International Symposium on ISCHEMIC HEART DISEASE: THE MAIN CAUSE OF MORBIDITY AND MORTALITY WORLDWIDE. WHAT CAN WE IMPROVE?

Rome (IT), July 05-07, 2017

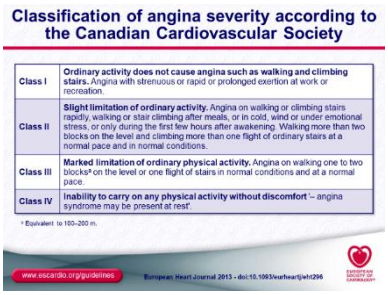
Highlights

Introduction

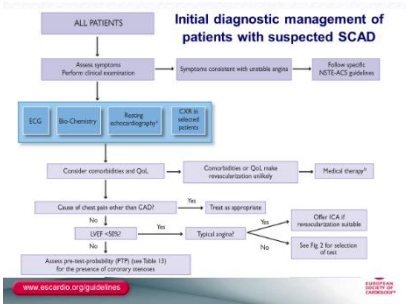
Prof. Crea, chairman of the symposium, opened the congress, by highlighting the high scientific level of this meeting, for the presence of all the top experts in ischemic heart disease coming from all the world. "1 out of 5 people die for ischemic heart disease and in our congress we will discuss on the way to improve diagnosis, prognosis and treatment" the speaker pointed out. The main topics discussed in this symposium were about ischemic heart disease and diagnosis, clinical presentations, acute coronary syndromes, Imaging and finally about heart failure. The congress has been attended by many of the top researchers of this field coming from all the world and by many young physicians attending the university of Rome.

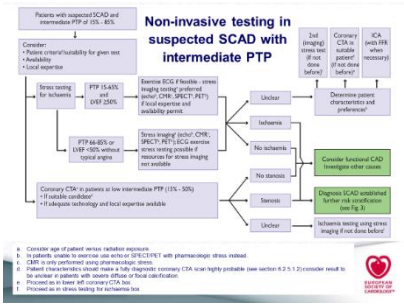
To follow the presentations of this congress, click on the link below: http://www.fondazione-menarini.it/Home/Eventi/Ischemic-heart-disease-the-main-cause-of-morbidity-and-mortality-worldwide-What-can-we-improve/Video-Slide … and, after having logged in, enter in the multimedia area.

The ESC guideline on stable coronary artery disease



The ESC guideline on stable coronary artery disease, was the topic discussed by Prof. Bax in his lecture. The speaker, coming from Leiden (NL), went deeper in his talk and presented very interesting data on the ESC guidelines, class of recommendations and level of evidence. In the main part of his lecture, the speaker talked about the classification of angina severity according to other guidelines like the Canadian Cardiovascular Society guideline and about the blood tests to be performed for the assessment of people with suspected SCAD for the optimization of treatment. Speaking about the traditional clinical classification of chest pain, Prof. Bax highlighted that this classification is very weak and subjective and it is necessary to perform other tests like the echocardiographic ones for the ejection fraction's measurement, or an exercise ECG test also if it is often negative in affected patients and the stress imaging only if the team has a sufficient expertise. The speaker presented also very interesting data on the initial diagnostic management of patients with suspected SCAD and highlighted the importance to start the investigation for comorbidities and quality of live data. In the second part of his lecture, the speaker presented a clinical case of a 62 years old symptomatic male patient and spoke about the tests to be performed for a correct diagnosis and treatment. More in particular Prof. Bax presented very interesting data on MRI and CT scan and highlighted that based on the results of the CT scan, it is possible to do the diagnosis, but if the result is unclear it is necessary to perform other tests. Finally, the speaker talked about the definitions of risk for various test modalities and *about the risk stratification by* invasive and non-invasive coronary arteriography in SCAD patients.





- What are the main points of the classification of angina based on the Canadian Cardiovascular Society guidelines?
- What are the main blood tests for the assessment of patients with suspected SCAD, based on the data presented by the speaker?
- What's about the initial diagnostic management of patients with suspected SCAD?
- Which do patients need for a non-invasive assessment of CAD, based on the data presented by the speaker?
- What are the tests to be performed in case of ischemia as an expression of a flow-limiting stenosis, based on the data presented by the speaker?
- What are the main characteristics of the MRI perfusion imaging, based on the data presented by the speaker?
- What's about the definitions of risk for various test modalities, based on the data presented by the speaker?

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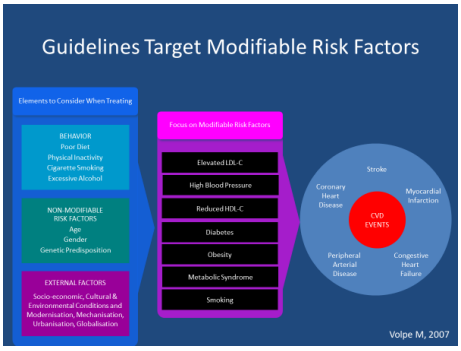
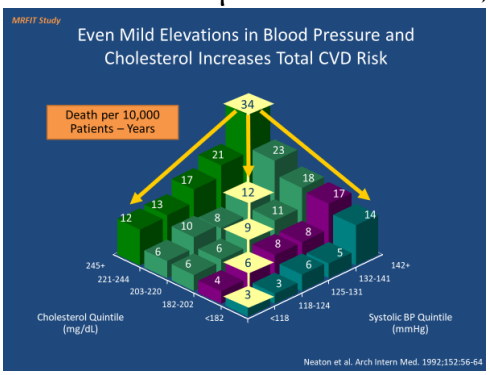
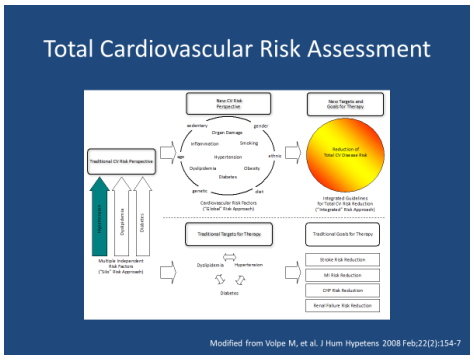
Prevention: how to reduce the burden of known risk factors?



Prof. Volpe from Rome (IT), spoke about "prevention: how to reduce the burden of known risk factors?" Going deeper in his lecture, the speaker presented very interesting data on the main risk factors for cardiovascular disease and pointed out that these ones are seen as individual actors, but biology does not work in an individually way and introduced the concept of the global burden of the morbidity constellation. In the main part of his lecture, Prof. Volpe presented very interesting data on the CVD prevention starting from the need to weigh any risk factor in association with the others. Prof. Volpe presented very interesting data on the effects of reducing blood pressure and cholesterol in an Asian Pacific population of about 600.000 people. In the second part of his lecture, the speaker talked about one of the main problems linked with prevention, characterized by the identification of the correct time and the correct intensity of therapy for the treatment of the risk factors for preventing, delaying or reduce the CVD risk; and in order to find out a comprehensive answer, Prof. Volpe presented a huge amount of very interesting data given by clinical and epidemiological studies and guideline recommendations. In conclusion, the speaker pointed out that it necessary to move from the single risk factors management for starting the treatment of all the risk factors taken together.





- What's about the global burden of the morbidity constellation from the speaker point of view?
- What's about the correlation between blood pressure and CVD risk, based on the data presented by the speaker?
- How early and how much should we treat risk factors to prevent or delay or reduce CVD, based on the data presented by the speaker?
- What's about the management of the main CVD risk factors from the speaker point of view?

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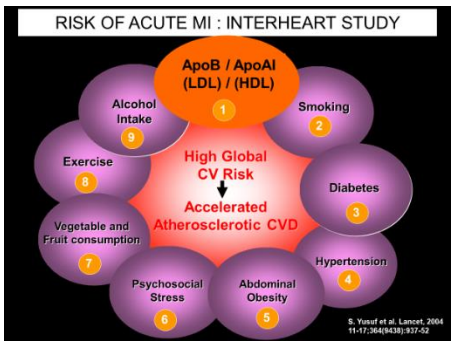
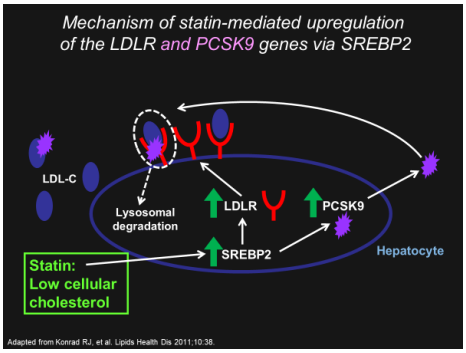
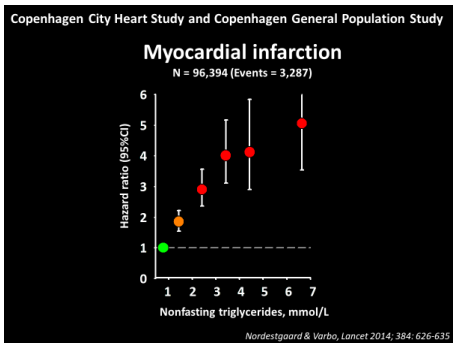
Prevention: how to reduce the residual risk?



