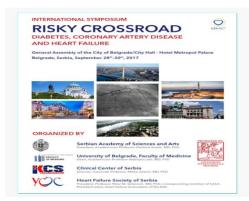
# International Congress RISKY CROSSROAD DIABETES, CORONARY ARTERY DISEASE AND HEART FAILURE

Belgrade, (RS), September 28th-30th, 2017 Highlights

#### Introduction



Prof. Seferović, chairman of the symposium, opened the congress, by highlighting the high scientific level of this meeting, focusing on risk crossroad on diabetes, coronary artery disease and heart failure, more in particular the speaker highlighted that this meeting has been dedicated to an update on diabetes, coronary artery disease and heart failure and their tight relationships, starting from epidemiology, through clinical findings, till to complications. The main topics discussed in this symposium were about

pathophysiology, molecular and translational findings, dysglycemia, risk evaluation and prevention, clinical aspects, diagnosis and treatment. The congress has been attended by many of the top researchers of this field coming from all the world and by many cardiologists and physicians, working on these topics.

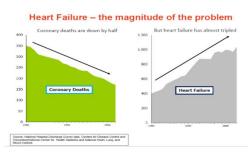
#### Acute heart failure and type 2 diabetes

**Heart Failure is a Worldwide Epidemic** 



Acute heart failure and type 2 diabetes, was the topic discussed by Prof. Filippatos in his lecture. The speaker, coming from Athens (GR), went deeper in his talk and presented very interesting data on epidemiology, by highlighting that those patients affected by glucose intolerance are at high risk of develop heart failure in the future. In the main part of his lecture, Prof. Filippatos, presented very interesting data on the burden of heart

failure, almost tripled from the 90<sup>th</sup> to 2015. More in particular the speaker talked about costs, survival rates and outcomes and highlighted that all these indices are quite poor. In the second part of his lecture, Prof. Filippatos presented very impressive data on the global burden of diabetes, pointing to the incredible number of estimated people with diabetes around the world: more than 600 million in the 2040. The speaker talked about



diagnosis and management of diabetic patients affected by HF, their clinical characteristics and outcomes. Finally, Prof. Filippatos presented very interesting data on the international registry

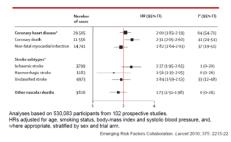


assessing medical practice with longitudinal observation for treatment of HF, on the main pathophysiologic mechanisms linked to female and male phenotypes and on therapy. In conclusion, the speaker pointed out that policy-makers, in order to prevent HF development in diabetic patients, urge to act on eight recommendations, where one of them concerns on the improvement of the patient education and support.

- What's about prevalence and incidence of Heart Failure by sex and age, based on the data presented by the speaker?
- What is the magnitude of the heart failure problem from the speaker point of view?
- What's about the global burden of diabetes, from the speaker point of view?
- What is the prevalence of diabetes in HF patients, based on the data presented by the speaker?
- What are the trends of diabetes prevalence among hospitalized HF patients, based on the data presented by the speaker?

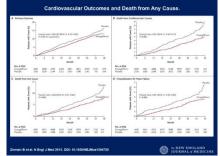
### Pharmacologic glycemic management and cardiovascular outcome trials: current status and future perspectives

#### Cardiovascular risk in diabetes



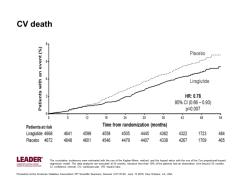
Prof. Lalić from Belgrade (RS), spoke about "Pharmacologic glycemic management and cardiovascular outcome trials: current status and future perspectives". Going deeper in his lecture, the speaker presented very interesting and impressive data on the cardiovascular risk in diabetic patients and talked about the CV risk related to

the established oral antihyperglycemics like metformin, Sus and TZDs.



In the main part of his lecture, the speaker presented very interesting data on the tight relationship between the glucose control and the reduction in the macrovascular disease incidence. More in particular Prof. Lalić talked about the main pharmacologic trials running in type 2 diabetic patients, treated with DPP-4 and SGLT2 inhibitors in order to find out

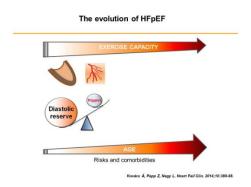
their effects on CVD and death. The speaker highlighted that SGLT2 inhibitors demonstrated



to be very effective in CVD prevention. Prof. Lalić, presented also very interesting data on the LEADR trial, where liraglitudine significantly reduced CV death, nonfatal myocardial infarction or non-fatal stroke but not hospitalization for heart failure in diabetic patients affected by CVD. Finally, the speaker pointed out that the American Diabetes Association has introduced empagliflozin and liraglutide as standards of medical care in patients with long-standing suboptimally controlled type 2 diabetes and established cardiovascular disease.

- What's about the CV risk and the main established oral antihyperglycemics, based on the data presented by the speaker?
- What is the relationship between glucose control and macrovascular disease, based on the data presented by the speaker?
- What's about the effect of empagliflozin cardiovascular outcomes and death, based on the data presented by the speaker?

