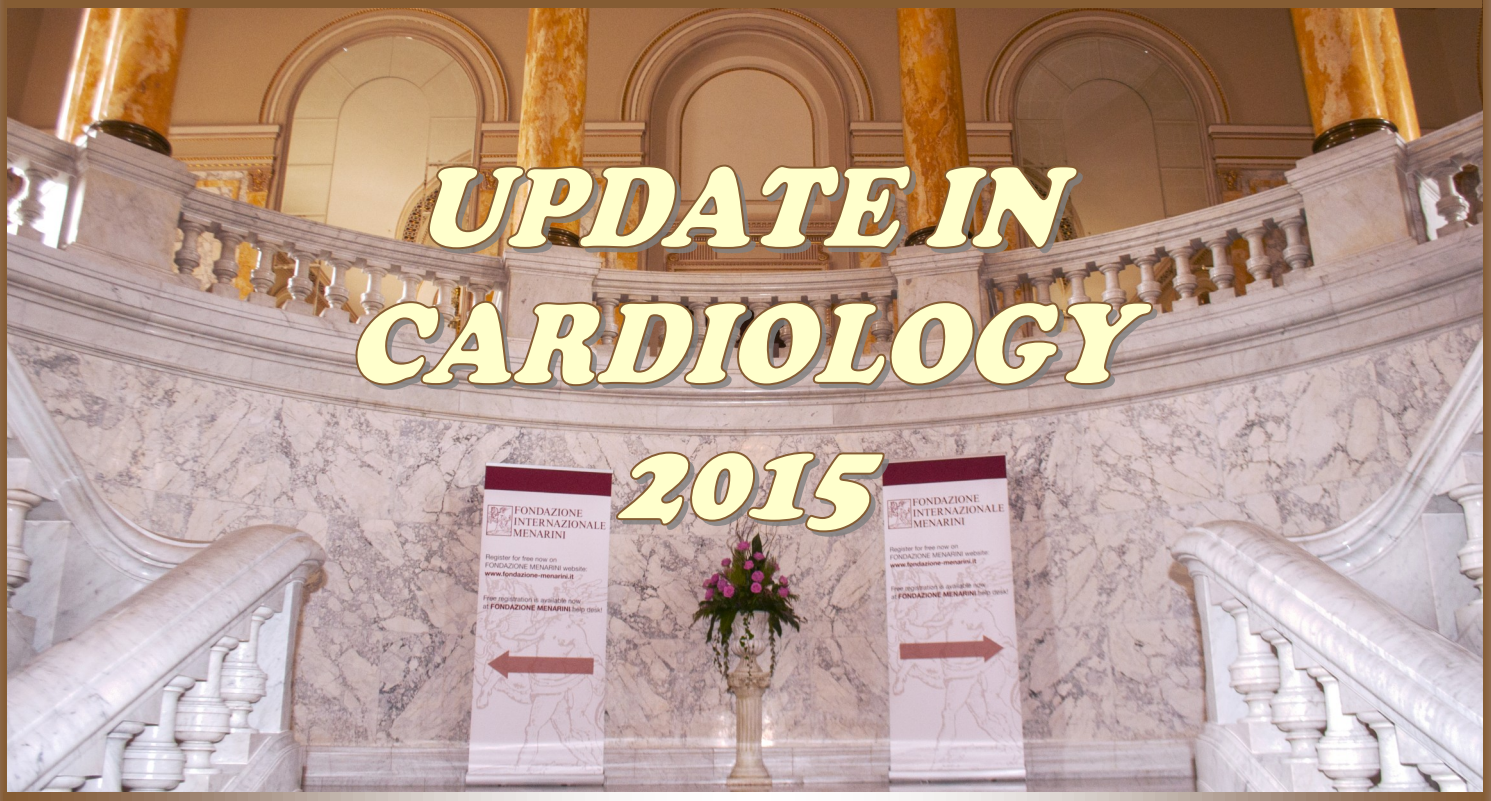

HIGHLIGHTS

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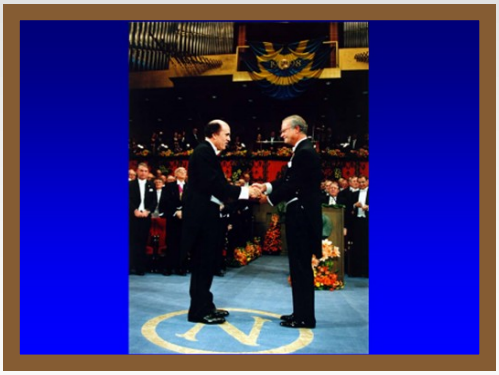
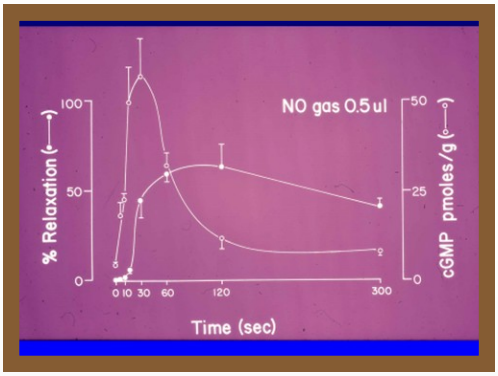
HIGHLIGHTS