"Prevention: how to reduce the residual risk?", was the topic Prof. Chapman spoke about in his lecture. The speaker coming from Paris (FR), presented very interesting data on the main risk factors taken together as high global CV risk and on the LDL causality related to the atherosclerosis vascular disease. Prof. Chapman highlighted that the EAS panel reviewed the evidence, based on the revision of separate meta-analyses of genetic studies, prospective epidemiological studies, mendelian randomization studies and randomized clinical trials. In the main part of his lecture, Prof. Chapman presented very interesting data given by clinical studies designed for the CVD secondary prevention and highlighted that many secondary prevention patients are still not at LDL-C goal despite the use of lipid-lowering drugs. The speaker talked also about the causes of the failure to attain the LDL-C goal and more in particular presented very interesting data on the defects of liver statins uptake, leading to the main statins adverse events on muscles. Prof. Chapman spoke also about the mechanism of statin-mediated upregulation of the LDL receptors and PCSK9 genes via SREBP2 and explained how this upregulation can lead to a low effect in LDL-C reduction. In the second part of his lecture, Prof. Chapman spoke about the PCSK9 inhibitors and about APO CIII and its effects on the lipoprotein metabolism.





The speaker highlighted that APO CIII has a direct effect also on LDL-C and not only on triglycerides. In the last part of his lecture, the speaker presented very interesting data on the tight relationship between the level of post-prandial triglycerides and the prevalence of MI, on the Human HDL metabolism and on the relationship between elevated HDL-C and mortality. In conclusion, Prof. Chapman pointed out that the main challenge in the future will be the possibility to address directly the atherosclerotic plaque at the coronary arterial level.

- **What's about the evidence of the LDL causality related to atherosclerotic vascular disease, based on the data presented by the speaker?**
- **What's about the LDL-C and the coronary plaque indices based on the data presented by the speaker?**
- **What is the residual risk in dyslipidemic patients in secondary prevention, based on the data presented by the speaker?**
- **What's about the correlation between elevated HDL-c and the risk of mortality, based on the data presented by the speaker?**

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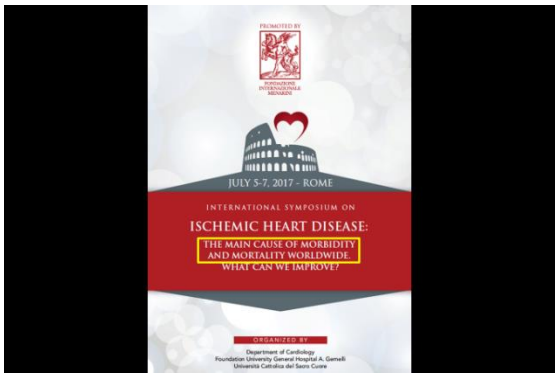
Inflammation and atherosclerosis: state of the art



Inflammation and atherosclerosis: state of the art, was the topic discussed by Prof. Libby. The speaker, coming from Boston (USA), spoke about the cardiovascular continuum revised. Going deeper in his lecture the speaker highlighted that during life we accumulate somatic mutation in blood WBC, leading to a rise in all-cause mortality but also in CVD risk mortality more than in cancer mortality. In the main part of his lecture, Prof. Libby, presented very interesting data explaining the relationship between atherosclerosis and the gene mutations at the bone marrows level. More in particular the speaker spoke about a mutation, the so called Tet2 mutation and its tight correlation with atherosclerosis. In the second part of his lecture, Prof. Libby spoke about the relationship between clonal hematopoiesis of indeterminate potential (CHIP) and the atherosclerotic events and finally presented very interesting data addressing the molecular mechanism at the genetic level, explaining the correlation between Tet2 gene mutation and cardiovascular disease outcome.

- What's about the cardiovascular continuum revised, based on the data presented by the speaker?
- Could atherosclerotic cardiovascular disease account for the rise in total mortality in patients with hematopoietic mutations based on the data presented by the speaker?
- Why does atherosclerosis associate with clonal hematopoietic of indeterminate potential, based on the data presented by the speaker?
- What's about the correlation between Tet2 mutation at the macrophages levels and LDL-C, based on the data presented by the speaker?
- What is the missing link between the hematopoietic mutations and the atherosclerotic cardiovascular risk from the speaker point of view?

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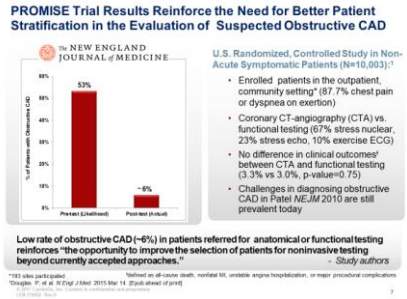
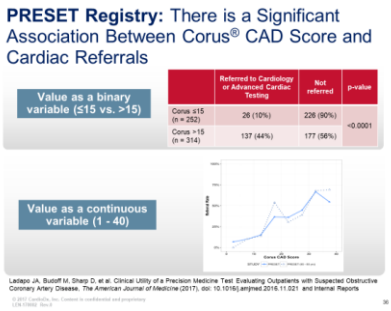
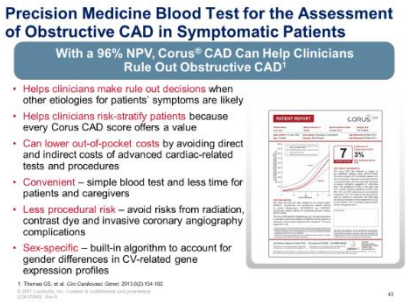
A novel whole blood RNA-based gene expression score to detect obstructive CAD in angina patients



A novel whole blood RNA-based gene expression score to detect obstructive CAD in angina patients, was the topic discussed by Prof. Boden in his keynote lecture. The speaker, coming from Boston (USA), talked about the clinical need of this novel score, the CORUS CAD overview, the review of the clinical validation studies and finally,about the utility of CORUS CAD in women. Going deeper in his lecture, Prof. Boden talked about the role of the standard exercise treadmill test in the CAD diagnosis and highlighted that it remains the preferred non-invasive diagnostic test in patients who are able to exercise, but "there is the need for a simple, safe non-invasive diagnostic test for detecting CAD particularly in women" the speaker pointed out. In the main part of his lecture, Prof. Boden presented very interesting data on the patients' profile who underwent to angiography for the detection of CAD lesions and talked about CORUS CAD that is a new, potentially disruptive technology with clinical utility in diagnosing subjects at low-risk for obstructive CAD, but with chest pain. The speaker presented very interesting data on CORUS CAD, more in particular on the analytical and clinical validity and utility, given by clinical validation studies running in low-risk CAD patients and highlighted that CORUS CAD presents a very high sensitivity and negative predictor value (NPV) from 90% to 96%. In the last part of his lecture, Prof. Boden presented other very interesting data given from Registry studies running in women at risk for CAD, demonstrating the clinical utility of CORUS CAD in these patients. In conclusion, Prof. Boden pointed out that thanks to a 96% of NPV, CORUS CAD can help physicians in ruling out obstructive CAD.





- What's about the normal angiography findings of CAD patients, based on the data presented by the speaker?
- What's about the PCI complications in women and man, based on the data presented by the speaker?
- What are the main CORUS CAD characteristics presented by the speaker?
- What are the patients not available for the CORUS CAD procedure, from the speaker point of view?
- What are the main clinical validation studies on CORUS CAD presented by the speaker?
- Why the CORUS CAD GES may be a more useful "Rule-out" test in women with suspected CAD, based on the data presented by the speaker?

