJM 2015;373:2117; 2016;375:323; 2017;377:644

**Liraglutide a GLP1-RA** (LEADER trial) is cardio/renoprotective  
NEJM 2016;375:323-334; 2017;377:339

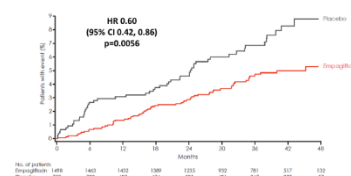
**DPP4 inhibitors** (MARLINA-T2D 2017 & CARMELINA 2018) **may be** renoprotective through **multiple off-target effects** (i.e. interaction of DPP4 with integrin  $\beta 1$ , preventing endothelial-mesenchymal transition and ultimately renal fibrosis)  
Diabetes Obes Metab 2017 online; Kidney Int 2015;88:429 & 479

Prof. Wanner coming from (Wurzburg (DE) spoke about “Improving diabetes outcomes: beyond glucose metabolism” and presented very interesting data on the standard of care in diabetic patients for reducing macro and microvascular outcomes. Going deeper in his lecture, Prof. Wanner talked about the new treatments like SGLT2 inhibitors, Liraglutide and DPP4 inhibitors able to reduce outcomes. In the main part of his lecture, the speaker presented the main data given from the EMPA-REG OUTCOME trial. More in particular Prof. Wanner talked about the effects of the SGLT2 inhibitors on all cause of mortality, cardiovascular death and hospitalization for heart failure.

Prevalent kidney disease: worsening of nephropathy



Hospitalisation for heart failure  
in prevalent kidney disease



Prof. Wanner, presented other very interesting data on the renal mechanism of action of the SGLT2 inhibitors and highlighted that these drugs are able to lower the intra-glomerular pressure and to reduce the incidence of the new onset or worsening of nephropathy in diabetic patients. In conclusion, the speaker pointed out that the SGLT2 inhibitors have very interesting effects at the renal level determining kidney protection.

- What's about the renal mechanism of the SGLT2 inhibitors, based on the data presented by the speaker?
- What is the effect of the standard-of-care in reducing macrovascular and microvascular outcomes in Type 2 diabetic patients, from the speaker point of view?
- What's about ketone bodies as energy source for the failing heart, based on the data presented by the speaker?
- How does diabetes cause glomerular hypertension, based on the data presented by the speaker?

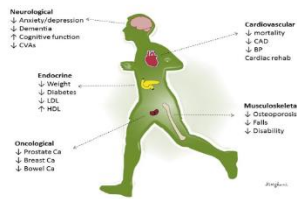
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# How can exercise training and diet influence risk management?

## Benefits of Exercise



Prof. Sharma from London (UK), spoke about “How can exercise training and diet influence risk management?” and presented very interesting data starting from the consideration that exercise and diet can prevent as well cardiovascular disease. Going deeper in his lecture, the speaker talked about the effects of physical activity and diet and presented very interesting data on the correlation

between physical activity and CVD where less is the exercise performed by people higher the CHD risk is. In the main part of his lecture, Prof. Sharma talked about the current physical activity guidelines for adults and children and highlighted that adults need to perform almost 30 minutes of moderate intensity physical activity for 5 days per week in order to take under control their CVD risk. In the second part of his lecture, the speaker presented very interesting data on the effect of diet for the CVD prevention. Speaking about the relationship between saturated fatty acids and all cause or mortality or CV disease Prof. Sharma highlighted that a systematic review and meta-analysis of observational studies have not found any association. In the last

## Dietary Benefits on the Cardiovascular System



## 2016 ESC Dietary Recommendations for Prevention of CVD

DIETARY RECOMMENDATIONS
<ul style="list-style-type: none"> <li>Saturated fatty acids to account for &lt; 10% of total energy expenditure, through replacement of polyunsaturated fatty acids.</li> <li>Trans unsaturated fatty acids; as little as possible, preferably no intake from processed food, and &lt;1% total energy intake from natural origin.</li> <li>&lt;5g salt per day.</li> <li>30-45g of fibre per day, preferably from wholegrain products.</li> <li>≥ 200 g fruit per day (2-3 servings).</li> <li>≥ 200g vegetables per day (2-3 servings).</li> <li>Fish 1-2 times per week, one of which to be oily fish</li> <li>30 g unsalted nuts per day.</li> <li>Alcohol 2 units per day for men and 1 unit for women</li> <li>Sugar-sweetened soft drinks and alcoholic beverages should be discouraged.</li> </ul>

Piepoli M et al. EHJ. 2016; 37: 2315-2381

part of his lecture, the speaker presented very interesting data on the effects of the replacement of the saturated fatty acids with the polyunsaturated ones on the metabolic profile and talked about the PURE study results. In conclusion Prof. Sharma pointed out that exercise for at least 150 minutes per week is recommended but with 600-750 minutes the benefits are greater.

- What are the benefits of exercise presented by the speaker?
- What are the dietary benefits on the cardiovascular system, based on the data presented by the speaker?
- What's about the PURE study results from the speaker point of view?
- What are the key points of the 2016 ESC dietary recommendations for CVD prevention, based on the data presented by the speaker?
- What's about primary CVD prevention with a Mediterranean diet, based on the data presented by the speaker?

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# Stable CAD: diagnosis: from symptoms to imaging

**ESC Guidelines-Stable Coronary Artery Disease**  
- Assessment of Pre-test probabilities (PTP) -

**Table 13** Clinical pre-test probabilities\* in patients with stable chest pain symptoms<sup>†</sup>

Age	Typical angina		Atypical angina		Non-anginal pain	
	Men	Women	Men	Women	Men	Women
20-29	18	28	20	10	10	5
30-39	18	27	20	14	20	8
40-49	27	47	40	30	34	13
50-59	84	58	58	38	44	17
60-69	88	68	68	37	54	24
70-79	88	76	79	47	62	33

**Table 4** Traditional clinical classification of chest pain

Typical angina (definite)	Plots all three of the following characteristics: • classical chest discomfort of non-traumatic quality and duration • provoked by exercise or emotional stress • relieved by rest within minutes.
Atypical angina (probable)	Plots two of three characteristics.
Non-anginal chest pain	Lacks or meets only one or none of the characteristics.

**Classification:**

- Age
- Gender
- Type of Symptoms

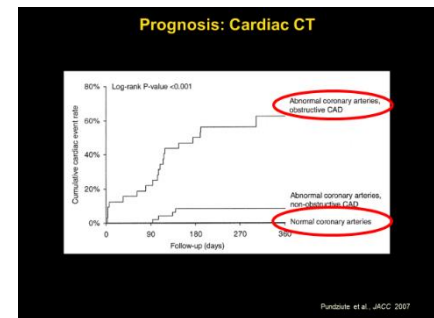
**Symptoms:**

- Typical angina
- Atypical angina
- Non-anginal CP

\*Reference: et al. Eur Heart J 2011

Prof. Manka from Zurich (CH), spoke about “Stable CAD: diagnosis: from symptoms to imaging”. More in particular, the speaker talked about the detection of CAD, the hemodynamic relevance of coronary stenosis, the assessment of viability and about the prognostic information given by the use of imaging. Going deeper in his lecture, Prof. Manka presented very interesting data pointing to the ESC guidelines on stable coronary artery disease assessment. In the main part of his lecture, the speaker

talked about the cardiac CT scan technique and presented very interesting data given from imaging studies running on patients affected by CVD, pointing to the high sensitive and predictive level of this technique. Prof. Manka presented other very interesting data on the prognostic value of the cardiac CT scan and talked about the functional imaging able to detect ischemia, pointing to the advantages of this technique compared to the anatomic imaging. The speaker presented very interesting data on cardiac MRI and highlighted that with this technique it is



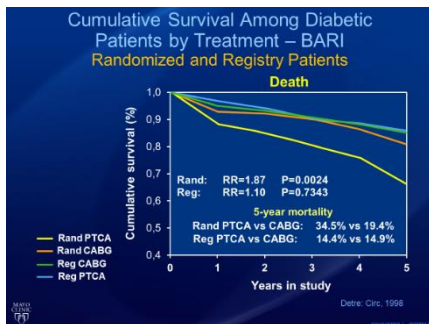
possible to quantify the myocardial ischemic burden in order to take any therapeutic decision. Prof. Manka talked also about the MR-INFROM study, designed for guiding the management of patients with stable coronary artery disease. Finally, the speaker presented very interesting data on the hybrid imaging MR/CT or MR/MR 3D fusion. In conclusion, Prof. Manka pointed out that the imaging of the hearth should be characterized by the integration of anatomy, morphology and function.

- What's about the ESC Guidelines on Stable Coronary Artery Disease, based on the data presented by the speaker?
- Why functional imaging is better than anatomic imaging for the stenosis detection, based on the data presented by the speaker?
- What's about the visualization of the Aorto-Coronary Bypasses, based on the data presented by the speaker?
- What are the key points of the functional imaging presented by the speaker?