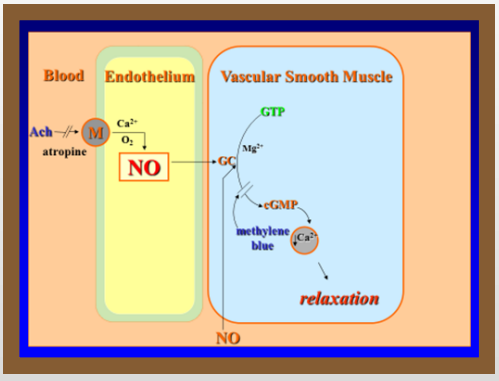
L.J. Ignarro
USA

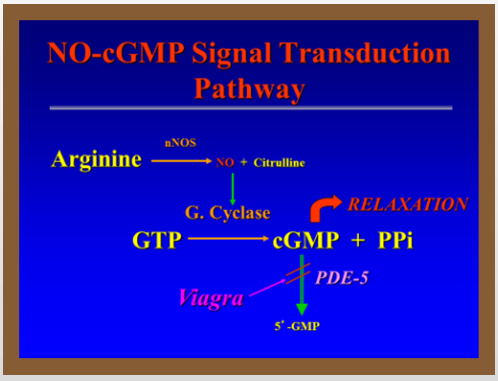
On the road to Stockholm: a Nobel mission



Prof. Luis Ignarro, Nobel Prize winner in 1998 for his discovery of Nitric Oxide, recounted the salient moments of his discovery of the principal endothelium-derived relaxing factor. The pharmacology of Nitric Oxide had been known for some time, one only has to think of the vasodilating effect of nitroglycerine discovered as far back as 1870, although what we did not know was the intimate physiological mechanism behind that effect. Could it be that Nitric Oxide, created from the metabolism of Nitryglycerine, was its mediator? The reply is: yes, and here you see the experiment that demonstrated it. Commencing from this demonstration, the pharmacological action of Nitric Oxide was described, characterised mainly by its relaxing effect on vascular musculature which determines a reduction in blood pressure in hypertensive patients, improves blood flow and reduces platelet aggregation. But what is its mechanism of action? In other words, what is the physiological relevancy of the cyclical NO/GMP system? This was the discovery of Prof. Ignarro, who after assiduously studying the enzyme cascade of Acetylcholinesterase at endothelium cell level, succeeded in demonstrating that the socalled EDRF (Endothelium-Derived Relaxing Factor), was none other than Nitric Oxide. A fundamental discovery which from 1992 acquired great visibility worldwide, in leading scientific journals and in the more important daily newspapers, to name but one, the first page of the New York Times. But to arrive at Nobel recognition, in all probability, an important helping hand came from a high-impact socio-medical clinical application: Nitric Oxide as a neurotransmitter that mediates the erectile function, in other words, Viagra. In March 1998 the marketing of Viagra commenced and in October of the same year the Nobel prize winner was announced. Does the story end here? Absolutely not, if anything it was the beginning of a new story, because the discovery of the physiological mechanism of Nitric Oxide has revolutionised modern Medicine, opening up the way to a whole series of applications and new drugs that are fundamental for the treatment of various pathologies, not only in the cardiovascular area.







What are the new applications? - - - What are the drugs? - - - What has changed after the discovery of Nitric Oxide in the Medicine of today?

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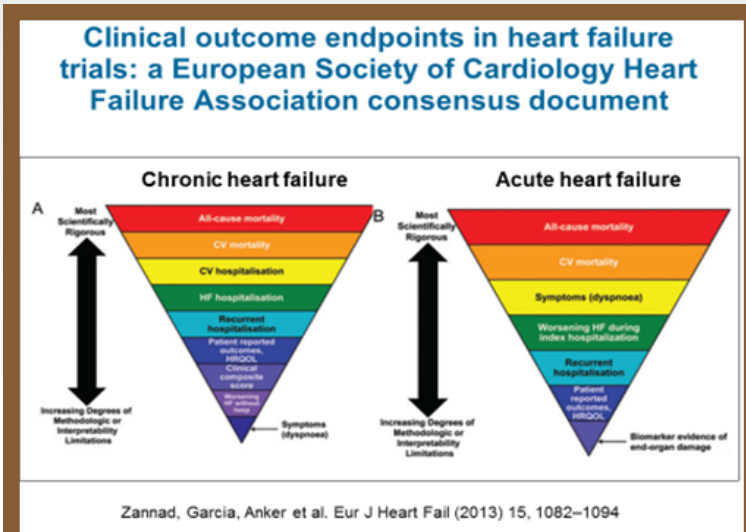
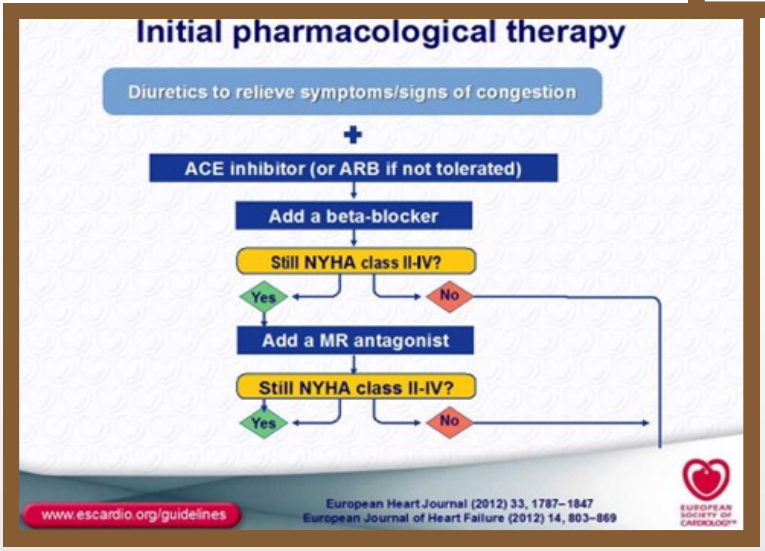
HIGHLIGHTS

M. Metra
Italy

Is extending the life of patients suffering from heart failure an achievable objective?