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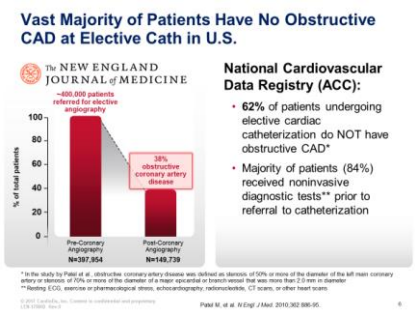
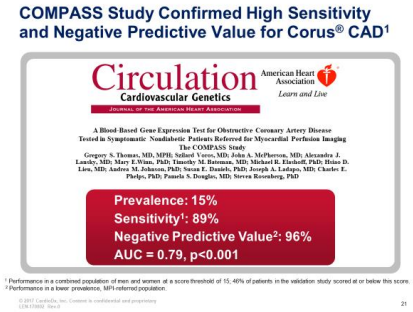
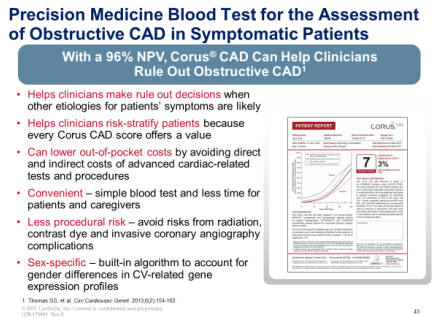
Functional tests



Functional tests, was the topic of Prof. Sechtem presentation. The speaker, coming from Stuttgart, (D), talked about the current ESC algorithm. Going deeper in his lecture, Prof. Sechtem presented very interesting data of other algorithms available for the CAD diagnosis, like the USA and the NICE ones and discussed the main similarities and differences between these algorithms. In the main part of his lecture, the speaker talked about the need for improving the diagnostic algorithms and presented very interesting data given by the main clinical studies running in patients who underwent to CAD diagnosis. More in particular Prof. Sechtem highlighted that the main biases between the different scores are about 20%, that is a very too high result and presented very interesting data on a new low-risk tool developed in 4631 PROMISE patients with CCTA at their initial test. Finally, Prof. Sechtem talked about the new NICE guideline on chest pain of recent onset and highlighted that the main novelties are represented by the abandonment of PTP, CAC zero and CCTA for typical, and atypical angina. In conclusion, the speaker pointed out that testing in patients with suspected CAD need to be improved.





- What is the current ESC algorithm, based on the data presented by the speaker?
- What are the main characteristics of the USA algorithm for the CAD detection, based on the data presented by the speaker?
- What are the main differences between the European, USA and NICE algorithms, based on the data presented by the speaker?
- Why should we improve diagnostic algorithms, based on the data presented by the speaker?
- Is an annual CV death/MI rate of 0.2%/year acceptable, based on the data presented by the speaker?

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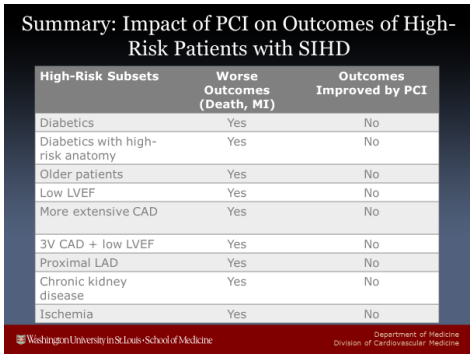
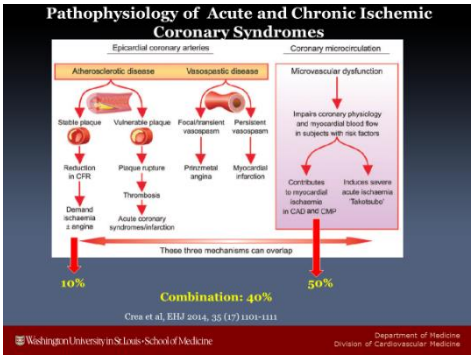
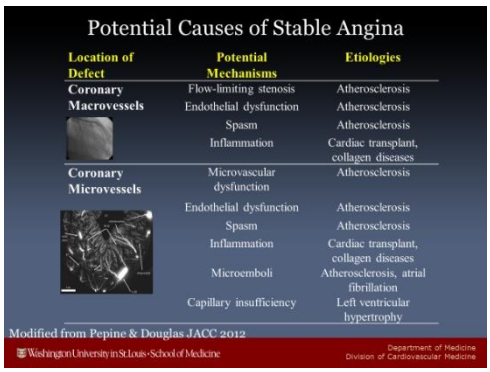
Do we need any testing at all?



Prof. Brown coming from St. Louis (USA) spoke about "Do we need any testing at all?" and presented very interesting data on the first three commandments of clinical medicine, that are do no harm, do not perform tests or procedures that do not improve quality of life and follow the data. Going deeper in his lecture, Prof. Brown presented two clinical cases on two patients, the first one a 61-years-old marketing executive affected by chest-pain without prior signs and symptoms of CAD and the second one a 42-years-old construction supervisor with elevated triglycerides with chest pain and highlighted that based on the USA and ESC guidelines the probability of IHD is based on the execution of Exercise ECG or Exercise MPI or echo depending on the guideline of reference. In the main part of his presentation, the speaker talked about the results on outcomes of the main clinical trials running in patients who underwent to PCI or surgery and highlighted that these are quite total negative. In the second part of his lecture, Prof. Brown presented very interesting data on the pathophysiology of the acute and chronic ischemic coronary syndromes and highlighted that only 10% of patients present atherosclerotic plaques in their coronary arteries, the 50% suffer from coronary microcirculation and the last 40% present a combined disease. Finally, the speaker presented a potentially alternative approach, based on the administration of medical therapy composed by aspirin, beta-blockers, ACE inhibitors, statins and nitrates. In conclusion, Prof. Brown pointed out that the recommended protocol for testing patients with stable angina is expensive and does not improve outcomes directly and there is the need for randomized trials for testing the strategy of initial medical therapy vs. other approaches to assess outcomes and cost-effectiveness.





- What's about the results of the main clinical trials on outcomes in patient who underwent to PCI or surgery based on the data presented by the speaker?
- What's about the alternative approach to patients with suspected anginal chest pain, based on the data presented by the speaker?
- What is the evolving role of CCTA in the workup of patients with suspected anginal chest pain, based on the data presented by the speaker?
- What are the key points of the pathophysiology of acute and chronic ischemic coronary syndromes presented by the speaker?

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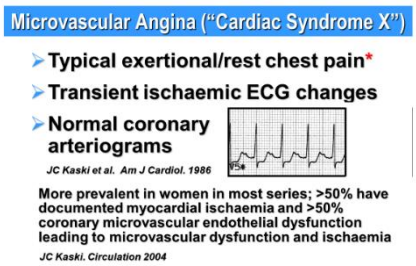
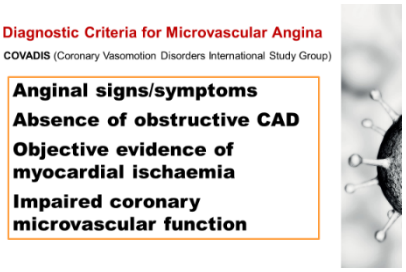
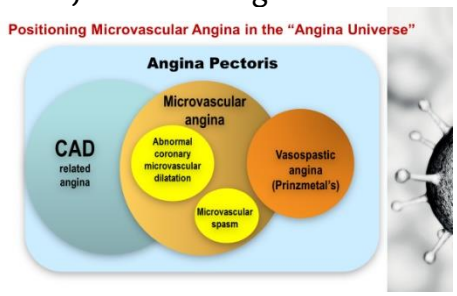
Microvascular angina



Prof. Kaski from London (UK), spoke about microvascular angina and presented very interesting data starting from the current angina paradigm. Going deeper in his lecture, Prof Kaski, talked about the many faces of angina and more in particular on angina in patients with normal coronary angiograms or non-obstructive coronary artery disease and its prevalence, costs and prognostic significance. In the main part of his lecture, Prof. Kaski presented very interesting data on the main characteristics of the microvascular angina and highlighted that it is more prevalent in women affected by documented myocardial ischaemia or coronary microvascular dysfunction. More in particular the speaker presented a huge amount of data given by clinical studies running in angina patients without obstructive CAD and spoke about the diagnostic criteria for microvascular angina. In the second part of his lecture, Prof. Kaski talked about the microvascular angina pathogenesis and pathophysiology and presented very interesting data on the main structural and functional mechanisms leading to coronary microvascular dysfunction in subjects with angina but normal arteries, like endothelial activation and dysfunction due to oestrogen deficiency, chronic inflammation or conventional risk factors for CAD. Finally, Prof. Kaski talked about the chronic stable angina treatment and presented very interesting data on the main treatment targets and the related drugs. In conclusion, the speaker pointed out that the current plaque-centred paradigm, is flawed and it is necessary to identify new, more effective, treatments.





- What are the main characteristics of the microvascular angina, based on the data presented by the speaker?
- What's about the low diagnostic predictivity of elective coronary angiography, based on the data presented by the speaker?
- How many women and men have signs and symptoms of myocardial angina without obstructive CAD, based on the data presented by the speaker?
- What are the main diagnostic criteria for microvascular dysfunction, based on the data presented by the speaker?
- What are the main populations that can be affected by microvascular angina, based on the data presented by the speaker?
- What's about the growing role of the microvascular dysfunction in angina pectoris and IHD?