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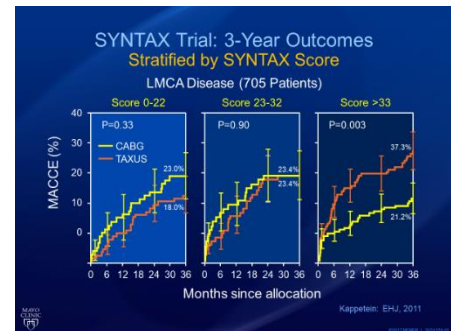
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## Stable CAD: CABG versus PCI

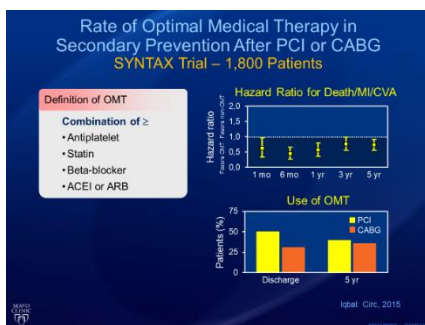


Prof. Gersh from Rochester (USA), spoke about “Stable CAD: CABG versus PCI”. More in particular, the speaker talked about the trials designed for the evaluation of the methods of revascularization and about their limits. Going deeper in his lecture, Prof. Gersh presented very interesting data on these limitations, more in particular the speaker discussed the contradictory data produced by registry studies on drug eluted stents, where in one study mortality is reduced by DES but in the

other one is increased. In the main part of his lecture, Prof. Gersh presented very interesting data on the comparison between the effects of CABG vs PCI from the efficacy and the safety point of view in diabetic patients running in BARI registry study and concluded that in general, diabetics go better with surgery. The speaker talked also about the comparison between CABG and PCI in patients with 3 vessel disease and highlighted that these patients have better outcome with CABG than with PCI. Prof. Gersh presented other very interesting data on the EXCEL trial comparing the effects of PCI vs CABG in patients



affected by LMCA disease and on the NOBLE trial running in the same patients and highlighted that for a better interpretation of these two studies longer-term follow-up is needed. Finally, the speaker talked about the impact of the coronary flow reserve on the cardiovascular outcomes in patients underwent to CABG or PCI. In conclusion, Prof. Gersh pointed out that at Mayo Clinic the cause of death in patients underwent to PCI have dramatically changed from the cardiac to the non-cardiac ones.



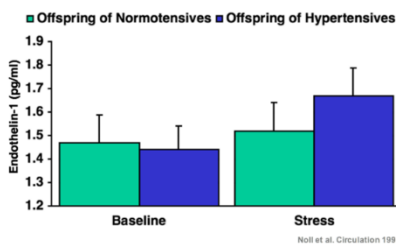
- What are the pros and the cons of CABG vs PCI in DM and HF patients, based on the data presented by the speaker?
- Did the patients enrolled in these trials have diabetes and HF, from the speaker point of view?
- What’s about CV mortality for CABG compared to medical therapy in diabetic and non-diabetic patients, from the speaker point of view?
- What are the main limitations of the study analysis presented by the speaker?

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# Takotsubo, an often-unrecognized acute heart disease

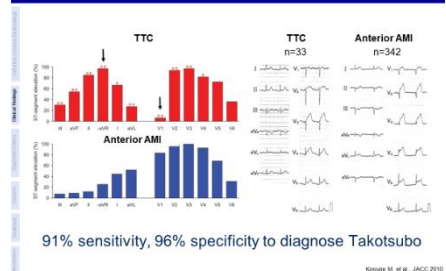
Mental Stress Increases Endothelin in Offspring of Hypertensive Parents



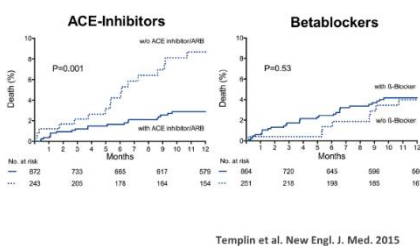
other very interesting data on the muscle sympathetic activity in these patients and talked about the relationship between Takotsubo and CAD. The speaker presented a huge amount of data in order to find out if there is any correlation between Takotsubo and CAD. Talking about imaging, Prof. Lüscher presented different types of Takotsubo cardiomyopathy and the typical images performed with

“Takotsubo, an often-unrecognized acute heart disease”, was the topic discussed by Prof. Lüscher, chairman of the symposium, more in particular the speaker presented very interesting data on the main characteristics of this syndrome. Going deeper in his lecture, the speaker talked about the endothelial function related to the acute mental stress, one of the mechanisms present in the Takotsubo syndrome. In the main part of his lecture, Prof. Lüscher presented

ECG Criteria: Takotsubo Cardiomyopathy vs. STEMI



TTC Long-Term Outcome: Effect of Drugs



echo. From the clinical point of view, the speaker pointed to the modified Mayo Clinic Diagnostic criteria for TTS and highlighted that this syndrome is more frequent in postmenopausal women. Finally, Prof. Lüscher presented very interesting data on the acute clinical course of this syndrome and on the long-term clinical outcome, pointing to its worse evolution. In conclusion, the speaker highlighted that Takotsubo cardiomyopathy resembles ACS, however symptoms, biomarkers and ECG changes, are different.

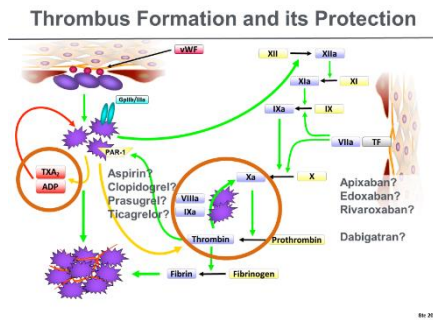
- Is there a correlation between endothelial function and Takotsubo syndrome, based on the data presented by the speaker?
- What's about the relationship between Takotsubo syndrome and coronary artery disease, from the speaker point of view?
- What are the main mechanisms of Takotsubo Syndrome presented by the speaker?
- What's about the clinical presentation of Takotsubo, based on the data presented by the speaker?
- What are the Long-Term clinical outcome of Takotsubo patients, based on the data presented by the speaker?

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# DAPT therapy: how long for whom?



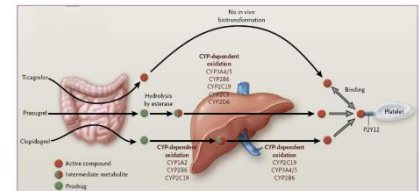
“DAPT therapy: how long for whom?” was the topic of Prof. Lüscher presentation. The speaker, coming from Zurich (CH), presented very interesting data starting from platelets and thrombus formation. Going deeper in his lecture, Prof. Lüscher talked about the main mechanisms leading to the thrombus formation and protection and highlighted the role played by factor Xa and thrombin. Talking about stent thrombosis, the speaker presented the main factors

contributing to its occurrence related to patients, stent type or also procedures performed on patients. Prof. Lüscher presented other very interesting data on the four steps in the interventional coronary intervention, characterized by balloon, stent, drug eluting stent and finally drug eluting scaffold. Talking about the opportunity to start with a dual

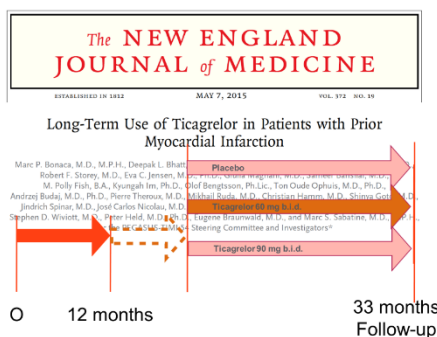
antiplatelet therapy after

PCI, Prof. Lüscher pointed to the importance of balance the two main risks, the first one represented by the ischemic risk and the second one related to the bleeding risk and the answer is tightly linked with the clinical conditions of any single patient. Finally, the speaker presented very interesting data on the future therapy developments mainly related to the use of the P2Y12 inhibitors alone and at different dosages or in association with NOAC.

## DAPT is not DAPT: Different Mechanisms of Action of P2Y<sub>12</sub> Inhibitors



## DAPT is not DAPT: The molecule matters

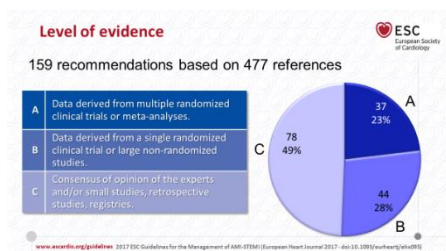


- What’s about the risk factor for stent thrombosis, from the speaker point of view?
- What are the four steps in Interventional coronary intervention, based on the data presented by the speaker?
- What are the main different mechanisms of action of the P2Y12 Inhibitors, based on the data presented by the speaker?
- What’s about the balance between ischemia and bleeding, based on the data presented by the speaker?

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# Management of STEMI patients according to the ESC Guidelines



The main topic of Prof. James presentation was “DAPT therapy: how long for whom?”. The speaker, coming from Uppsala (SE), presented very interesting data on 2017 ESC guidelines for the management of STEMI patients. Going deeper in his lecture, Prof. James talked about the novelties characterizing these guidelines. More in particular, in the main part of his lecture,

the speaker presented very interesting data on MINOCA and Quality indicators, on the patients’ strategy selection and the time delays, on the time limits for opening an IRA, on the ECG findings at presentation, on the time to angiography after fibrinolysis and finally on patients taking anticoagulants.