Heart Failure is a pathology that is still characterised by a high mortality rate. Prof. Metra from Brescia presented interesting data on the outcome of patients suffering from heart failure. Firstly, not all patients with heart failure are afflicted by the same mortality. In fact much depends on the presence of a reduced or well-conserved ejection fraction; and the outcome changes again in the event of acute failure. Patients with a reduced ejection fraction appear to benefit more from the treatment protocols in use compared with those with a preserved ejection fraction. The introduction of ACE inhibitors associated with Beta-Blockers has significantly improved the prognosis in terms of reduction of mortality in patients with reduced ejection fraction, but not in those with preserved ejection fraction. New drugs being studied are also showing positive effects for this category of patients. However, in the case in which the ejection fraction is preserved, no data are presently available to show an improvement in prognosis in terms of mortality with no pharmacological treatment. The prevailing hypothesis is that the inflammatory processes, which are anyhow present in these patients, are principally responsible for this phenomenon. As to acute failure, one of the main problems is correlated organ damage, accompanied by the effects of concomitant pathologies.





What are the most effective new drugs? - - - What are the factors that prevent improvement of the prognosis of patients with preserved ejection fraction?

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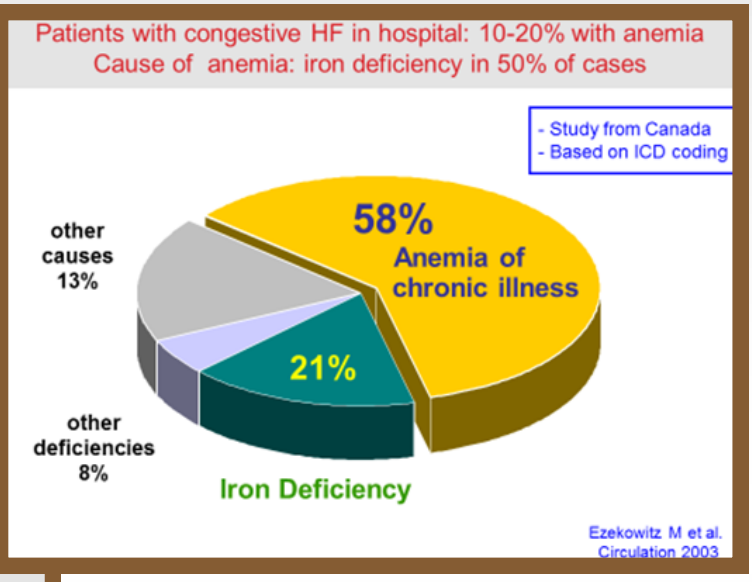
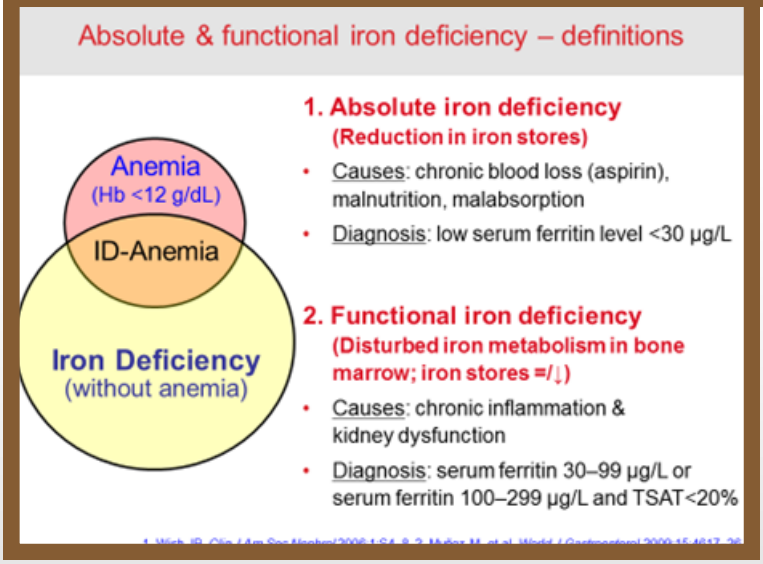
HIGHLIGHTS

S.D. Anker
Germany

To what extent does Iron deficiency affect the evolution and prognosis of patients with Heart Failure?

Prof. Anker from Gottingen presented some very interesting data on the impact of iron deficiency in patients suffering from heart failure. These patients may have various comorbidities, including different forms of anemia. Why do patients with heart failure have an iron deficiency incidence of over 20%? The problem is partly due to diet. Iron is in fact particularly present in fruit and vegetables, foods that are increasingly lacking in people's standard diets.





In addition, another problem is related to the typical inflammatory state of patients suffering from heart failure. Inflammation in fact reduces iron uptake quite significantly. Is anemia or iron deficiency more dangerous for patients with heart failure? In other words, which of the two pathological conditions has the worse influence on prognosis? Iron deficit exposes patients with heart failure to a prognosis that is significantly worse than the concomitant presence of anemia. It is therefore fundamental to opt for an effective replacement therapy. Nevertheless, the administration of iron does not always succeed in correcting anemia, or rather, in restoring HB to normal levels, but also in these cases it improves the outcome of heart failure.

What is the target tissue of iron molecules? - - - What is the impact of martial therapy on hospitalisation?