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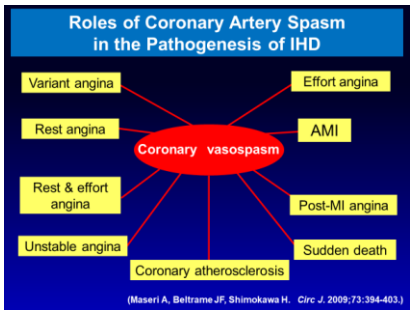
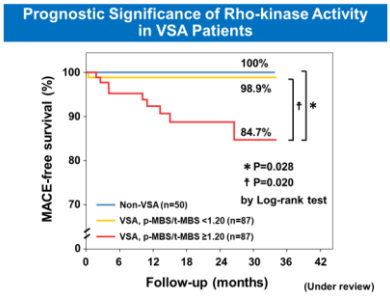
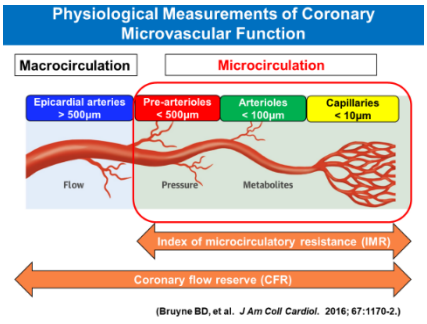
Vasospastic angina



Prof. Shimokawa from Senday (J), spoke about Vasospastic angina. More in particular, the speaker talked about pathophysiology, the central role of Rho-kinase, the possible role of the coronary adventitia and finally about the future perspectives. Going deeper in his lecture, Prof. Shimokawa presented very interesting data on many experimental studies running in his center on the role played by the coronary vasospasm and on the effects of the Rho-kinase on the gene-expressions. More in particular the speaker presented other data on the effects of the Rho-kinase inhibitors on the coronary spasm and on patients affected by the microvascular angina. In the main part of his lecture, Prof. Shimokawa talked about the discovery of new biomarkers like the enhanced Rho-kinase activity in VSA patients. Finally, the speaker presented very interesting data on the possible role played by the coronary adventitia, starting from the observation that in VSA patients there is an enhanced formation of vasa vasorum. More in particular Prof. Shimokawa presented other very interesting data, demonstrating that there is a very tight correlation between coronary adventitia VV and vasoconstriction in VSA patients. In the last part of his presentation, the speaker talked about a clinical project, that is the International Prospective Registry of VSA patients, involving many countries from around the world and about the International Prospective Registry of CMD aiming to the physiological measurements of the coronary microvascular function.





- What is the possible role of the adventitial vasa vasorum in the pathogenesis of the coronary artery spasm, based on the data presented by the speaker?
- What are the roles of the coronary artery spasm in the IHD pathogenesis, based on the data presented by the speaker?
- What are the main mechanisms of coronary spasm presented by the speaker?
- What's about the role played by the Rho-kinase pathway in the pathogenesis of the cardiovascular diseases, based on the data presented by the speaker?
- What are the main effects of Rho-kinase on the gene expressions, based on the data presented by the speaker?
- What's about the chemical structure of Fasudil and hydroxyfasudil presented by the speaker?

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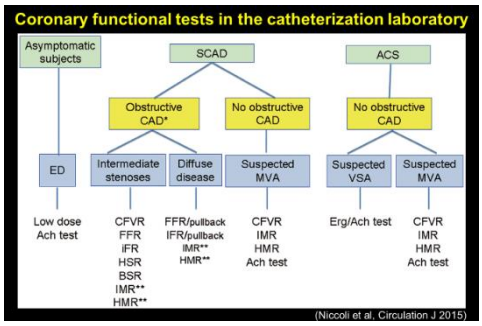
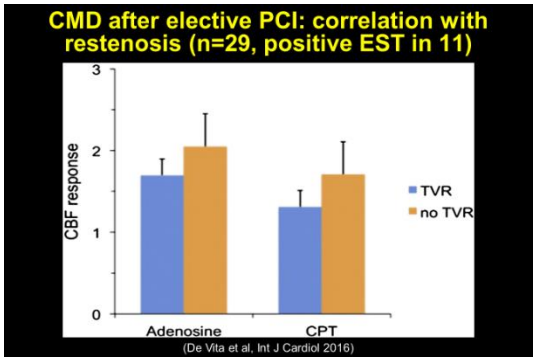
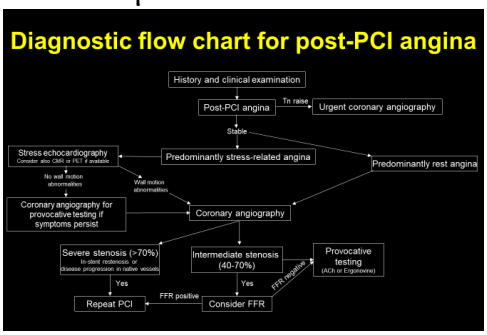
Type 3 coronary microvascular dysfunction



Type 3 coronary microvascular dysfunction, was the topic discussed by Prof. Crea from Rome (IT), more in particular the speaker talked about the classification of the microvascular dysfunction, divided in 4 types, where the third one is about patients affected by microvascular dysfunction and obstructive CAD. In the main part of his presentation the speaker talked about the type 3 CMD impact on outcome and symptoms starting from the coronary functional tests. More in particular Prof. Crea highlighted the role of the Acetylcholine test able to detect an impaired dilatory function and the role of adenosine in inducing hyperaemia as another way for the detection of the impaired dilatory function. The speaker presented other very interesting data, showing that the presence of CMD has a worse impact on the cardiac mortality in patients affected by stable angina. In the second part of his lecture, Prof. Crea presented very interesting data on the impact the type 3 CMD has on symptoms, starting from the presentation of a clinical case of a patient affected by angina also after PCI. Finally, the speaker talked about the structural and the functional causes leading to the recurrent or the persistence of angina and presented a very interesting diagnostic flow chart for post-PCI angina. In conclusion Prof. Crea, pointed out that in SA patients the presence of CMD, independently predict the outcome and in these patients the symptoms are frequently caused by CMD as revealed by the persistence of angina after PCI.





- What's about the correlation between stable angina and the defects in the coronary flow reserve, based on the data presented by the speaker?
- What is the impact of CMD on the outcome of patients with stable angina, based on the data presented by the speaker?
- What are the main structural and functional causes leading to recurrent or persistent angina based on the data presented by the speaker?
- What are the key points of the diagnostic flow chart for patients suffering from post-PCI angina, presented by the speaker?

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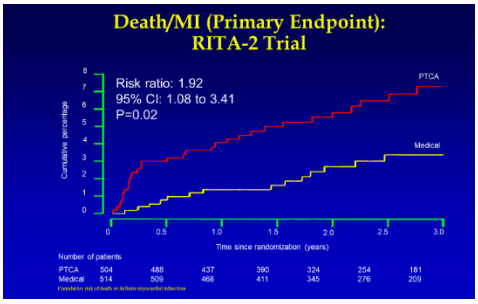
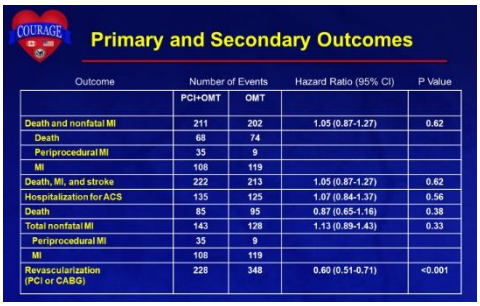
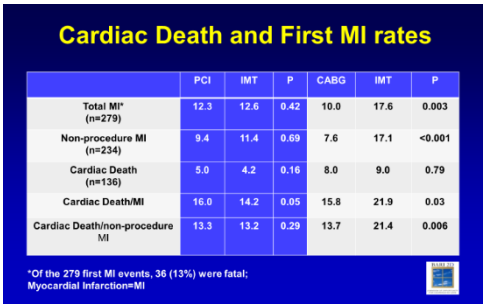
Stable ischemic heart disease: does myocardial revascularization improve the outcome?



Prof. Weintraub from Newark (USA), presented very interesting data on "Stable ischemic heart disease: does myocardial revascularization improve the outcome?". More in particular the speaker talked about the comparison between CABG and Medical Therapy. Going deeper in his lecture the speaker presented very interesting data given from the main clinical trials running in patients affected by CAD who underwent to CABG, PCI or Medical Therapy. More in particular Prof. Weintraub talked about the results of the COURAGE study, comparing PCI+OMT vs OMT alone and highlighted that there are no statistical differences in the two groups on the survival free of death from any cause and myocardial infarction. The speaker talked also about other studies like the ten years follow-up survival of the medicine, angioplasty, or surgery study (MASS-II) running in patients affected by multivessel coronary artery disease and the BARI 2D trial. In conclusion, Prof. Weintraub pointed out that PCI as an initial management strategy does not reduce the incidence of death or MI and that the risk factors control with a therapeutic lifestyle and appropriate pharmacology remains the cornerstone of therapy for reducing recurrent events.