**What is new in 2017 Guidelines on AMI-STEMI**

2017 NEW / REVISED CONCEPTS

<b>MINOCA AND QUALITY INDICATORS:</b>	<ul style="list-style-type: none"> <li>New chapters dedicated to these topics.</li> </ul>
<b>STRATEGY SELECTION AND TIME DELAYS:</b>	<ul style="list-style-type: none"> <li>Clear definition of first medical contact (FMC).</li> <li>Definition of “time 0” to choose reperfusion strategy (i.e. the strategy clock starts at the time of “STEMI diagnosis”).</li> <li>Selection of PCI over fibrinolysis when anticipated delay from “STEMI diagnosis” to wire crossing is <math>\leq 120</math> min.</li> <li>Maximum delay time from “STEMI diagnosis” to choice of fibrinolysis agent is set in 10 min.</li> <li>“Close to balloon” term eliminated from guidelines.</li> </ul>
<b>TIME LIMITS FOR ROUTINE OPENING OF AN IRA:</b>	<ul style="list-style-type: none"> <li>0-12h (Class I), 12-48h (Class IIa), &gt;48h (Class III).</li> </ul>
<b>ELECTROCARDIOGRAM AT PRESENTATION:</b>	<ul style="list-style-type: none"> <li>Left and right bundle branch block considered equal for recommending urgent angiography if ischaemic symptoms.</li> </ul>
<b>TIME TO ANGIOGRAPHY AFTER FIBRINOLYSIS:</b>	<ul style="list-style-type: none"> <li>Timeframe is set at 2-24h after successful fibrinolysis.</li> </ul>
<b>PATIENTS TAKING ANTICOAGULANTS:</b>	<ul style="list-style-type: none"> <li>Acute and chronic management presented.</li> </ul>

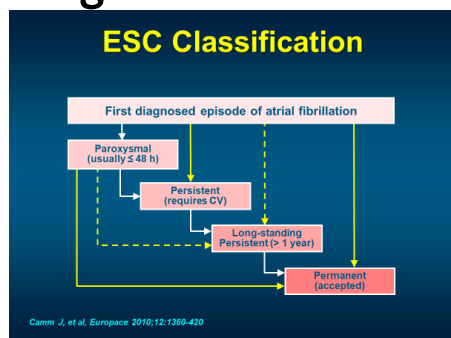
www.escardio.org/guidelines 2017 ESC Guidelines for the Management of AMI-STEMI (European Heart Journal 2017; doi:10.1093/eurheartj/ehw309)

- What are the classes of recommendations of these new guidelines, based on the data presented by the speaker?
- What is new in 2017 Guidelines on AMI-STEMI, from the speaker point of view?
- What’s about the new quality indicators, presented by the speaker?
- What’s about the reperfusion strategies in the infarct-related artery, according to time from symptoms onset, based on the data presented by the speaker?
- What’s about novelties in PCI and fibrinolysis strategies, presented by the speaker?
- What are the 2017 new recommendations, presented by the speaker?
- What’s about the doses of the anti-thrombotic agents, based on the data presented by the speaker?

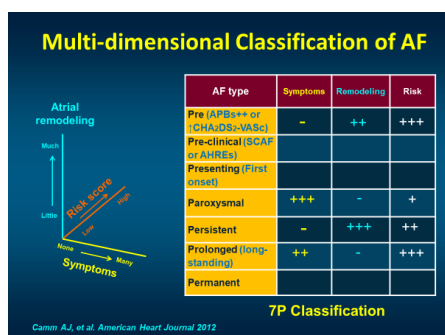
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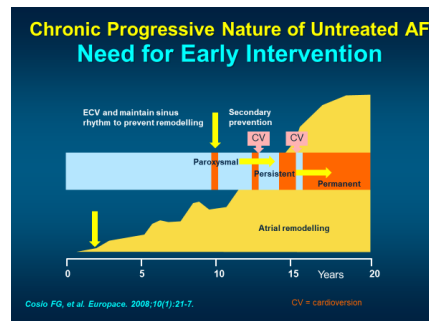
# Diagnosis and classification of AF



talked about the ESC AF classification, based on the AF pattern, pointing to the temporal varieties of AF divided into intermittent and non-intermittent. Prof. Camm pointed out that with the new classification, persistent AF has been divided into three sub types like: early persistent, continuous and long-standing. In the main part of his lecture, the speaker



“Diagnosis and classification of AF”, was the topic discussed by Prof. Camm from London (UK). More in particular the speaker presented very interesting data starting from the diagnosis of AF. Going deeper in his lecture, Prof. Camm talked about the incidence of the subclinical atrial fibrillation and presented very interesting data comparing the acute vs the chronic forms of atrial fibrillation. More in particular the speaker presented very interesting data on the chronic progressive nature of the untreated atrial fibrillation and highlighted that the non-paroxysmal atrial fibrillation is tight related to stroke. Prof. Camm presented other very interesting data on the differences between paroxysmal and persistent atrial fibrillation related to the LA ablation therapy. Finally, the speaker presented the multi-dimensional classification of AF.

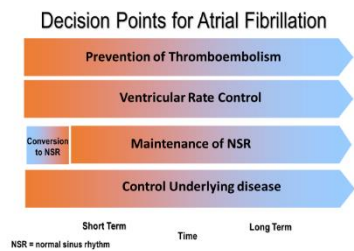


- What is the new definition of the permanent atrial fibrillation presented by the speaker?
- What are the main indications for catheter ablation of symptomatic atrial fibrillation, based on the data presented by the speaker?
- What's about the multi-dimensional AF classification, based on the data presented by the speaker?
- What's about the evaluation of the substrate for AF presented by the speaker?

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# Medical therapy of AF



“Medical therapy of AF”, was the topic discussed by Prof. Kerr Saraiva from Sao Paulo (BR), more in particular the speaker talked about the burden of AF in Latin America and about the decision points for atrial fibrillation. Going deeper in his lecture Prof. Kerr Saraiva presented very interesting data on the correct approach for controlling heart rate in atrial fibrillation, given from the ESC

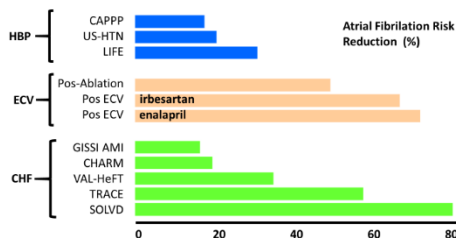
guidelines recommendations and talked about the effect of beta-blockers in AF patients. The speaker presented also very interesting data given from a clinical study on the use of digoxin in AF patients, by highlighting that this drug increases mortality in these patients. In the main part of his lecture, Prof. Kerr Saraiva talked about cardioversion and presented very interesting data given from the ESC guidelines, where the initiation of a long-term rhythm control therapy is recommended for improving

ESC 2016 Guidelines - Antiarrhythmic drugs

Drug	Route	1 <sup>st</sup> dose	Follow-up dose	Notes
Prevalence	Oral	200-300 mg	N/A	Hypotension, atrio-fibrosis with 1:1 conduction, QT prolongation. Avoid in patients with 1:1 conduction and/or significant structural heart disease.
Amiodarone	IV	5-7 mg/kg over 10 min	50 mg/kg as a maximum over 3-7 hours	Phlebitis, hypotension, bradycardia, sinus block, slow ventricular rate. Delayed conversion to sinus rhythm (8-12 hours).
Propafenone	IV	1.5-2 mg/kg over 10 min		Hypotension, atrio-fibrosis with 1:1 conduction, QT prolongation. Avoid in patients with 1:1 conduction and/or significant structural heart disease.
Fluticase <sup>a</sup>	IV	1 mg over 10 min	1 mg over 10 min after waiting for 10 min	QT prolongation, polymorphic ventricular tachycardias/depression (5-10% of patients) with slow ventricular rate. Avoid in patients with QT prolongation, hypotension, severe LVD or low ejection fraction.
Verapamil	IV	3 mg/kg over 10 min	2 mg/kg over 10 min after waiting for 10 min	Hypotension, non-sustained ventricular arrhythmias, QT and QRS prolongation. Avoid in patients with SBP <100 mmHg, recent (30 days) ACS, NYHA Class III and IV heart failure, QT interval prolongation, bradycardia, QTc >440 ms and severe aortic stenosis.

ACS = acute coronary syndrome; AF = atrio-ventricular; 1:1 conduction = 1:1 conduction; LVD = left ventricular dysfunction; NYHA = New York Heart Association; SBP = systolic blood pressure.  
<sup>a</sup> Use a large peripheral vessel and change to oral amiodarone within 24 h of IV (oral line) administration.  
<sup>b</sup> Fluticase is only available in selected European countries.

Reduction of AF incidence in ACE Inhibitors and ARB's trials



symptoms in AF patients. Finally, the speaker presented very interesting data on the control of the underlying diseases, like hypertension, CAD, MI and HF. More in particular, Prof. Kerr Saraiva talked about drug treatment and presented very interesting data on the reduction of AF incidence with ACE inhibitors and ARBs given from clinical trials running on these patients.

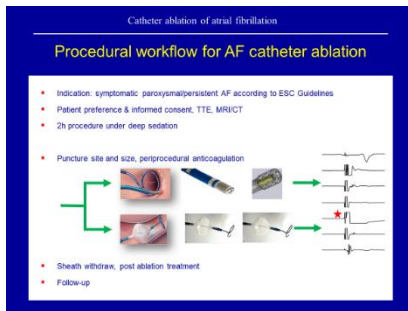
- What are the key points of the acute heart rate control in atrial fibrillation, based on the data presented by the speaker?
- What's about the long-term heart rate control from the speaker point of view?
- What's about the ESC 2016 guidelines on antiarrhythmic drugs, based on the data presented by the speaker?
- What's about the recommendations on pharmacotherapy for the management of patients with concomitant diseases, from the speaker point of view?

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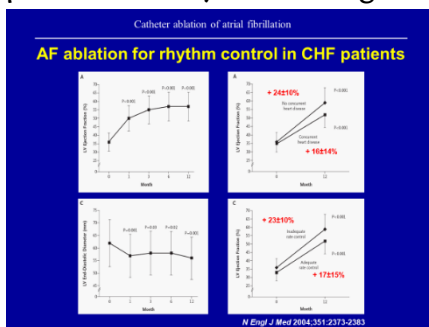
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# Catheter ablation of AF

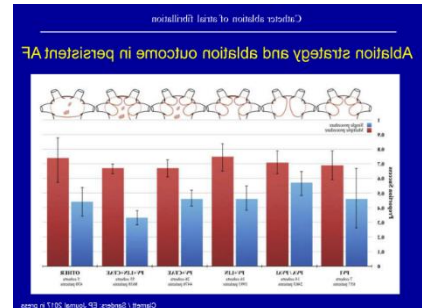


procedure workflow and on the rhythm outcome of AF catheter ablation. More in particular the speaker talked about the ablation strategies, the related outcomes and about complications like stroke, vascular complications and silent stroke. In the second part of his lecture, Prof. Hindricks presented very interesting data on the catheter ablation in



Prof. Hindricks from Leipzig (DE), presented very interesting data on “Catheter ablation of AF”. Going deeper in his lecture, the speaker talked about a review of the current status of AF catheter ablation, pointing to the main ESC guidelines indications for AF catheter ablation, starting from the real clinical data given from patients treated in his center. In the main part of his lecture, Prof. Hindricks presented very

interesting data on the



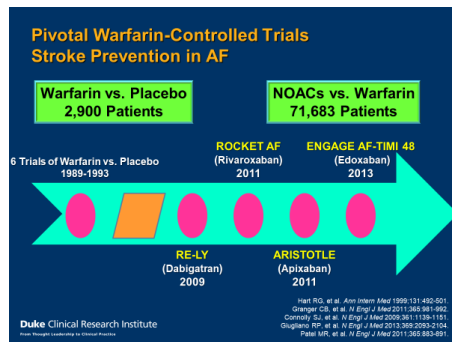
asymptomatic AF patients, where the results were controversial. Finally, the speaker talked about catheter ablation in AF patients affected by HF. The new data presented by the speaker were positive and favourable for performing this procedure in these patients, more in particular in those with advanced HF and reduced EF. In conclusion, the speaker pointed out that novel technologies may further improve the ablation procedure and the outcome by reducing the AF recurrence rate.