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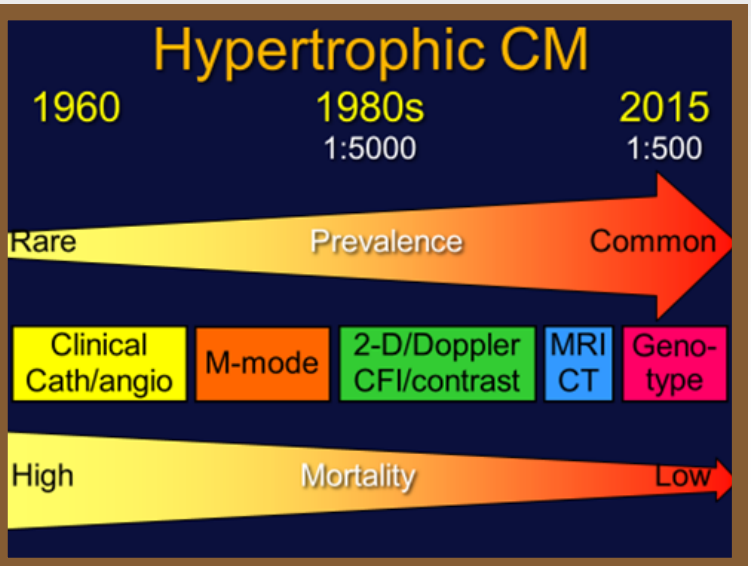
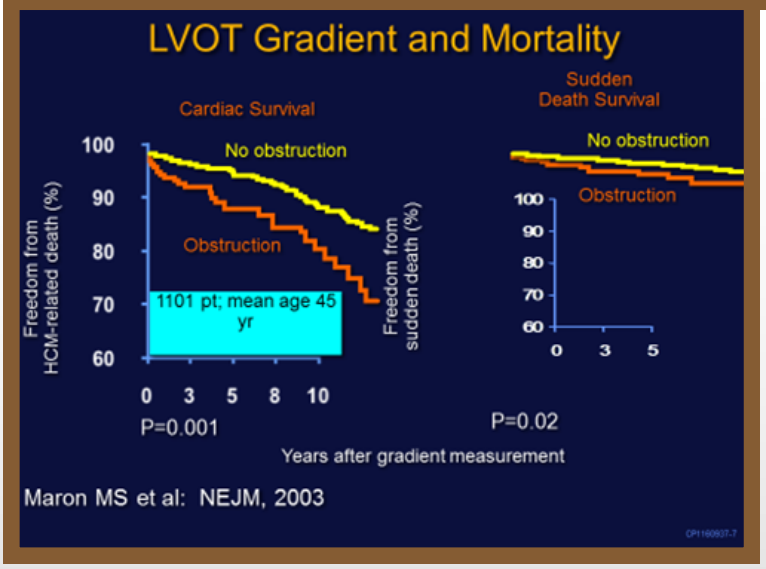
HIGHLIGHTS

B. Khandheria
USA

Hypertrophic cardiomyopathy: what has changed since 1960?

Prof. Khandheria from Wisconsin presented very interesting data on hypertrophic cardiomyopathy, a pathology characterised by a high degree of heterogenicity. Nowadays the diagnosis is made genetically, in the past it was only clinically based. This has enabled the diagnosis of a significantly greater number of patients, but has also modified the prognosis, passing from a high to a very low mortality rate. Genetic alterations at the basis of this pathology determine important alterations in the sarcomeres of myocytes which cause hypertrophy. Not all the forms of cardiomyopathy are the same in terms of outcome: the prognosis of patients who present a situation compatible with obstruction of the left ventricle is significantly worse than for patients without obstruction. Treatment too is strictly related to the different phenotypes in which the pathology is present and differs from pharmacological to surgical where, in particular and well-defined cases, the latter is resolutive and has a decidedly favourable prognosis. Lastly, from the point of view of prognosis, a decidedly unfavourable association is that with Obstructive Sleep Apnea Syndrome.





What is the most effective treatment strategy? - - - What are the most effective prevention strategies in the presence of hypertrophic cardiomyopathy?

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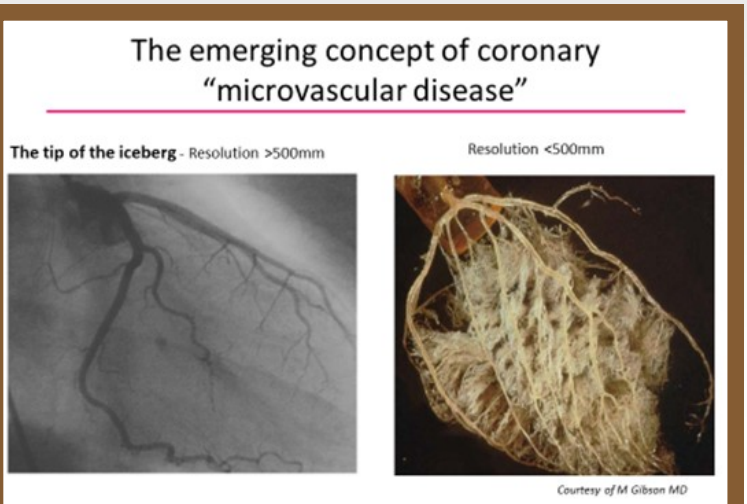
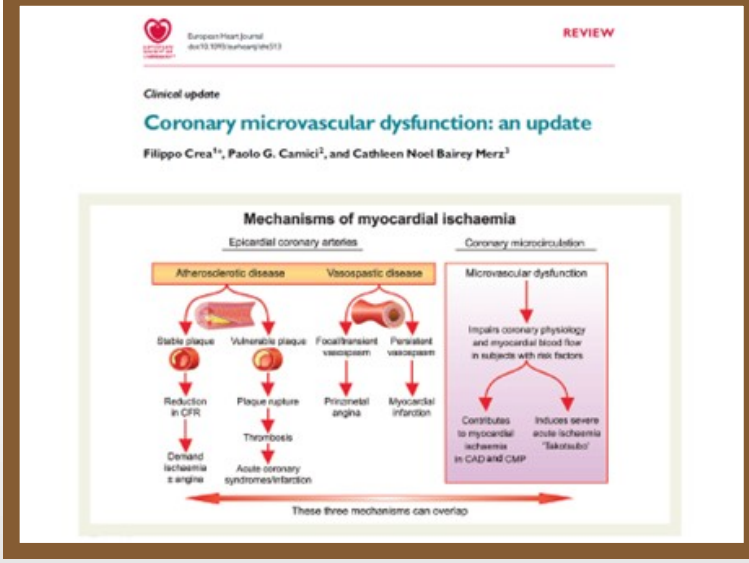
HIGHLIGHTS