Outcome	Number of Events		Hazard Ratio (95% CI)	P Value
	PCI+OMT	OMT		
Death and nonfatal MI	211	202	1.05 (0.87-1.27)	0.62
Death	68	74		
Periprocedural MI	35	9		
MI	108	119		
Death, MI, and stroke	222	213	1.05 (0.87-1.27)	0.62
Hospitalization for ACS	135	125	1.07 (0.84-1.37)	0.56
Death	85	95	0.87 (0.65-1.16)	0.38
Total nonfatal MI	143	128	1.13 (0.89-1.43)	0.33
Periprocedural MI	35	9		
MI	108	119		
Revascularization (PCI or CABG)	228	348	0.60 (0.51-0.71)	<0.001



- What are the main data affording for CABG, based on the data presented by the speaker?
- What are the main results of the MASS-II trial, based on the data presented by the speaker?
- What' about the effect on survival of the prompt revascularization in type 2 diabetic patients, based on the data presented by the speaker?
- Why do we need non-randomized approaches from the speaker point of view?
- What's about the decline in mortality, based on the data presented by the speaker?
- What are the future advances discussed by the speaker?
- What's about the problem of generalizability from the speaker point of view?

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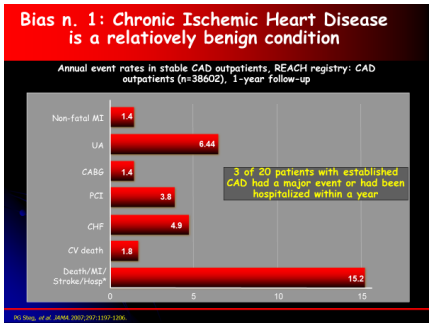
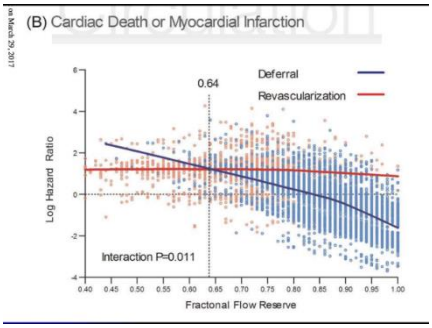
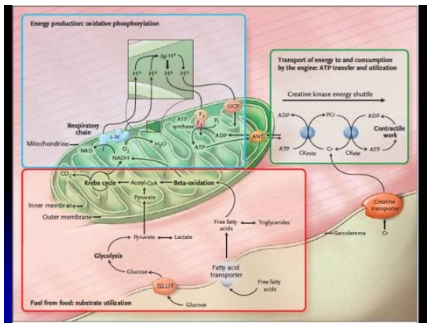
Can we do any better with antianginal treatment?



"Can we do any better with antianginal treatment?" was the topic of Prof. Marzilli presentation. The speaker, coming from Pisa (IT), presented very interesting data starting from the discussion on the main biases related to the chronic ischemic heart disease (CIHD) diagnosis and management. The first one refers to the idea that CIHD is a relatively benign condition, despite 3 of 20 patients with established CAD have a major event or that CAD is strictly correlated only with coronary atherosclerosis despite the data demonstrate that the prevalence of obstruction is only present in a minority of CIHD patients. Another bias presented by the speaker refers to the idea that the stenosis removal is an effective cure for CIHD, despite a lot of data demonstrate the contrary. Prof. Marzilli talked also about the fourth bias, that is the idea that the more accurate measure of the stenosis severity is able to improve the PCI results, despite the data published this year on circulation, demonstrate exactly the contrary. The fifth bias presented by the speaker, refers to the idea that we know why the atherosclerotic lesions cause myocardial ischemia, but in the reality ischemia is due to many physiopathological processes than the only atherosclerotic one. The last bias Prof. Marzilli talked about was the idea that an adequate blood supply prevents myocardial ischemia, despite the fact that blood does not deliver ATP and also the heart has no storage of ATP, that means that ischemia is related to the failure of mitochondria in ATP production. In conclusion, Prof. Marzilli pointed out that physicians have to stop to confuse myocardial ischemia with coronary atherosclerosis if we want to gain progresses in the HID management.





- **What's about the effectiveness of the medical therapy during time, from the speaker point of view?**
- **What is the prevalence of coronary stenosis in the reality compared to the guidelines prediction, based on the data presented by the speaker?**
- **What is the essence of IHD, from the speaker point of view?**
- **What about the correlation between cardiac death and revascularization procedures, based on the data presented by the speaker?**
- **What are the main results of the COURAGE trial presented by the speaker?**

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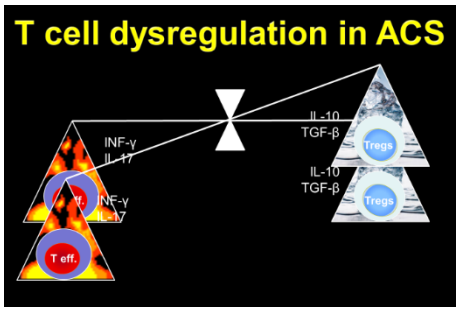
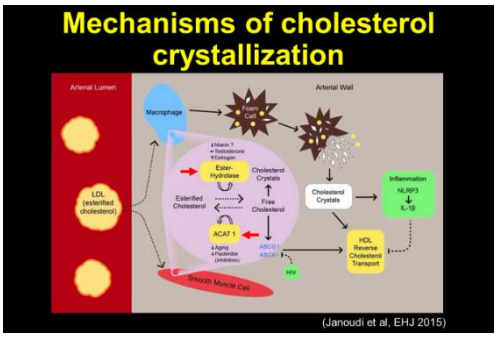
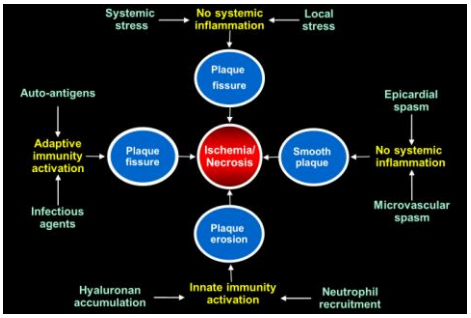
An overview of ACS



The main topic of Prof. Crea presentation was "an overview of ACS". The speaker, coming from Rome (IT), presented very interesting data on the pathophysiology and pathogenesis of the acute coronary syndromes. More in particular Prof. Crea went deeper in his lecture and presented very interesting data on the T cell dysregulation in ACS leading to the adaptive immune activation, the plaque fissuring and the ischemic/necrotic lesions. Prof. Crea talked also about other very important pathogenetic factors that obtain the same result through other pathways. Going deeper in his lecture, the speaker presented very interesting data on other causes leading to plaque fissuring like the activity of the cholesterol crystal, or the mechanisms leading to the plaque erosion through the myeloperoxidase activation, the neutrophils recruitment and the enhanced hyaluronidase expression. In the main part of his lecture, Prof. Crea presented other very interesting data on the other plaque fissuring mechanisms present in almost the 30% of patients, like the coronary spasm due to the presence of the enhanced Rho-kinase activity. Prof. Crea spoke also about the CANTOS study and presented very interesting data on the reduction of the cardiovascular events obtained with the canakinumab administration.





- What are the main mechanisms of the T cell dysregulation in ACS patients?
- What are the main unique adaptive immune signatures in ACS presented by the speaker?
- What's about the expanded CV continuum, based on the data presented by the speaker?
- What's about the pathogenesis of plaque fissure other than inflammation from the speaker point of view?
- What are the main mechanisms of plaque fissuring due to cholesterol crystallization, based on the data presented by the speaker?
- What are the key points of the clinical implications related to the plaque fissuring mechanisms presented by the speaker?