- What’s about the good indications for AF catheter ablation, presented by the speaker?
- What are the main complications of atrial fibrillation catheter ablation, based on the data presented by the speaker?
- What’s about catheter ablation in asymptomatic AF patients?
- What are the main results of the CASTLE AF trial, presented by the speaker?

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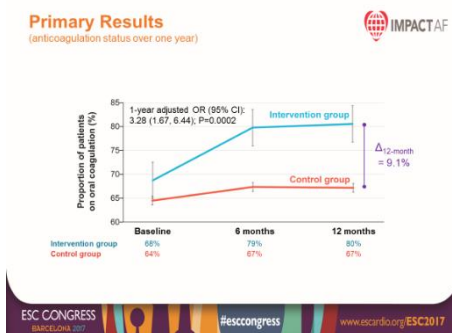
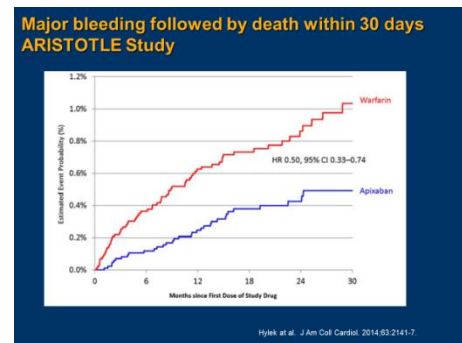
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# Stroke Prevention in patients with AF: What is new in 2017?



Prof. Lopez from Durham (USA), spoke about “Stroke Prevention in patients with AF: What is new in 2017?” and presented very interesting data on the oral anticoagulation therapy as an effective strategy for preventing stroke. Going deeper in his lecture, the speaker talked about the risk-benefit assessment of this therapy aimed to prevent stroke, but at risk of bleeding. In the main part of his lecture, Prof. Lopez presented very interesting data on the use of NOACs compared to warfarin from an efficacy and safety point of view. The speaker presented also other data given from the ARISTOTLE study designed for study the intracranial haemorrhage in patients receiving anticoagulant therapy. Prof. Lopez talked also about the dose selection based on outcomes and presented very interesting data given from the PIONEER study designed

for providing evidences of the reduction of bleeding when the antithrombotic regimens are reduced. Prof. Lopez talked also about the RE-DUAL-PCI trial and discussed the data produced by this study and presented his personal feeling about it. Finally, the speaker talked about the IMPACT AF study running in his clinical center, designed for improving the anticoagulant treatment of patients with atrial fibrillation. In conclusion, Prof. Lopez pointed out that preventing stroke is the key of this therapy and bleeding is the cost to pay and dosing of OAC is critical.

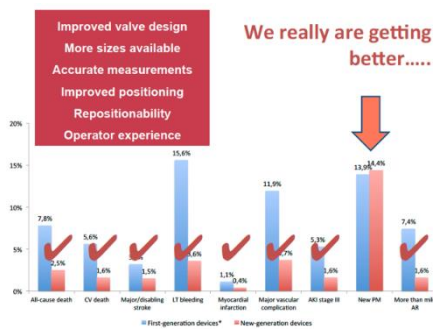


- What's about the new anticoagulants compared to warfarin regarding the intracranial haemorrhage, presented by the speaker?
- What's about the NOAC Antidotes, based on the data presented by the speaker?
- What's about the correlation between AF, CAD and Antithrombotic Therapy, based on the data presented by the speaker?
- What is the interpretation of the PIONEER results, presented by the speaker?
- What's about the results on stroke of the IMPACT AF trial, presented by the speaker?

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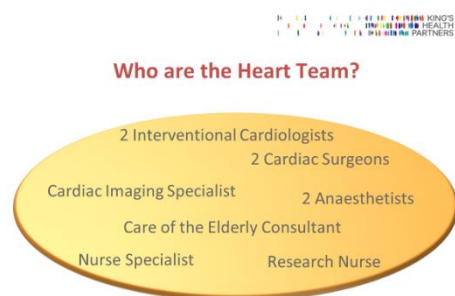
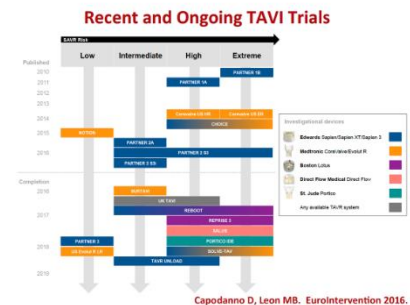
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# TAVI: state of the art



“TAVI: state of the art”, was the topic discussed by Prof. Prendergast from London (UK), more in particular the speaker talked about TAVI as an established and simple treatment for inoperable and high risk aortic stenosis patients. Going deeper in his lecture, Prof. Prendergast presented very interesting data given from the UK TAVI registry, demonstrating that the results of this procedure have been dramatically improved in these last 15 years. In the main part of his

lecture, the speaker presented very interesting data given from the recent and ongoing TAVI trials and highlighted that these trials have been powered by a heavy technology characterized by the development of new TAVI systems. In the second part of his lecture, Prof. Prendergast talked about the remaining questions on TAVI procedure like, device durability, development of endocarditis or stroke, the need for permanent pacemaker, the non-transfemoral access and



finally on the problems linked with the bicuspid valves. and presented very interesting data given from the clinical trials running in patients with such problems. Finally, the speaker talked about the new ESC guidelines and highlighting that TAVI has been considered the treatment of choice for high risk patients and presented very interesting data on the heart valve centers, managed by the so called “Heart team”, composed by many specialists in different cardiological fields.

- What’s about TAVI from the speaker point of view?
- What are the main recent and ongoing trials on TAVI, presented by the speaker?
- What are the main advantages of the new TAVI system, based on the data presented by the speaker?
- What’s about the remaining questions on TAVI from the speaker point of view?
- Who are the Heart Team?

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# The role of imaging

Echocardiography in Valve Disease		
ASE / AHA Appropriate Use Criteria		
Indication	TTE for Evaluation of Valvular Function Member or Class	Appropriate use score (1-6)
34.	Initial evaluation when there is a reasonable suspicion of valvular or structural heart disease	A (5)
37.	Pre-operative evaluation of aortic valve disease with a change in clinical status or cardiac exam or to guide therapy	A (5)
38.	TTE for Evaluation of Valvular Function Native Valvular Stenosis	
39.	Routine surveillance (1-2 y) of mild valvular stenosis without a change in clinical status or cardiac exam	A (1)
41.	Routine surveillance (1-2 y) of moderate or severe valvular stenosis without a change in clinical status or cardiac exam	A (5)
45.	Routine surveillance (1-2 y) of moderate or severe valvular regurgitation without a change in clinical status or cardiac exam	A (5)
47.	TTE for Evaluation of Valvular Function Prosthetic Valves	
48.	Initial postoperative evaluation of prosthetic valve for establishment of baseline	A (5)
49.	Routine surveillance (1-2 y) after valve replacement of prosthetic valve for baseline or suspected valve dysfunction	A (1)
50.	Evaluation of prosthetic valve with suspected dysfunction or a change in clinical status or cardiac exam	A (5)
51.	Pre-operative evaluation of known prosthetic valve dysfunction when it would change management or guide therapy	A (5)
52.	TTE for Evaluation of Valvular Function Infective Endocarditis (Native or Prosthetic Valves)	
53.	Initial evaluation of suspected infective endocarditis with positive blood cultures or a new murmur	A (5)
55.	Pre-operative evaluation of infective endocarditis at high risk for progression or complication or with a change in clinical status or cardiac exam	A (5)

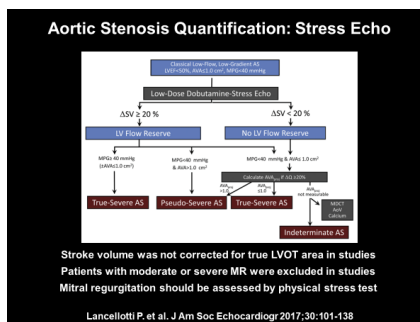
Douglas et al. J Am Soc Echocardiogr 2011;24:229-267

Prof. Tanner from Zurich (CH), spoke about “The role of imaging” and presented very interesting data starting from the 3 D imaging of a valve disease reconstruction. Going deeper in his lecture, the speaker talked about the echocardiography application criteria in valve disease and presented very interesting data on the interval for follow-up, indicated every 4-5 years, but in case of progressive lesion every 6 months. In the main part of his lecture, Prof.