P.G. Camici
Italy

Ischemic heart disease and dysfunction of cardiac microcirculation: two closely correlated phenomenons

The coronary vascular tree is classically represented by a series of relatively large blood vessels, as they appear in the angiograph. Nevertheless, this image is light years away from reality. The coronary vascular tree is in fact also characterised by a series of little vessels which, beginning with the larger coronary arteries, cover the cardiac tissue like an intricate forest, non visualised on the angiograph; the so-called "coronary microcirculation". Starting from this consideration, Prof. Camici from Milan addressed the theme of dysfunction of the coronary microcirculation, seen from different angles, both physiological and parapathological, and clinical. But, from a vascular point of view, what is the mechanism that determines dysfunction of the microcirculation? Not just one mechanism, but a series of mechanisms exist, mainly characterised by changes in vascular structure, such as intima media thickness with narrowing of the vascular lumen and functional alterations, responsible for the onset of ischemia of varying gravity. In general, functional lesions of the microcirculation are secondary to endothelial dysfunction. There is also a third mechanism, known as "extra vascular", determined by compression of the small vessels in the microcirculation, located in the cardiac wall, in those situations in which diastolic pressure remains excessively high, determining compression.





What are the main clinical conditions in which dysfunction of the microcirculation may be present? - - - How can dysfunction of the microcirculation by diagnosed?

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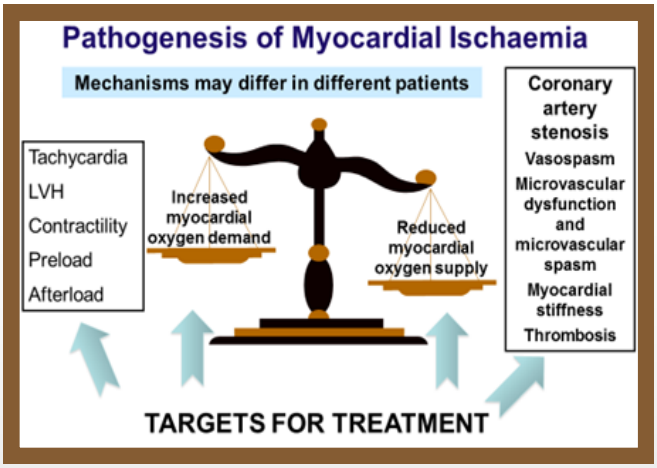
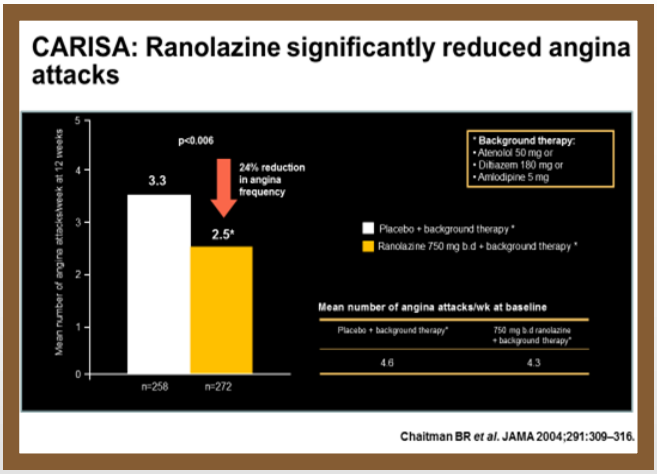
HIGHLIGHTS

J.C. Kaski
UK

How to manage Stable Chronic Angina: the role of new drugs

Stable Chronic Angina affects in particular people over the age of 65; it is common and disabling, the management of which, as Prof. Kaski from London maintains, currently presents wide margins for improvement. Not all patients suffering from stable chronic angina manage to benefit from the positive effects of treatment, either because they are too elderly or because they are not eligible for revascularization, due to the presence of adverse events related to pharmacological treatment or to the permanence of an anomalous vasomotor tone. In other cases a form of angina is present related to dysfunction of the microcirculation, responsible for the failure of painful symptomatology to remit even after CABG or PCI. It is therefore fundamental to prescribe treatment that will effectively affect the underlying pathogenetic mechanism. The pathogenesis of stable chronic angina is complex and above all differs from patient to patient. For this reason new specific drugs are on the market or under study for treating this pathology, each with different mechanisms of action. Among these we mention Ranolazine, a late sodium current inhibitor, especially indicated for patients suffering from stable angina who are insufficiently controlled or who do not tolerate first line anti-anginal therapies. Besides Ranolazine, Prof. Kaski presented data on studies conducted on other molecules, e.g.. Nicorandil and Trimetazidine.