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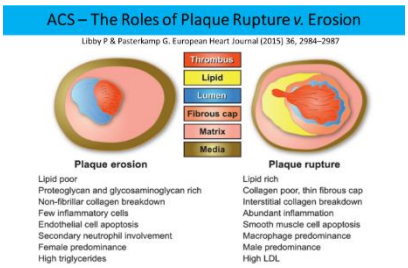
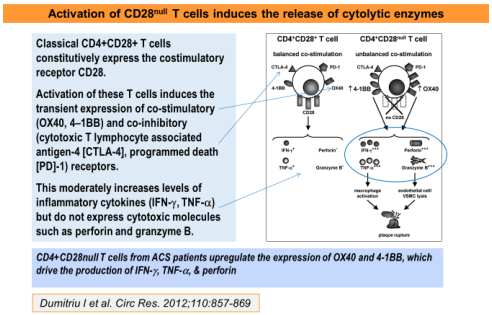
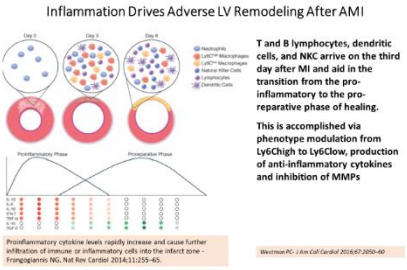
Role of inflammation in ACS



Prof. Kaski from London (UK), spoke about Role of inflammation in ACS and presented very interesting data on inflammation as a trigger, or as a result of ACS and AMI. Going deeper in his lecture, Prof. Kaski presented very interesting data on the impact of inflammation on the post-ACS clinical outcomes and on inflammation as a therapeutic target. More in particular the speaker presented very interesting data on the plaque rupture and on the inflammatory mechanisms that can play a major role in most of the processes leading to ACS. In the main part of his lecture, Prof. Kaski talked about the roles played by the processes of plaque rupture vs erosion in ACS patients and presented very interesting data on the main processes of inflammation in ACS patients also from the clinical point of view, like the relationship between Rheumatoid arthritis or Lupus Erythematosus and the risk of MI. In the second part of his lecture, Prof. Kaski spoke about the composition of the vulnerable plaque, characterized by the presence of macrophages, pro-inflammatory cytokines, T-cell infiltration and activated platelets and presented very interesting data given by experimental studies on all these elements, the CD4+CD28 null T cells and their potent cytotoxic machinery. Speaking about platelets and inflammation in ACS patients, Prof. Kaski highlighted the pro-inflammatory role of platelets and the relationship between inflammation and thrombosis. Finally, the speaker presented very interesting data on the relationship between inflammation and recurrent post-MI events, more in particular on inflammation as a driver of adverse LV remodelling after acute MI. In conclusion, Prof. Kaski pointed out that the innate and the adaptive immunity play a key role in coronary plaque instability and that T-cells, neutrophils, the inflammasome and macrophages may be potential therapeutic targets.





- Why is ACS a changing paradigm, based on the data presented by the speaker?
- Can we find EGFR T790M in the blood, based on the data presented by the speaker?
- What's about the relationship between rheumatoid arthritis and risk of MI, based on the data presented by the speaker?
- What's about the relationship between CD4 and CD28- T cells and the coronary artery disease presented by the speaker?
- What are the main mechanisms leading to the widespread inflammation in ACS patients, based on the data presented by the speaker?

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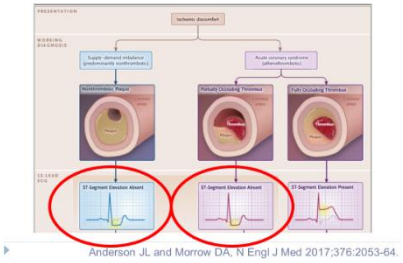
Role of thrombosis

Similar ECG presentation of type 1 and type 2 MI



Anderson JL and Morrow DA. N Engl J Med 2017;376:2053-64.

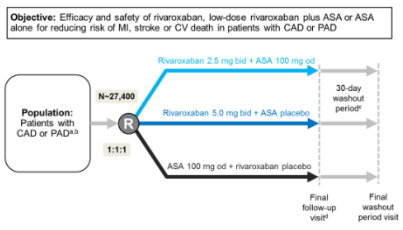
Role of thrombosis, was the topic discussed by Prof. De Caterina from Chieti (IT). More in particular the speaker presented very interesting data on thrombosis in various subsets of ACS, on the antithrombosis treatment around revascularization and finally on the long-term treatments. Talking about thrombosis in ACS patients, the speaker presented very interesting data on Atherothrombosis as the MI type 1 cause and its ECG presentation. Prof. De Caterina highlighted that it is very similar to the type 2 cause, but with very different therapies to be applied for. The speaker presented also very interesting data given by clinical studies running in NSTEMI patients, highlighting the close relationship between thrombosis, thrombolysis and the antiplatelet therapy, but also the ineffectiveness of antithrombotic therapies in certain MI subset I and II. Talking about antithrombotic treatments around revascularization, Prof. De Caterina presented very interesting data on the combination of 2 antiplatelet agents against the stent thrombosis. Going deeper in his lecture, the speaker presented a huge amount of data given from many clinical trials running in MI revascularized patients treated with combined antiplatelet therapy and highlighted the effects of the $P2Y_{12}$ inhibitors on the reduction of the stent thrombosis. Finally, Prof. De Caterina presented very interesting data on the log-term treatment thanks to the COMPASS study design and results. In conclusion, Prof. De Caterina pointed out that the stent thrombosis largely depends on $P2Y_{12}$ platelet stimulation and the combination between a $P2Y_{12}$ inhibitor and an anticoagulant is as effective as a classical "triple therapy" with aspirin, clopidogrel and an oral anticoagulant.

Stent thrombosis is not increased by omitting aspirin in the presence of a $P2Y_{12}$ inhibitor!!

	Double therapy (n=297)	Triple therapy (n=284)	Hazard ratio (95% CI)	p value
Combined secondary endpoint	31 (11·1%)	50 (17·6%)	0·60 (0·38–0·94)	0·025
Death				
All-cause	7 (2·5%)	18 (6·3%)	0·39 (0·16–0·93)	0·027
Cardiac	3 (1·1%)	7 (2·5%)	0·43 (0·11–1·66)	0·207
Non-cardiac	4 (1·4%)	11 (3·9%)	0·36 (0·11–1·13)	0·069
Stent thrombosis				
Any	4 (1·4%)	9 (3·2%)	0·44 (0·14–1·44)	0·165
Definite	1 (0·4%)	3 (1·1%)	0·33 (0·03–3·22)	0·319
Probable	0	2 (0·7%)	NA	0·161
Possible	3 (1·1%)	4 (1·4%)	0·75 (0·17–3·30)	0·708

DeWilde W. et al. Lancet 2013;381:1107–15

COMPASS Study Design



De Caterina R and Goto S, Vascul Pharmacol 2016; 81:1-14

- **What are the main considerations about the ISIS-2 and subsequent antithrombosis treatments in MI patients, based on the data presented by the speaker?**
- **What is the effect on stent thrombosis of the addition of an anticoagulant to DAPT, based on the data presented by the speaker?**
- **What are the Key points of the COMPASS study, based on the data presented by the speaker?**

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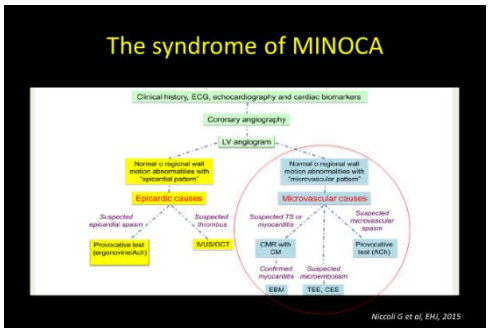
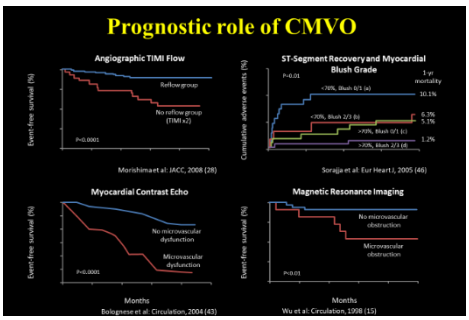
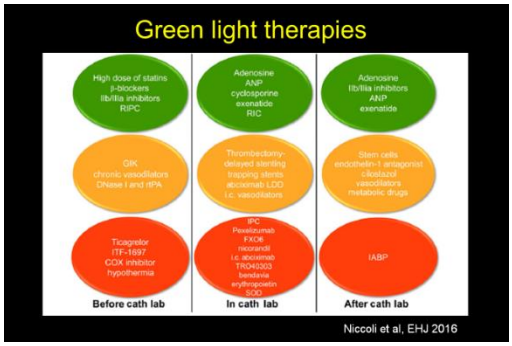
Role of coronary microvascular dysfunction



Prof. Niccoli from Rome (IT), spoke about the role of the coronary microvascular dysfunction. More in particular, the speaker talked about the pathogenesis of the coronary microvascular dysfunction (CMD) in MI patients with normal coronary arteries and coronary artery disease. Going deeper in his lecture, Prof. Niccoli presented very interesting data on the microcirculatory dysfunction in ST-elevation MI patients, by highlighting that the CMD has a prognostic role for the prediction of the acute coronary events. In the main part of his lecture, the speaker talked about the chronic microvascular obstruction (CMVO), its pathogenesis, its diagnostic tool and its prognostic role in MI patients. Talking about CMVO diagnosis the speaker highlighted the role played by MRI also for its prognostic value in patients affected by myocardial haemorrhage. Prof. Niccoli spoke also about the role played by the infart size from the prognostic point of view. In the second part of his lecture, the speaker presented very interesting data on the multiple therapeutic targets and on the controversial, promising and ineffective therapies against reperfusion injury. More in particular the speaker talked about high dose statins, IV metoprolol, exenatide, colchicine and about cyclosporine as a paradigmatic example. In conclusion, Prof. Niccoli pointed out that CMD is increasingly recognized as a pathogenetic factor in acute MI and, most importantly, the microcirculation has a strong impact after reperfusion when the CMVO does occur.