Tanner presented very interesting three-dimensional imaging data of a patient affected by mitral regurgitation due to valve prolapse caused by a tendon rupture. The images were clear and the valve regurgitation was well detected. The speaker highlighted that in mitral valve regurgitation, the echo approach is indispensable for a correct management. In the second part of his lecture, Prof. Tanner talked about the application of the colour doppler

technique in patients with aortic stenosis and in a more severe context for the contemporary presence of the two defects, the mitral regurgitation and the aortic stenosis. The speaker presented also very interesting imaging data on the correct stroke volume calculation, the pressure recovery and on the degree of calcification for a better aortic stenosis quantification. Finally, Prof. Tanner presented some recommendations for a better approach to these types of patients in a clinical practice setting



- What's about the 3D echo application in mitral valve regurgitation, based on the data presented by the speaker?
- What's about the 3D echo in patients with aortic stenosis, based on the data presented by the speaker?
- What are the main problems related to the aortic stenosis quantification, based on the data presented by the speaker?
- What to do in clinical practice from the speaker point of view?

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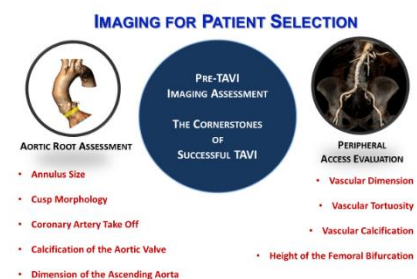
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# Patient selection for TAVI

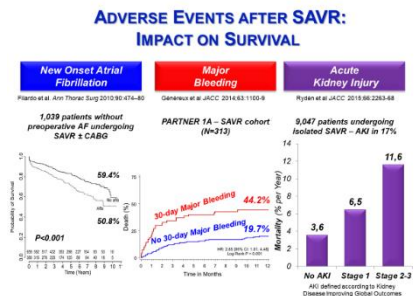
CRITERIA TO GUIDE THE HEART TEAM		
	FAVOURS TAVI	FAVOURS SAVR
CLINICAL CHARACTERISTICS	<ul style="list-style-type: none"> <li>Presence of aortic coarctation (not adequate for catheterisation)</li> <li>Age &gt;75 years</li> <li>Previous cardiac surgery</li> <li>Frailty</li> <li>Renal disability and conditions that may affect the rehabilitation process after the procedure</li> </ul>	<ul style="list-style-type: none"> <li>Age &lt;75 years</li> <li>Suspicion of endocarditis</li> </ul>
ANATOMICAL AND TECHNICAL ASPECTS	<ul style="list-style-type: none"> <li>Favourable access for transcatheter TAVI</li> <li>Severity of aortic regurgitation</li> <li>Proximal aorta</li> <li>Presence of other coronary bypass grafts at risk when coronary is performed</li> <li>Expected patient growth/development</li> <li>Severe chest deformation or scoliosis</li> </ul>	<ul style="list-style-type: none"> <li>Unfavourable access (any) for TAVI</li> <li>Short distance between coronary ostia and aortic valve annulus</li> <li>Size of aortic annulus out of range for TAVI</li> <li>Aortic root morphology unfavourable for TAVI</li> <li>Valve morphology (bicuspid, degree of calcification, calcification pattern) unfavourable for TAVI</li> <li>Presence of thrombi in aorta or LV</li> </ul>
ASSOCIATED CONDITIONS REQUIRING INTERVENTION	<ul style="list-style-type: none"> <li>Severe CAD requiring revascularisation by CABG</li> <li>Severe primary mitral valve disease, which could be treated surgically</li> <li>Severe tricuspid valve disease</li> <li>Aneurysm of the ascending aorta</li> <li>Significant hyperlipidaemia requiring intervention</li> </ul>	

that the Regulatory Authorities put the cut-off at 75 years old as the age that divides surgery from TAVI application in patients undergoing valve replacement implantation. In the main part of his lecture, the speaker presented a huge amount



“Patient selection for TAVI” was the topic discussed by Prof. Windecker. The speaker, coming from Berne (CH), presented very interesting data on the main characteristics of the TAVI procedure for a total valve replacement. Going deeper in his lecture, the speaker talked about the risk assessment of TAVI comparing to Surgery and presented the current available TAVI risk scores. Prof. Windecker pointed out

of data on the main conditions, like frailty, that drive the choice of TAVI instead of surgery in such patients. Talking about outcomes the speaker pointed out that TAVI is associated with better clinical outcomes and also in the early peri-procedures recovery. Finally, Prof. Windecker presented very interesting data on the pre-TAVI imaging assessment, of high importance for a successful TAVI and talked about the main anatomic factors favouring TAVI or SAVR.



- What's about the evolution of the clinical evidence on TAVI and SAVR, based on the data presented by the speaker?
- What are the criteria to guide the clinical team in the choice between TAVI and SAVR, presented by the speaker?
- What are the key factors for the choice of TAVI or SAVR from the speaker point of view?
- What are the main adverse events after TAVI and SAVR, presented by the speaker?
- What are the anatomic factors favouring TAVI or SARV, presented by the speaker?

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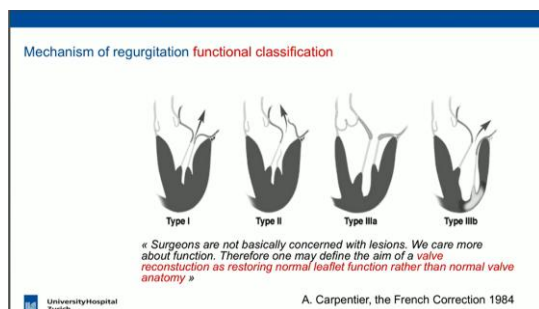
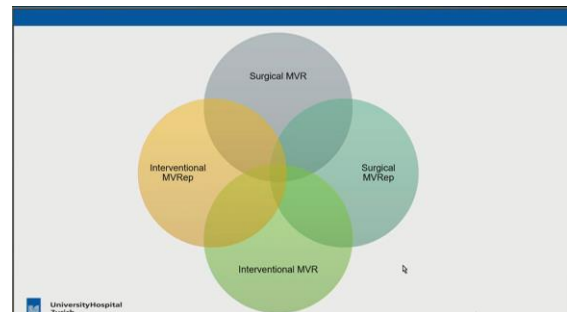
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# Percutaneous mitral valve repair



Prof. Maisano from Zurich (CH), spoke about "Percutaneous mitral valve repair". More in particular, the speaker talked about the evolution of the Alfieri procedure starting from the open approach to the percutaneous approach. Going deeper in his lecture, Prof. Maisano presented very interesting data on the structure vs function in a percutaneous setting and highlighted the expanding portfolio

of the transcatheter approach, like the MitraClip system. The speaker pointed out that this procedure is not palliative at all, if performed in a correct way with the right patient. Prof. Maisano presented very interesting data on a patient apparently not available for a such type of procedure, who underwent to MitraClip and resolved his cardiac problems. In the second part of



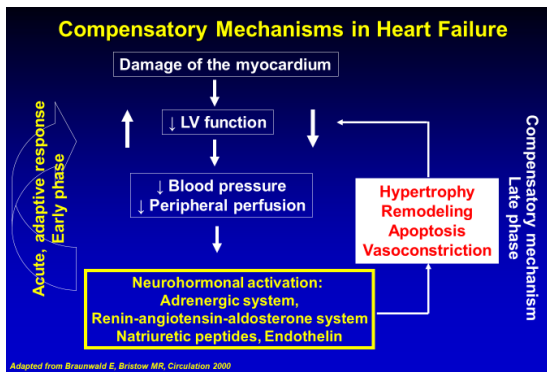
his lecture, the speaker talked about the possibility to combine MitraClip and annuloplasty in order to obtain a better result in patients affected by mitral regurgitation. Finally, Prof. Maisano presented very interesting data on the possibility to perform mitral valve replacement, also if this procedure is in a preliminary phase, the speaker pointed out. In conclusion, Prof. Maisano pointed out that surgery is important and non-replaceable at all.

- Which patients should be selected for the MitraClip procedure, based on the data presented by the speaker?
- What is the final outcome of this procedure, from the speaker point of view?
- What's about the MitraClip and annuloplasty combination, based on the data presented by the speaker?
- What are the main problems related to the mitral valve replacement, based on the data presented by the speaker?

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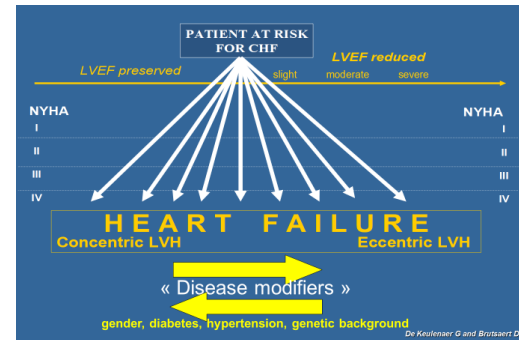
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# New HF ESC Guidelines – definition and classification of HF

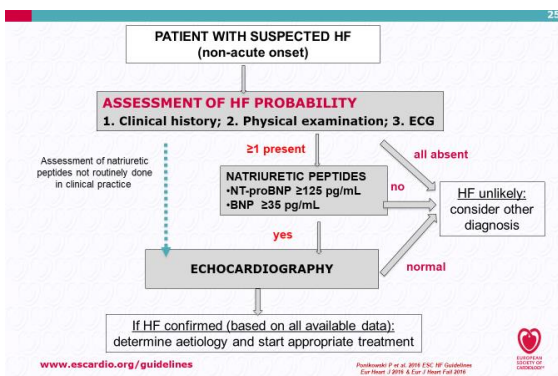


“New HF ESC Guidelines – definition and classification of HF”, was the topic discussed by Prof. Ponikowski from Wroclaw (PL), more in particular the speaker talked about definition, classification and pathomechanisms undergoing HF. Going deeper in his lecture, the speaker presented very interesting data on the compensatory mechanisms activated in HF patients, leading to some other alterations in our body which need for acute and

adaptive responses. In the main part of his lecture, Prof. Ponikowski talked about the ACCF/AHA stages of HF and highlighted that the stage A was not included in the definition of Heart Failure of the 2012 ESC guidelines. The speaker pointed out that in the new 2016 ESC guidelines the pre-HF state has been included. More in particular Prof. Ponikowski presented very interesting data given from the new 2016 ESC guidelines on Heart Failure, in order to



explain new concepts on classification of HF based on the different symptoms/signs state of the patients and characterized by the presence of three categories: HF with reduced, midrange and preserved EF. Talking about diagnosis Prof. Ponikowski pointed out that the assessment of the HF probability composed by clinical history, physical examination and ECG, is a duty for GPs in order to make possible the HF diagnosis in an early phase.