What are the main pathogenetic means of angina caused by dysfunction of the microcirculation? - - - What are the effects of the new anti-anginal agents? - - - Are other molecules being studied?

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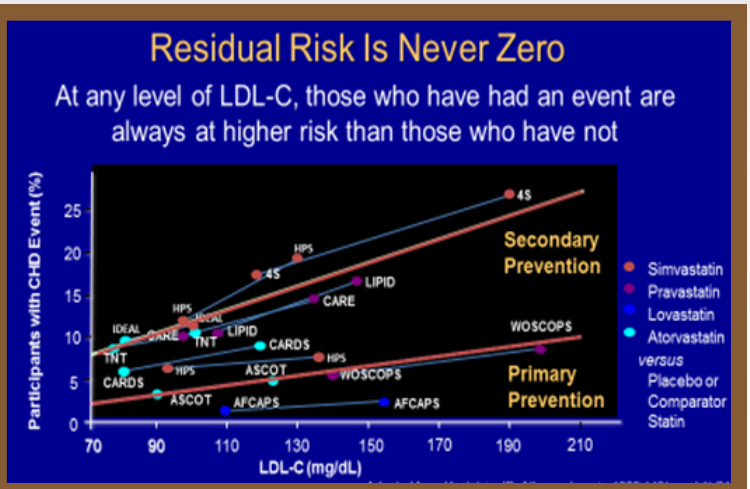
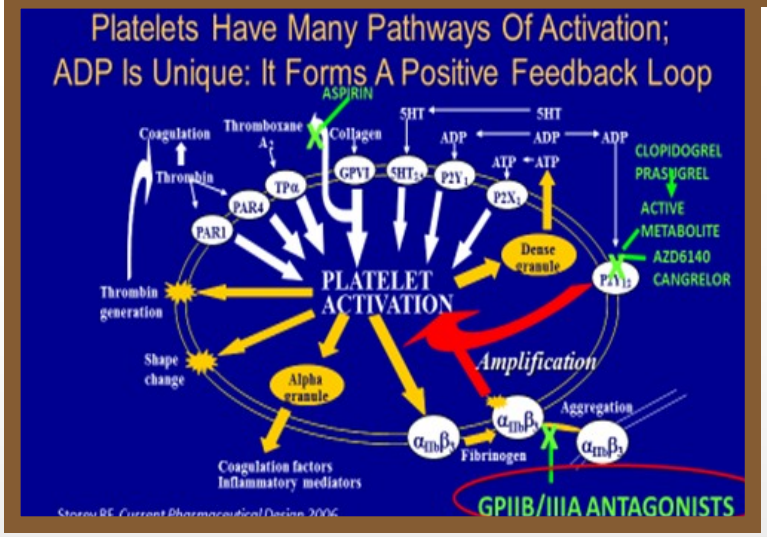
HIGHLIGHTS

A. De Franco
USA

Antiplatelet therapy in patients with coronary disease: state of the art

Prof. De Franco from Wisconsin introduced this important, albeit delicate subject, with the question: "How many of you would recommend to a patient, family member, or yourself, an antiplatelet therapy or even an aspirin after stenting?" The data collected from recent studies on the subject are, to say the least, contradictory. When should antiplatelet therapy be suspended after implanting a stent? Or even recommend aspirin-based





treatment for primary prevention? It should be remembered that there is a 15% increase in the risk of developing a myocardial event during the year following suspension of antiplatelet therapy. Another fundamental aspect concerns the fact that not all antiplatelet therapies are the same, in fact some drugs interact with various different receptors. But how long should treatment last? Less than a year or more than a year? How should the risk of bleeding in long-term anti-coagulant therapy be considered? In the case of triple therapy, does aspirin continue to play a role of primary importance? And, lastly, how does the patient react when faced with these drugs? In other words, are patients compliant with the therapy?

What are the results of major studies on patients being treated with antiplatelet drugs? - - - Is the effectiveness of this therapy in patients with stents consistent with that seen in those without stents? - - - What costs must the patient sustain in the event of using the new oral anticoagulants?