- **What's about the green light therapies for reperfusion injury, based on the data presented by the speaker?**
- **What are the key points of the EUROSTRATEGY proposal study, based on the data presented by the speaker?**
- **What are the main colchicine effects in MI patients presented by the speaker?**
- **What's about the exenatide effects in MI patients, based on the data presented by the speaker?**

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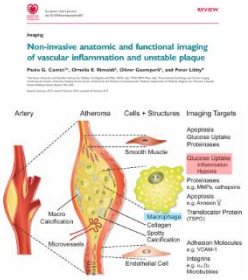
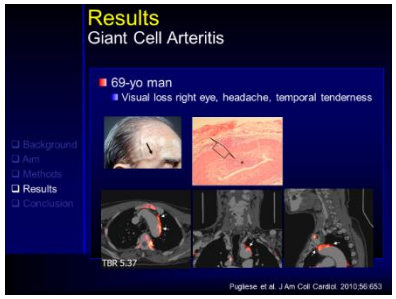
Non-invasive imaging



Non-invasive imaging, was the topic discussed by Prof. Camici from Milan (IT), more in particular the speaker talked about the development of the human coronary atherosclerosis and thrombosis. Going deeper in his lecture, Prof. Camici presented very interesting data on the plaque progression and on the spectrum of STEMI and NSTEMI Acute Coronary Syndrome. In the main part of his lecture, the speaker talked about the plaque inflammation, the non-invasive methods for his detection, the role played by Hypoxia for the glucose uptake in the human macrophages and about a Translocator protein, the so called PK11195, that specifically binds to macrophages as a marker of the activated phagocytes. Prof. Camici presented also very interesting data given by imaging studies running in patients affected by chronic autoimmune diseases. In the second part of his lecture, Prof. Camici talked about the involvement of the vasa vasorum in the pathophysiology of atherosclerosis and presented very interesting data on the contribution of the neovascularization to the plaque growth given by an imaging study on the detection of the in-vivo carotid plaque. More in particular the speaker talked about the study objectives, design, flowchart and results.



- What are the main causes of coronary thrombosis presented by the speaker?
- What is the effect of hypoxia on the human macrophages, based on the data presented by the speaker?
- What are the main characteristics of the PK11195 protein, based on the data presented by the speaker?
- What is the effect of the steroid treatment on the PK11195 vascular uptake?
- What's about the contribution of neovascularization to the plaque growth, based on the data presented by the speaker
- What are the main characteristics of the IMPLAC study, presented by the speaker?

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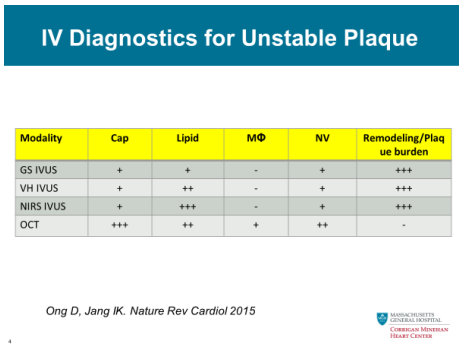
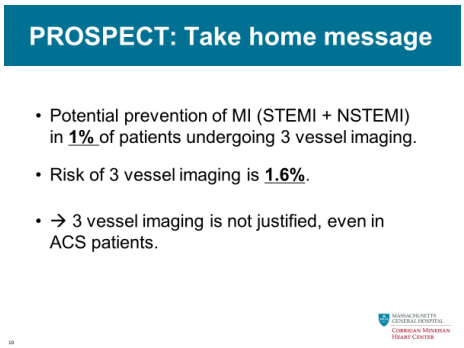
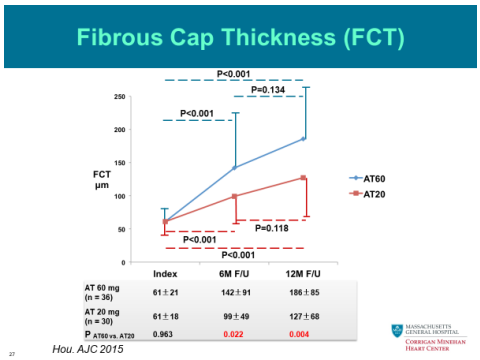
Invasive imaging



Prof. Jang from Boston (USA), presented very interesting data on Invasive imaging, starting from the concept of the unstable plaque that is prone to erosion but not yet disrupted. Going deeper in his lecture, Prof. Jang presented very interesting data on the diagnosis for unstable plaque thanks to the application of IVUS or OCT modalities and discussed the main differences of these methodologies. More in particular Prof. Jang spoke about many imaging studies and presented very interesting data starting from the PROSPECT study, showing that in order to prevent 1 cardiac death it is necessary to treat at least 100 patients. Prof. Jang pointed out that the risk of 3 vessel imaging is about 1.6%, that means it is not justified the 3-vessel imaging application even in ACS patients. The speaker presented other very interesting data given by clinical studies on ACS patients who underwent to imaging for their plaques diagnosis. More in particular Prof. Jang talked about the MGH OCT Registry and the YELLOW II study and presented objectives, methods, study design and finally the main results, showing that the pursuit of the unstable plaques may not be cost effective and may increase the risk. In conclusion, Prof. Jang pointed out that the intravascular imaging of unstable plaques is not ready for any clinical application.





- What's about the differences between IVUS and OCT, based on the data presented by the speaker?
- Why trying to detect "unstable plaque" using an intravascular modality from the speaker point of view?
- What are the main important components of the unstable plaque, based on the data presented by the speaker?
- What are the main independent predictors of lesion events in the PROSPECT study, based on the data presented by the speaker?

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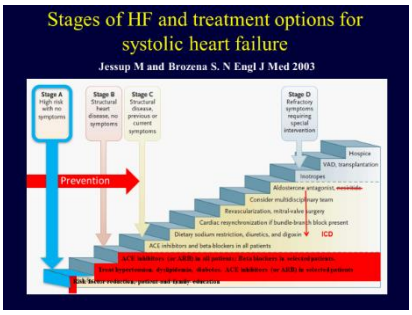
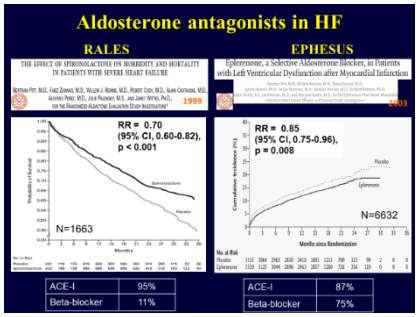
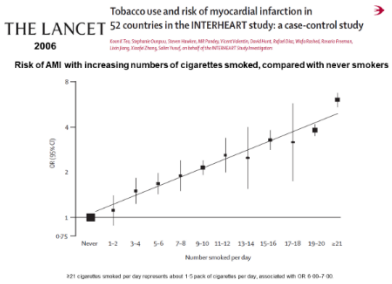
The pandemics of heart failure with reduced ejection fraction: a look to the future



Prof. Pfeffer from Boston (USA), spoke about "the pandemics of heart failure with reduced ejection fraction: a look to the future" and presented very interesting data starting from the economic burden of hospitalizations for heart failure. Going deeper in his lecture, Prof. Pfeffer talked about the need for preventive and public health strategies specifically tailored to the local epidemiological characteristics and presented very interesting data given by the main clinical studies running in HF patients, on the effects of different antihypertensive drugs. More in particular the speaker talked about the HF stages and the treatment options for patients affected by systolic heart failure. In the main part of his lecture, Prof. Pfeffer presented very interesting data given by the main clinical studies running in HF patients on the effects of the main antihypertensive therapies on their outcome. More in particular the speaker talked about the effect of diuretics and statins in a primary prevention setting. Speaking about prevention in patients affected by ventricular systolic dysfunction, Prof. Pfeffer presented very interesting data on the effects of ACE inhibitors. In patients with structural disease, the speaker presented other very interesting data on the effects of Beta-blockers, by highlighting the incredible result on the mortality reduction and about the effects of the aldosterone-antagonists. In the last part of his presentation, the speaker talked about the angiotensin-neprilysin inhibitors and on the results of the TOPCAT study and the related biases due to the very different populations enrolled in the study. Finally, Prof. Pfeffer presented very interesting data on the multivariable predictors of HF, by highlighting that all these factors work together for the HF development. In conclusion, Prof. Pfeffer pointed out that the cardiovascular disease is a continuum and its necessary to stop the CVD evolution since its first steps, working on patients for the modification of their life style.