- What's about the ACCF/AHA stages of Heart Failure, based on the data presented by the speaker?
- What do the ESC Heart Failure Guidelines tell about prevention, based on the data presented by the speaker?
- What is the new classification of Heart Failure, presented by the speaker?
- What are the mechanisms involved in the autonomic disturbances of HF, presented by the speaker?

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graph TD
    A[Patients suspected to have heart failure] --> B[ASSESSMENT OF HF PROBABILITY]
    B --> C[1. Clinical history: History of CAD MI, revascularization; History of arterial hypertension; Exposure to cardiotoxic drugs; Disorientation. Use of diuretics, Cytotoxics / paracetamol nocturnal dyspnea]
    B --> D[2. Physical examination: Rales, bilateral ankle edema, heart murmur, jugular venous distation, laterally displaced/cracked apical beat]
    B --> E[3. ECG, any abnormality]
    C --> F[Assessment of natriuretic peptides not routinely done in clinical practice]
    F --> G[NATURETIC PEPTIDES]
    G --> H["≥ 1 present  
NT-proBNP ≥ 125 pg/ml  
BNP ≥ 35 pg/ml"]
    H --> I[No]
    H --> J[Yes]
    I --> K[HF unlikely: consider other diagnosis]
    J --> L[ECHOCARDIOGRAPHY]
    K --> L
    L --> M[Normal]
    L --> N[If HF confirmed (based on all available data): determine etiology and start appropriate treatment]
    M --> N
  
```

**Patients suspected to have heart failure**

**ASSESSMENT OF HF PROBABILITY**

1. Clinical history: History of CAD MI, revascularization; History of arterial hypertension; Exposure to cardiotoxic drugs; Disorientation. Use of diuretics, Cytotoxics / paracetamol nocturnal dyspnea
2. Physical examination: Rales, bilateral ankle edema, heart murmur, jugular venous distation, laterally displaced/cracked apical beat
3. ECG, any abnormality

Assessment of natriuretic peptides not routinely done in clinical practice

**NATURETIC PEPTIDES**

≥ 1 present  
NT-proBNP ≥ 125 pg/ml  
BNP ≥ 35 pg/ml

No

Yes

**HF unlikely: consider other diagnosis**

**ECHOCARDIOGRAPHY**





Normal

**If HF confirmed (based on all available data): determine etiology and start appropriate treatment**

**Heart Failure Guidelines  
EHJ / EAHF 2016**

## Life saving treatments

Palliative Drugs	Neurohormonal Drugs	Devices	ARNI
Pre-1980	1980s	1990s	2000s
2010s	2016		



Digitalis Diuretics

ACE-I

ICDs

CRT, CRT-D

LVAD

Sensing Devices

Iron


ARNI

$\beta$ -Blockers

MR-Antagonists

Transplantation

Ivabradine



University Hospital Zurich

Schmidhuber et al. 2017

### Key Point 4 - Comorbidities!

The diagram illustrates the complex interplay of comorbidities in HIV/AIDS. At the center is the **HEART**, which is connected to various other organs and systems:

- LIVER:** Shows **Angiogenesis** and **Hepatocyte** involvement.
- LUNG:** Shows **Neutrophilosis**, **HIV**, and **Fibrocyte** involvement.
- IMMUNE SYSTEM:** Shows **CD4+ T cells**, **Macrophage**, **Lymphocyte**, and **TGF-β** involvement.
- BONE:** Shows **Osteocyte** and **FGF 23** involvement.
- KIDNEYS & ADRENALS:** Shows **Ang II**, **Ras**, **Angiotensin II**, **Adrenal cortex cell**, and **Adrenal medulla cell** involvement.

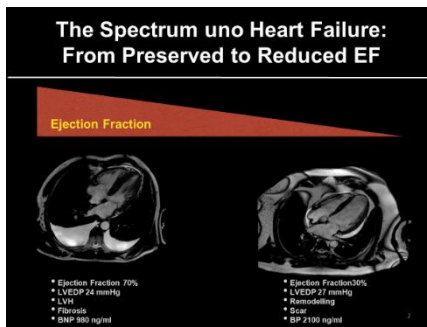
The **HEART** itself is connected to **Atrial myocyte**, **Ventricular myocyte**, **Endothelial cell**, and **Smooth muscle cell**.

Source: Buglioni A, Burnett JR, Cox CH, Aitken 2011

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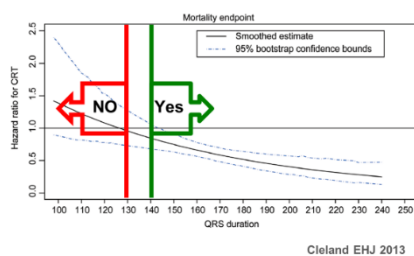


# Pharmacological treatment of HF



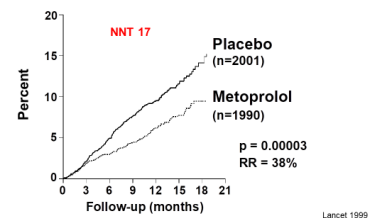
blockers. In the main part of his lecture, the speaker presented very interesting data given from the PARADIGM-HF trial, on the effects of LCZ696 that is an angiotensin-receptor-neprilysin-inhibitor (ARNI). Prof. Lüscher talked also about the effects of the mineralocorticoid receptor antagonists and presented very interesting data given from the EMPHASIS trial. In the

The Dos and Dont's of CRT: QRS Duration



“Pharmacological treatment of HF” was the topic discussed by Prof. Lüscher. The speaker, coming from Zurich (CH), presented very interesting data on the therapeutic aim in CHF patients. Going deeper in his lecture, Prof. Lüscher talked about symptoms and survival and presented very interesting data given from clinical trials running in HF patients on therapy. More in particular the speaker discussed the data on ACE inhibitors, ARBs, diuretics and  $\beta$ -

Influence of Metoprolol on Cardiovascular Mortality in Congestive Heart Failure (MERIT-HF)



the second part of his lecture, the speaker talked about Ivabradine, Empagliflozin and about ICD and CRT. More in particular Prof. Lüscher presented very interesting data given from the CARE-HF and the EchoCRT trials and highlighted that CRT can be performed only in patients with a QRS duration more than 140 mmsec. Finally, the speaker pointed out that the association between CRT and pharmacological treatment can significantly improve the outcome of the HF

patients.

- What's about the Neurohumoral Regulation of the Cardiovascular System, based on the data presented by the speaker?
- What are the long-term results of the CONSENSUS trial, presented by the speaker?
- What's about the LCZ696 effect in HF patients, based on the data presented by the speaker?
- What is the effect of the ARNIs in HF patients from the speaker point of view?
- What's about CRT in HF patients based on the data presented by the speaker?

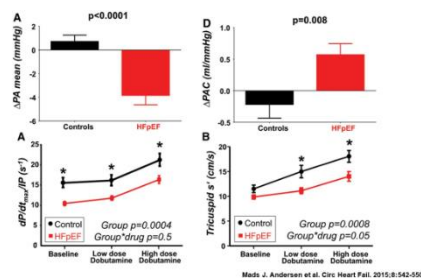
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# HF with preserved systolic function

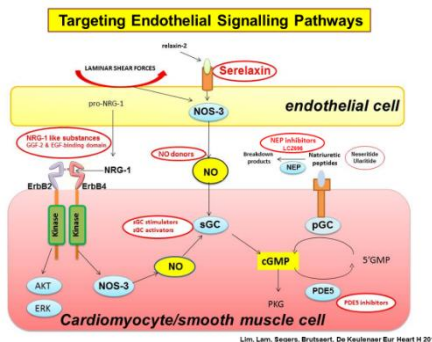
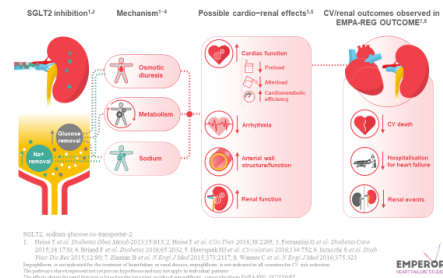
Prof. Lam from Singapore (SGP), spoke about “HF with preserved systolic function”. More in particular, the speaker talked about 5 potential mechanisms for therapies of patients affected by HF with preserved EF. Going deeper in her lecture, Prof. Lam presented very interesting data on an experimental treatment characterized by the opening of an interatrial shunt in order to reduce the left atrial pressure responsible for the LA remodelling and

## β-agonists in HFpEF/PH



dysfunction. In the main part of her lecture, the speaker talked also about another experimental treatment aimed to reduce the pulmonary hypertension and the RV dysfunction, characterized by the infusion of butamine as a β-agonist, with a significant improvement in cardiac functions. Prof. Lam presented also very interesting data given from obese patients affected by HFpEF, characterized by a significant volume expansion and treated with the SGLT2 inhibitors, that

## Role for SGLT2i?



in special populations.

- Is there a role for SGLT2 inhibitors for the treatment of HFpEF patients, based on the data presented by the speaker?
- What are the main results of the physical exercise in HFpEF patients from the speaker point of view?
- What's about the effect of Sildenafil in HFpEF patients, based on the data presented by the speaker?
- What's about the PARAMOUNT and the PARAGON trials, based on the data presented by the speaker?

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# Comorbidities in HF

Aetiology and comorbidity HF-REF/HF-PEF

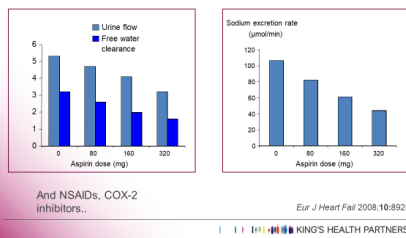
Medical history	LVSD (%)	No LVSD (%)	p value
Ischaemic heart disease (IHD)	50.8	39.8	<0.001
Atrial fibrillation	20.7	21.9	=0.886
Acute myocardial infarction (AMI)	30	16.3	<0.001
Valve disease	23.3	32.8	<0.001
Hypertension	52.2	60.6	<0.001
Chronic renal impairment*	6.9	10.3	=0.461
Diabetes	32.7	32.6	=0.923
Asthma	8.3	9.0	=0.025
Coronary obstructive pulmonary disease	16.8	19.3	<0.001

National Heart Failure Audit 2015/16

KING'S HEALTH PARTNERS

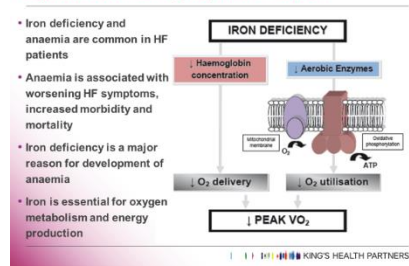
in particular Prof. McDonagh presented very interesting data, showing that iron deficiency is the main cause of anemia in these patients and discussed the guidelines recommendations for anemia diagnosis. In the second part of her lecture, the speaker talked about diabetes and its relationship with HF and presented very interesting data on the effect of the hypoglycaemic agents in HF patients. Prof. McDonagh presented other very interesting data on the correlation between sleep disorders breathing and HF and highlighted that central sleep apnea is associated with a worse outcome in these patients. The speaker talked also about renal dysfunction and HF and highlighted that it is of high importance do not use industrial doses