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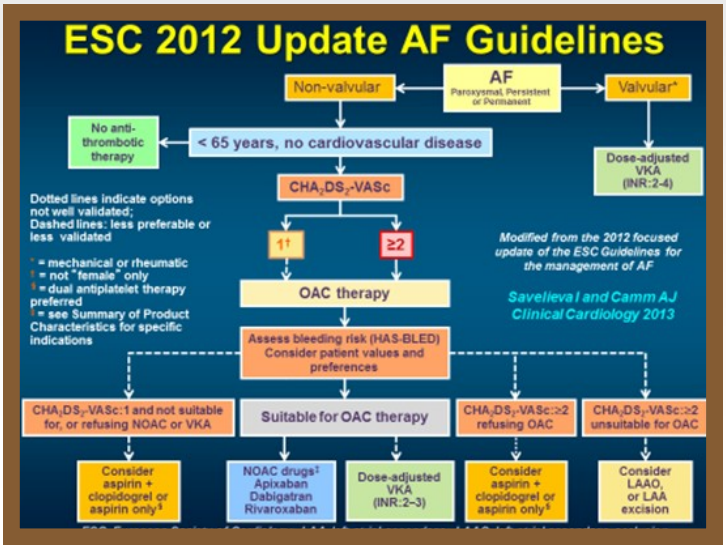
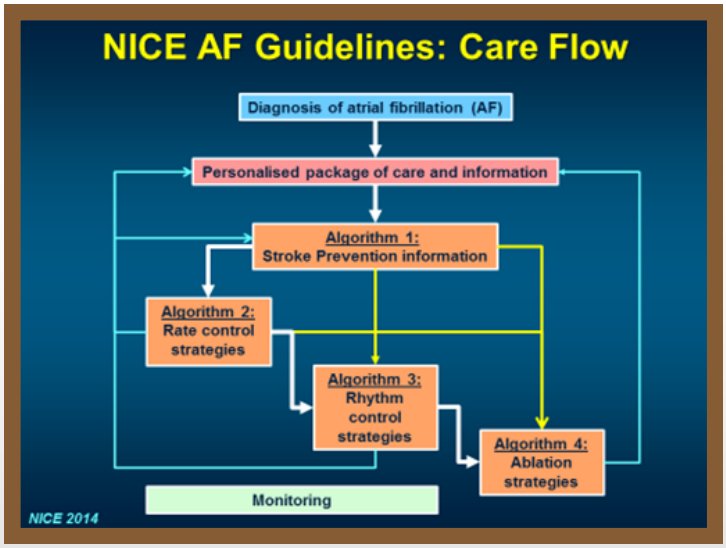
HIGHLIGHTS

J. Camm
UK

What is the position of the Guidelines in the management of Atrial Fibrillation?

Prof. Camm from London, tackled this subject, beginning with the fact that over the last 24 months at least 10 international guidelines on atrial fibrillation have been published. On the other hand, this theme is of primary importance if one considers that atrial fibrillation is responsible for 1% of the world's mortality rate. An initial aspect to be born in mind is that the guidelines are affected by the political and cultural context in which they are issued, for example in the United States they are closely related to decisions of the Regulatory Body, the FDA. In Europe, since there are still differences among the member countries it is more difficult to create unitary guidelines that reflect the state of the art present in all the countries. Lastly, again in Europe, unlike the United States, the guidelines are perceived more as a support to the physician's decision-making than as rules to be followed. The National Institute of Health guidelines are the only ones based on a cost/benefit evaluation. These divide the management of atrial fibrillation into three algorithms dedicated to: control of frequency, control of rhythm and ablative strategies. These three algorithms are at the core of medical discussion, since the results of trials conducted on the specific themes are often contradictory.





What drugs and what life-styles should be recommended? - - - When should ablation be chosen as elective treatment? - - - These are some of the problems on which Prof. Camm focused in his report.

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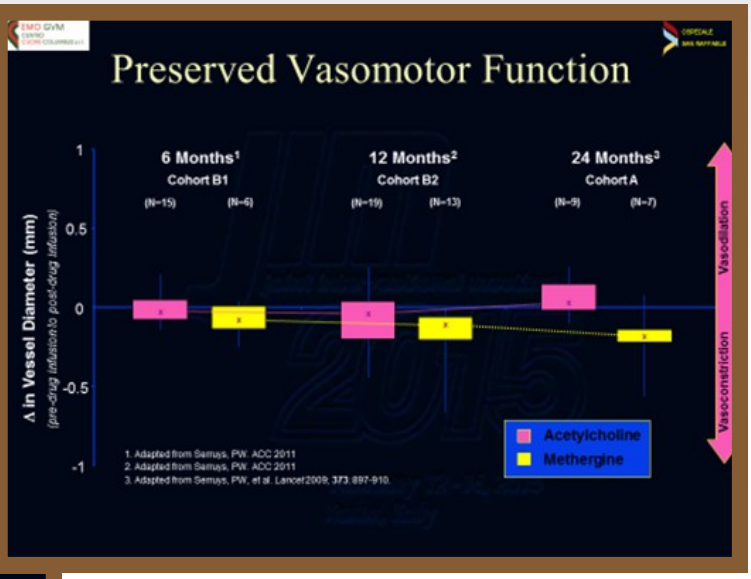
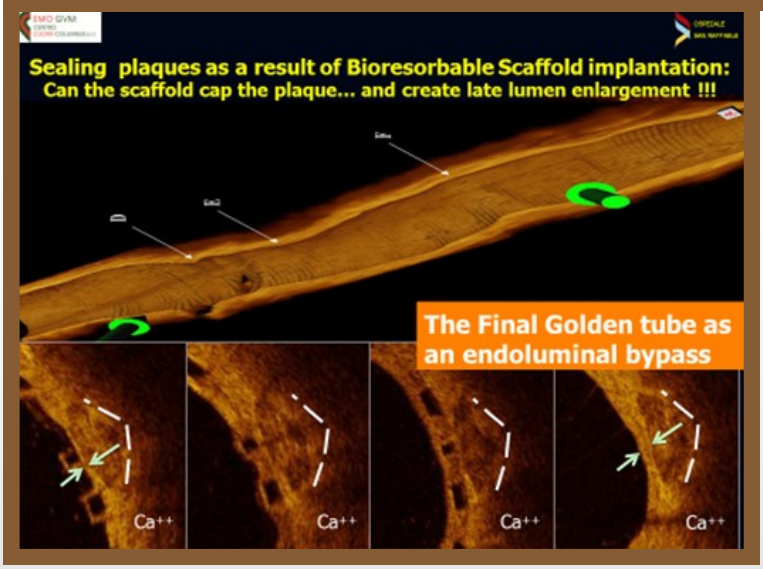
HIGHLIGHTS

A. Colombo
Italy

The absorbable stent: a concrete alternative to the traditional approach ?