- What's about heart failure as an aging phenomenon, based on the data presented by the speaker?
- What's about the mean discharge age in men and women for the first hospitalization for heart failure from the 1986 to 2010, based on the data presented by the speaker?
- What is the risk of acute MI associated with the exposure to multiple risk factors, based on the data presented by the speaker?
- What are the main multivariable predictors of Heart Failure presented by the speaker?

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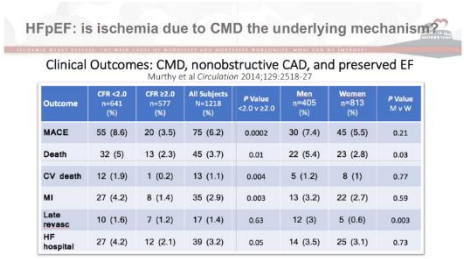
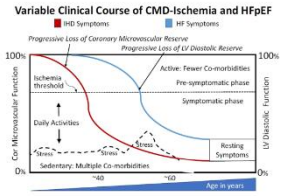
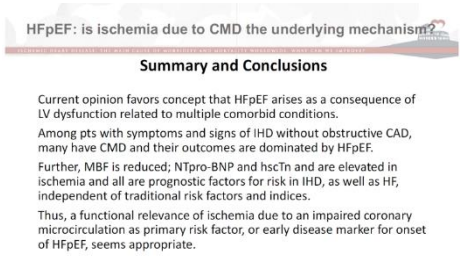
Role of ischemia



Role of ischemia, was the topic discussed by Prof. Pepine from Gainesville (USA), more in particular the speaker talked about the HFpEF and its links with CMD. Going deeper in his lecture, Prof. Pepine presented very interesting data on the multi-morbidity of CMD in HFpEF patients and spoke about the clinical outcomes of patients affected by CMD, non-obstructive CAD and preserved HF. More in particular the speaker presented a huge amount of very interesting data, given by the main clinical trials running in HFpEF patients and highlighted that a functional relevance of ischemia due to an impaired coronary microcirculation as primary risk factor, or early disease marker for the onset of HFpEF, seems appropriate. Finally, Prof. Pepine talked about the pathogenesis processes in HFpEF, by highlighting the central role of the microvascular ischemia.





- What is the underling mechanism leading to ischemia in HFpEF patients, based on the data presented by the speaker?
- Is ischemia due to coronary microvascular dysfunction a bridge to HFpEF, from the speaker point of view?
- What are the key points of the microvascular ischemia-HFpEF hypothesis, presented by the speaker?
- What are the main biomarkers useful to inform on mechanisms and to determine the prognosis, based on the data presented by the speaker?
- What's about the evidences that link endothelium with the LV relaxation?

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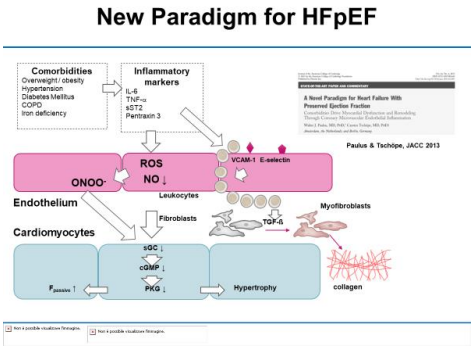
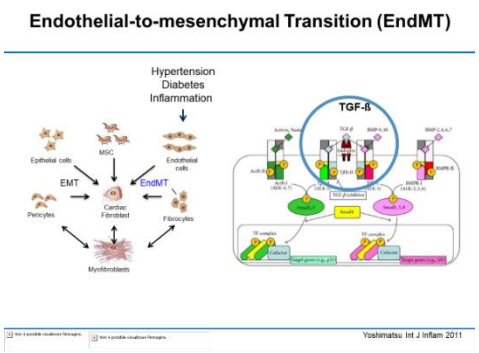
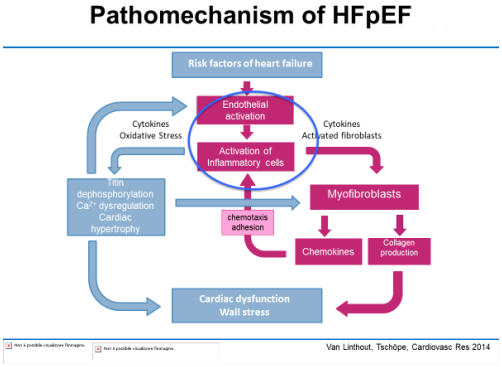
Role of microvascular inflammation



Prof. Van Linthout from Berlin (D), spoke about the role of microvascular inflammation and presented very interesting data starting from the prognosis of HF. Going deeper in her lecture, Prof. Van Linthout talked about the relationship between inflammation and HF and presented very interesting data on the structural causes of the microvascular dysfunction. In the main part of her lecture, the speaker talked about the main circulating biomarkers associated with the onset of HFpEF and presented very interesting data on the microvascular circulation and the adhesion molecules, by highlighting that inflammation is the trigger factor for the development of fibrosis, very typical in HFpEF patients, leading to the diastolic dysfunction. In the second part of her lecture, Prof. Linthout presented very interesting data on the endothelium-to-mesenchymal transition process, as a consequence of the hypertension, diabetes and inflammation effects on the endothelial cells. The speaker talked also about the endothelial nitric oxide2, the oxidative stress and its correlation with the development of the interstitial cardiac fibrosis. Finally, Prof. Linthout spoke about the effect of inflammation on the cardiomyocyte function leading to stiffness, CA^{2+} dysbalance and cardiomyocyte hypertrophy. In conclusion, the speaker pointed out that in the pathomechanism of HFpEF the endothelial activation and the activation of the inflammatory cells play a central role.





- **What is the impact of TGF β on the in vitro human cardiac fibroblasts, based on the data presented by the speaker?**
- **What are the key points of the new paradigm for HFpEF presented by the speaker?**
- **What is the role played by myocardial titin and collagen in the onset of the cardiac diastolic dysfunction, based on the data presented by the speaker?**
- **What are the structural causes of the microvascular dysfunction, based on the data presented by the speaker?**

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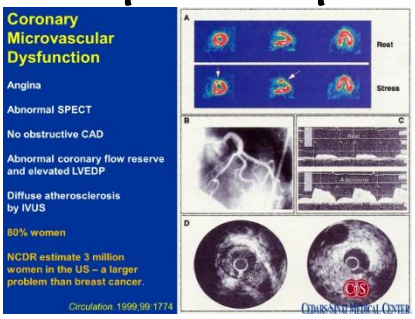
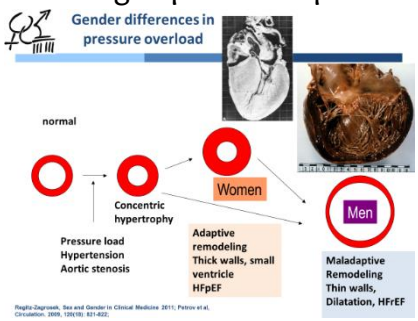
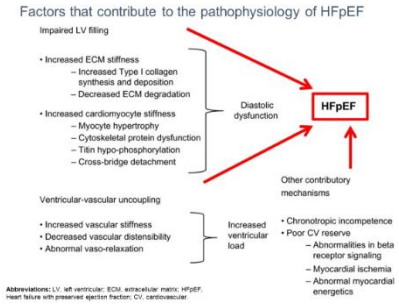
Therapeutic implications



"Therapeutic implications" was the topic discusses by Prof. Bairey Merz. The speaker coming from Los Angeles (USA), presented very interesting data on the coronary microvascular dysfunction and the main clinical characteristics of these patients, by highlighting that this finding is particular present in women, with an estimation burden of about 3 million women in the USA. Going deeper in her lecture, Prof. Bairey Merz talked about the potential causes and consequences of the coronary microvascular dysfunction and about the gender-related HFpEF mechanisms. In the main part of her lecture, the speaker presented very interesting data on the main therapeutic targets and highlighted that the preliminary data given by experimental studies support the correlation between CNMD and HFpEF and that anti-ischemic, anti-metabolic and anti-fibrotic therapies should be tested in these patients. In conclusion, Prof. Bairey Merz pointed out that the WISE data suggest that the CMD prevention and treatment could prevent HFpEF.





- What are the main gender-related HFpEF mechanisms, based on the data presented by the speaker?
- What are the main factors that contribute to the pathophysiology of HFpEF presented by the speaker?
- What are the main gender differences in pressure overload, based on the data presented by the speaker?
- What's bout the correlation between CMD and the left ventricular concentric remodelling, based on the data presented by the speaker?

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