Stop aspirin



“Comorbidities in HF”, was the topic discussed by Prof. McDonagh from London (UK), more in particular the speaker talked about some non-cardiac comorbidities like diabetes, chronic renal impairment, asthma and COPD. Going deeper in her lecture, Prof. McDonagh presented very interesting data on the importance of these comorbidities in HF patients. In the main part of her lecture, the speaker talked about anemia and iron deficiency as one of the main finding affecting HF patients, more

Impact of iron deficiency on patients with CHF



of diuretics because they can worse outcome as well as do not use aspirin. Finally, Prof. McDonagh talked about COPD and Asthma and their relationship with HF. The speaker highlighted that these patients have to be treated with cardioselective  $\beta$ -blockers. Speaking about depression Prof. McDonagh pointed out that this finding is common and it is associated with poor prognosis and that the selective serotonin reuptake inhibitors are safe and effective.

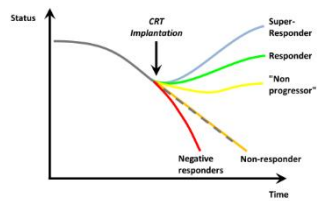
- Why comorbidities are important in HF patients, based on the data presented by the speaker?
- What are the main problem with anaemia and iron deficiency from the speaker point of view?
- What is the prevalence of iron deficiency in patients with CHF?
- What's about hypoglycaemic agents and HF, based on the data presented by the speaker?
- What's about ACE inhibitors, ARBs and MRA and the renal function, based on the data presented by the speaker?
- What's about the correlation between HF and depression, from the speaker point of view?

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# Devices and interventions

## Cardiac resynchronisation therapy

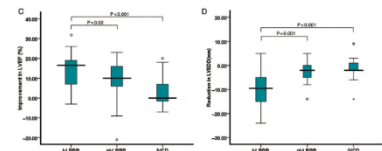


Marini, PNAS 2014; 111: 1707-1711

Prof. Breitenstein from Zurich (CH), presented very interesting data on “Devices and interventions”. More in particular the speaker talked about CRT and presented very interesting data on the outcome of the CRT implantation characterized by the presence of super responder, responder, non-responder and non-progressor patients and the impossibility to predict before, in what group any patient can fall. In the main part of his

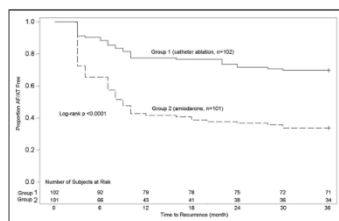
lecture, Prof. Breitenstein presented very interesting data given from the clinical trials designed for CRT evaluation. The speaker presented also other data on ICD and highlighted that the younger patients seem to have significant benefits in mortality compared to standard therapy. Prof. Breitenstein talked also about the ICD complications and presented very interesting data on the risk of sudden death and the possibility

## Cardiac resynchronisation therapy



Tan et al. European Heart Journal 2015; 35: 1489-1498

## AF ablation in heart failure patients - AATAC



Di Blase et al. Circulation 2015; 131: 1627-1634

to give an affordable answer with the subcutaneous ICD. In the second part of his lecture, Prof. Breitenstein talked about the AF ablation in HF patients and presented very interesting data given from many clinical trials like the AATAC and the CASTLE AF studies. In conclusion, the speaker pointed out that CRT and ICD are an established part of the heart failure treatment and that the catheter ablation for AF seems to be of benefit for the HF patients.

- What's about the main characteristics of CRT, based on the data presented by the speaker?
- What's about ICD and its protection from sudden cardiac death, based on the data presented by the speaker?
- What are the main results of the ICD-Danish trial, presented by the speaker?
- What are the most important complications of an ICD, from the speaker point of view?
- What are the main results of the CASTLE AF trial, presented by the speaker?

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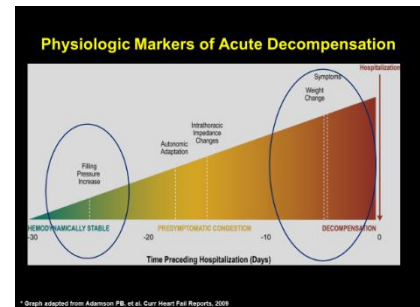


# Causes and pathophysiological mechanisms of acute heart failure

A PRACTICAL APPROACH TO DIFFERENTIATING AHFS	
1. Hypertensive group:	<ul style="list-style-type: none"> <li>- female</li> <li>- normal LVEF</li> <li>- in-hospital mortality rate - 2%</li> <li>(with 5% mortality and 30% readmission rates within 60-90 days of discharge)</li> </ul>
2. Normotensive group:	<ul style="list-style-type: none"> <li>- low LVEF</li> <li>- signs and symptoms of pulmonary/systemic congestion (oedema) before and at the time of admission</li> <li>- in-hospital mortality rate - 3%</li> <li>(with 7% mortality and 30% readmission rates within 60-90 days of discharge)</li> </ul>
3. Hypotensive group:	<ul style="list-style-type: none"> <li>- low SBP levels (<math>\leq 120</math> mm Hg) at the time of presentation</li> <li>- low LVEF</li> <li>(mortality rate 7% during hospitalization &amp; with 14% mortality and 30% readmission rates within 60-90 days of discharge)</li> </ul>

“Causes and pathophysiological mechanisms of acute heart failure”, was the topic discussed by Prof. Mehra from Wroclaw (PL), more in particular the speaker talked about the AHF syndromes and more in particular on the one characterized by the worsening of the chronic HF. Going deeper in his lecture, the speaker presented very interesting data on the main causes leading to the presentation of an acute decompensated heart failure starting from the tight relationship between troponin and natriuretic peptide levels

and AHF prognosis. In the main part of his lecture, Prof. Mehra talked about the effect that the high BP has on the AHF outcome and presented very interesting data on a practical approach to differentiate AHF characterized by the presence of three groups of patients, the first one with high BP, the second one normotensive but with low EF and the last one hypotensive with low SBP and low EF. The speaker presented other very interesting data on some signs, classically considered as important from a prognostic point of view, like daily weight measurements, filling pressure and other physiological markers of acute compensation and talked about a novel hypothesis based on the increase of the filling pressure before the ADHF, depending on the prior increase of the effective circulatory volume. In order to better explain this hypothesis, the speaker presented very interesting data on the contribution to the systemic decompensation typical of the acute decompensated HF of three systems like the abdominal, the renal and the intestinal circulation. Finally, Prof. Mehra talked about the braking phenomena characterized by the loss of power of diuretics despite the increase of their dosage and the presence of a conserved circulating volume and about the relationship between GUT microbiota alterations and decompensated HF.



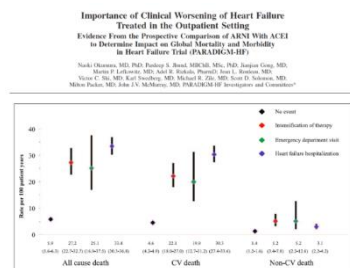
Tackling Abdominal Contributions to Advanced Heart Failure	
• Focus on Central Venous Congestion	<ul style="list-style-type: none"> <li>- “the earlier, the better”?</li> </ul>
• Reduce Intra-abdominal Pressure	<ul style="list-style-type: none"> <li>- Ascites is NOT a pre-requisite</li> </ul>
• Alter the Gut Microbiome	<ul style="list-style-type: none"> <li>- Rifaximin</li> </ul>

- What is the relationship between troponin and natriuretic peptide and HF, based on the data presented by the speaker?
- What’s about the practical approach for differentiating AHF patients, presented by the speaker?
- What’s about the main “Precipitating” factors presented by the speaker?
- What are the main problems with “Conventional Wisdom”, based on the data presented by the speaker?
- Do daily weight measurements help from the speaker point of view?
- What are the key points of the new hypothesis presented by the speaker?
- What’s about the abdominal contributions to cardiorenal dysfunction in advanced heart failure, based on the data presented by the speaker?

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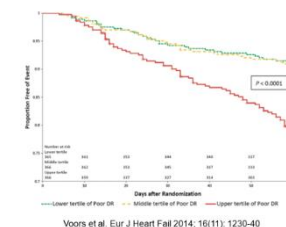
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# Management of acute HF