Prof. Colombo spoke on absorbable stents, a new treatment option with a potentiality that still has to be expressed. The use of this new type of device offers some unquestionable advantages, for example: they facilitate treatment of restenosis, maintain the by-pass option open in the event of necessity, there are no stent-related inflammatory reactions, possibility of using this route to administer "in situ" drugs which cannot be administered systemically, lastly greater options in paediatric surgery. Other important aspects concern maintenance of the vasomotor function and the capacity to promote, during the following months, implant and reabsorption, a form of vascular remodelling which *de facto* determines a widening of the lumen. Prof Colombo presented personal data with which he demonstrated how this technique can be applied also to those cases which up until now have been considered solvable only by surgery or also with poor possibilities of success.





Are there any data on the incidence of a greater number of events in patients treated with these new stents? - - - What are the effects, at vascular level, of the application of these new devices?

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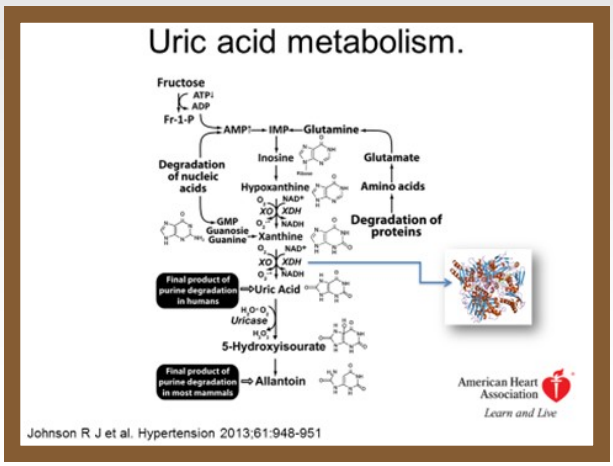
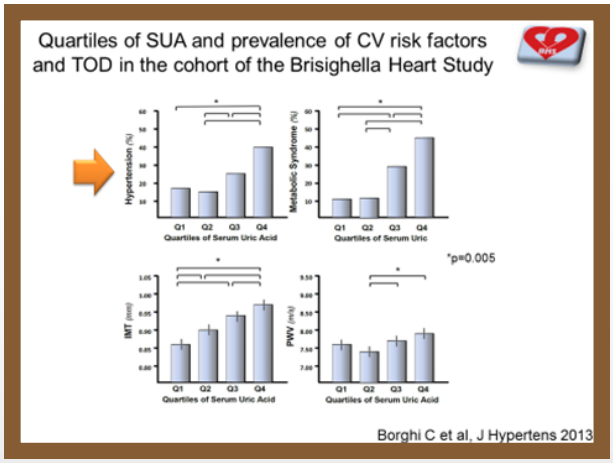
HIGHLIGHTS

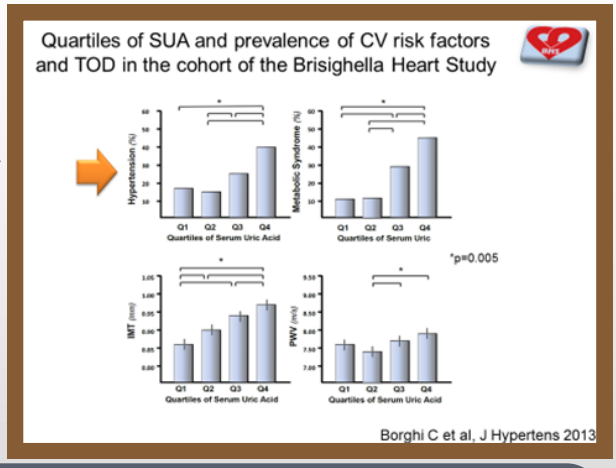
C. Borghi
Italy

Uric Acid and Hypertension: A new means of prevention?

Prof. Borghi from Bologna spoke on this decidedly innovative problem, even though the correlation between uric acid and hypertension has been known since 1975 when Prof. Bulpitt observed that 40-60% of hypertensive patients suffered from a state of hyperuricemia and 50% of patients suffering from gout were also hypertensive. The prevalence of hyperuricemia in the population is far greater than that of gout and this data are even more important since those involved are asymptomatic hyperuricemic subjects, suggesting that the connection between hyperuricemia and gout, while important, is surpassed by another connection, that between hyperuricemia, hypertension and cardiovascular disease. And this connection is gradually becoming more evident. Prof. Borghi presented a series of recently published data which show how the increase in cardiovascular risk factors, such as hypertension, BMI, total cholesterol, glomerular filtration, corresponds to a similarly significant increase in serum levels of uric acid. The reduction of uric acid in blood levels may contribute to the reduction of cardiovascular events in hypertensive patients. In addition, subjects suffering from hyperuricemia are destined to become precociously hypertensive compared with non-hyperuricemic subjects. Among the factors predicting development of hypertension in adulthood, the presence of hyperuricemia in adolescents is one of the most important. Similarly important is a correct diet, with a limited amount of fructose-rich drinks. But what are the effects of the pharmacological treatment of hyperuricemic states? The data produced are particularly interesting, the administration of Xanthine Oxidase inhibitors, of which Febuxostat is a valid representative, improve control of blood pressure and prevent vascular damage.







What is the intimate connection in terms of metabolism, between uric acid and cardiovascular disease? - - - What is the role of Xanthine Oxidase? - - - What studies are underway on Xanthine Oxidase inhibitors and what do they aim to demonstrate?

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HIGHLIGHTS

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