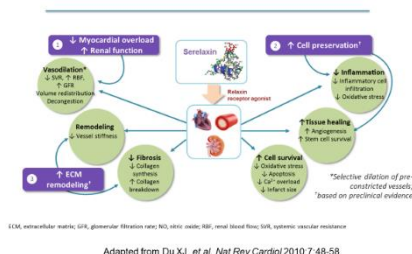


event. In the main part of his lecture, the speaker talked about the main results of the clinical trials running in acute HF patients and treated with loop diuretics, showing that these compounds at high dosage worsen the outcome. Prof. Metra, presented other very interesting data on the effects of spironolactone in AHF and highlighted that this approach seems to have no effects compared to placebo. Speaking about the effects of vasodilators in

Survival curves for Death or HF/RF readmission through day 60 in patients subdivided by WRF and Diuretic response. An analysis from RELAX-AHF



## Serelaxin in the pathophysiology of acute HF



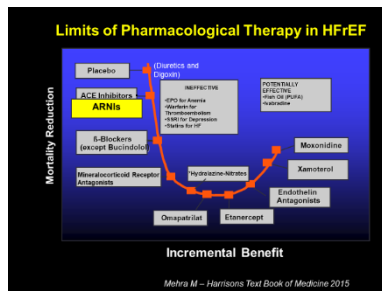
AHF Prof. Metra, pointed out that their use is more useful than diuretics but no demonstration of their efficacy has been performed till now. Finally, the speaker talked about new drugs like the biased ligands of the angiotensin II type 1 receptor, ularitide and serelaxin and presented very interesting data showing that in order to develop these new therapies there are some problems mainly due to the difficulty to run trials in such high-risk population with a well- balanced patient selection.

- What's about the treatment of acute HF recommended in the 2016 ESC guidelines, based on the data presented by the speaker?
- What's about the algorithm for the management of patients with acute heart failure, presented by the speaker?
- What is the diuretic response in acute heart failure, based on the data presented by the speaker?
- What's about the new drugs for the treatment of AHF patients, presented by the speaker?

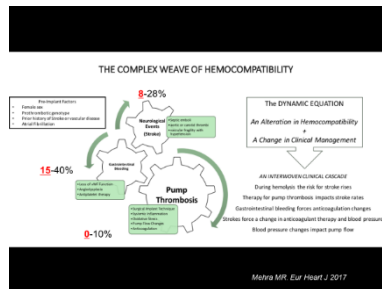
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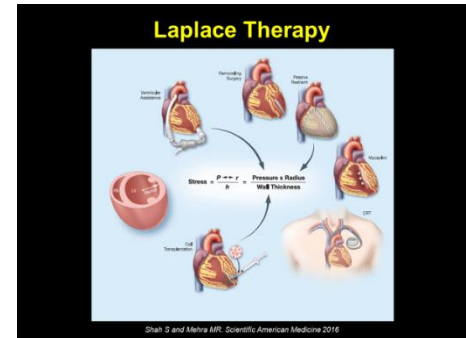
# Advanced therapy in advanced heart failure



presented very interesting data on the Laplace therapy and more in particular on the implantation of a ventricular assist device characterized by the prolongation of the life for more than 12 months in almost the 68% of patients.



Prof. Mehra from Wroclaw (PL), spoke about “Advanced therapy in advanced heart failure”. More in particular, the speaker talked about the advanced therapy starting from the limits of the pharmacological therapy in HFrEF patients. Going deeper in his lecture, the speaker talked about the triggers as a referral for advanced therapy and presented very interesting data on the Laplace therapy and more in particular on the implantation of a ventricular assist device characterized by the prolongation of the life for more than 12 months in almost the 68% of patients. In the main part of this lecture, Prof. Mehra talked about a new theory called “hemocompatibility” and presented very interesting data, showing that an alteration in hemocompatibility and a change in clinical management can produce very impressive results in term of reduction of bleeding and stroke in patients implanted with these innovative devices.

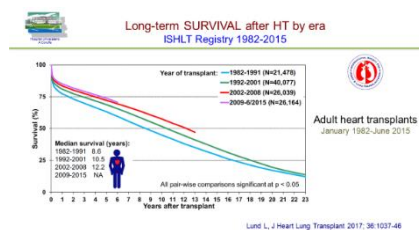


- What’s about the ENDURANCE study, based on the data presented by the speaker?
- What’s about the acquired von Willebrand Disease as a hemocompatibility biomarker presented by the speaker?
- Why are the neurological events not been reduced, from the speaker point of view?

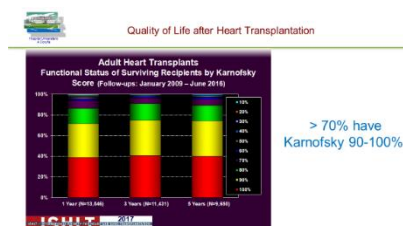
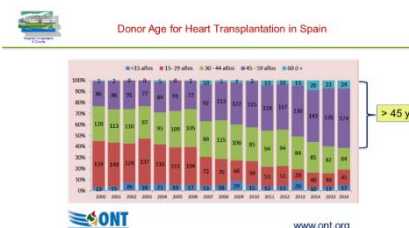
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# Heart transplantation



causes of death, the speaker pointed out that one of the main causes of death is related to the poor conditions of the recipients. In the main part of her lecture, Prof. Crespo-Leiro talked about the changes of the recipient population, composed by older patients, or younger by with complex congenital heart diseases or affected by other organ failures. The speaker presented also very interesting data on donors and the changes characterizing this population like age. Prof. Crespo-Leiro talked also about the relationship between the long-term survival after HT and the donor age and about the waiting list time. In the second part of her lecture the speaker presented very interesting data on the use of the temporary mechanical circulatory support as a direct bridge to heart transplantation and on the ex-vivo perfusion of donor hearts. Prof. Crespo-Leiro presented also very interesting data on rejection, more in particular she talked about acute rejection, rejection during the first year after HT and about the pathophysiology of the chronic graft failure. The speaker highlighted that the paradigm of monitoring rejection is changing, more in particular thanks to the inclusion of mRNA and Dd-cfDNA in it.



Prof. Crespo-Leiro presented also very interesting data on HT immunosuppression and talked about the compounds involved. Finally, the speaker talked about quality of life, pointing to that more than 70% of patients transplanted in the hospital of La-Coruna have normal quality of life.

- What's about the main significant risk factors for 1 year mortality, based on the data presented by the speaker?
- What is the upper limit of age for the cardiac transplantation, based on the data presented by the speaker?
- What's about rejection as a systemic reaction, based on the data presented by the speaker?
- What is the 2016 Organ Donation rate, presented by the speaker?
- What are the leading cause of death after HT, based on the data presented by the speaker?
- What are the key topics of the HT Immunosuppression in 2017, presented by the speaker?

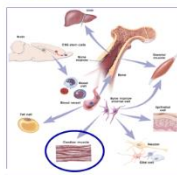
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# The future of stem cell therapy and cardiac regeneration

## „Stem Cell Plasticity“ - The Initial Idea behind Cardiac Stem Cell Therapy



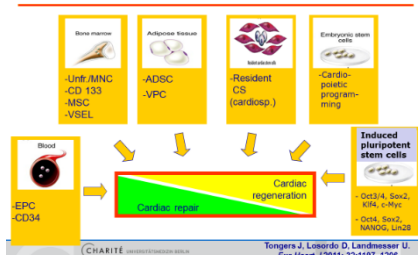
„Stem Cell Plasticity“: Capacity of BM stem cells to „transdifferentiate“ outside their lineage boundaries

CHARITÉ

National Institutes of Health (2002)

the developing concepts on cardiac regeneration and presented very interesting data on the optimal source of stem cells, like the human embryonic stem-cells, but also the ones derived from fibroblasts.

## Optimal source of stem/progenitor cells for cardiac repair or regeneration ?



CHARITÉ

Tongers J, Lüscher D, Landmesser U. Eur Heart J 2011; 32:1197-1206

Prof. Landmesser from Berlin (DE), talked about “The future of stem cell therapy and cardiac regeneration”. Going deeper in his lecture, the speaker presented very interesting data on the history of stem cell therapy, more in particular on the bone marrow-cell application in patients after MI and about the early randomized, controlled trails of BMC therapy post MI.

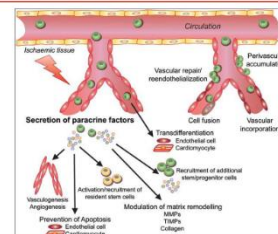
In the main part of his lecture, Prof. Landmesser talked about

the developing concepts on cardiac regeneration and presented very interesting data on the optimal source of stem cells, like the human embryonic stem-cells, but also the ones derived from fibroblasts.

Finally, Prof. Landmesser

presented very impressive data on the heart regeneration in zebrafish and in adult mice and on one phase 1 study running in HF patients treated with a new compound called cimaglermin alfa that is a neuregulin 1, a compound able to makes heart muscle. In conclusion, the speaker pointed out that the future promises the development of new technology able to induce cardiac repair and regeneration.

## Proposed mechanisms of cardiac repair by bone marrow/circulating blood-derived cell-based therapies



CHARITÉ

Tongers J, Lüscher D, Landmesser U. Eur Heart J 2011; 32:1197-1206

- How did stem cell therapy start, based on the data presented by the speaker?
- What are the developing concepts of the cardiac regeneration, presented by the speaker?
- What does the future hold from the speaker point of view?
- What's about the optimal source of stem/progenitor cells for cardiac repair or regeneration, based on the data presented by the speaker?
- What are the main strategies for the replacement of the lost cardiomyocytes presented by the speaker?

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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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