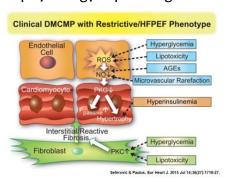
### Molecular and pathophysiological mechanisms of coronary artery disease/heart failure in type 2 diabetes



Molecular and pathophysiological mechanisms of coronary artery disease/heart failure in type 2 diabetes, was the topic Prof. Papp spoke about in his lecture. The speaker coming from Debrecen (HU), presented very interesting data on diastolic heart failure and more in particular he spoke about the pathomechanism of HF with preserved ejection fraction. In the main part of his lecture, Prof. Papp presented very interesting data on pathophysiology, pointing to the

importance of reserve in the onset of systolic and

diastolic heart failure. The speaker talked also about therapy and highlighted that in order to find a very effective treatment for patients affected by HF with preserved ejection fraction, phenotyping is crucial. In the second part of his lecture, Prof. Papp presented very interesting data on the correlation between diabetes, diabetic cardiomyopathy and HFpEF. More in particular, the speaker highlighted that at the basis of the diabetic cardiomyopathy there is a lot of



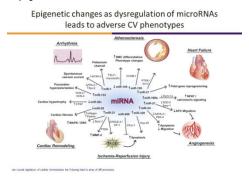
oxidative stress, the same in HFpEF and presented very interesting data on the NO-cGMP-PKG



pathway as a potential pharmacological target in HFpEF patients affected by diabetes. Prof. Papp presented also very interesting data given from clinical trials in HFpEF patients with type 2 diabetes treated with the phosphodiesterase-5A inhibitor vardenafil and other very interesting and innovative drugs pointing to other pharmacological targets in HFpEF patients. In conclusion, the speaker pointed out that the links between Type 2 diabetes and HFpEF may help to understand their nature.

- Is diabetic cardiomyopathy related to HFpEF, based on the data presented by the speaker?
- Does the type of diabetes matter in the pathophysiology of the diabetic cardiomyopathy, from the speaker point of view?
- What's about the pathophysiologic background of HFpEF, based on the data presented by the speaker?
- Can we mobilize the NO-cGMP-PKG pathway in HFpEF patients, based on the data presented by the speaker?
- What's about the effects of vardenafil in HFpEF patients with T2DM, based on the data presented by the speaker?

#### Epigenetic signature and coronary artery disease/heart failure in type 2 diabetes: a clinical perspective



"Epigenetic signature and coronary artery disease/heart failure in type 2 diabetes: a clinical perspective", was the topic discussed by Prof. Cosentino. The speaker, coming from Stockholm (SE) presented very impressive data, starting from the definition of epigenetics epigenomics. Going deeper in his lecture, Prof. Cosentino, talked about epigenome, pointing to the epigenomic landscape in different human cells. The speaker talked also about the link between genome and adverse CV

phenotypes. by the epigenetic highlighting the role played mechanisms in the gene expression leading to CVD and Diabetes. In the main part of his lecture, the speaker presented very interesting data on the effects of epigenetics in the development of these diseases starting from the miRNAs landscape in the diabetic heart. In the second part of his lecture, Prof. Cosentino talked about the link between inflammation and the diabetic vascular complications presented very interesting experimental data on the NF-kB signalling in diabetes. More in particular the speaker talked

Understanding NF-kB signalling in diabetes DIABETES NF-kB ?

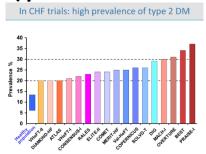
Glucose Fluctuations drive persistent epigenetic changes

about the role played by methyltransferase Se7 in the vascular disease phenotype in type 2 diabetic patients. Finally, Prof. Cosentino talked about the so called bad legacy effect of hyperglycemia responsible for the pathological circle activation between ROS and PKC  $\beta$  and the role played by p66shc. The speaker presented very interesting experimental data, demonstrating that type 2 DM is associated with an epigenetic remodelling in p66Shc, pointing to the role played by the glucose fluctuations in driving many epigenetic changes.

- What's about the differences between epigenetics and epigenomics, based on the data presented by the speaker?
- What is the functional impact of miRNAs in the development of CVD and diabetes, from the speaker point of view?
- What's about the role played by inflammation in the onset of the diabetic vascular complications, based on the data presented by the speaker?
- What's about the role played by p66<sup>shc</sup> for the development of the residual risk in type 2 diabetic patients, based on the data presented by the speaker?

To follow the presentations of this congress, click on the link below: http://www.fondazione-menarini.it/Home/Eventi/Risky-crossroad-diabetes-coronary-artery-disease-andheart-failure/Video-Slide ... and, after having logged in, enter in the multimedia area.

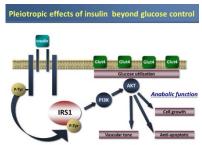
### Insulin resistance, coronary artery disease and heart failure in type 2 diabetes

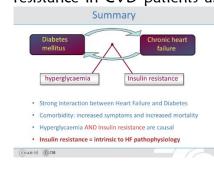


"Insulin resistance, coronary artery disease and heart failure in type 2 diabetes", was the topic discussed by Prof. Doehner in his lecture. The speaker, coming from Berlin (DE), talked about the tight relationship between diabetes and HF. Going deeper in his lecture, Prof. Doehner presented very interesting data on the

increasing prevalence of diabetes and HF and on their mutual interaction and aggravation. In the

main part of his lecture, the speaker talked about this interaction and presented very interesting data on their pathophysiological mechanisms. More in particular Prof. Doehner talked about the pleiotropic effects of insulin beyond the glucose control and presented very interesting data on the effects due to insulin resistance in CVD patients and on its pleiotropic actions. In the

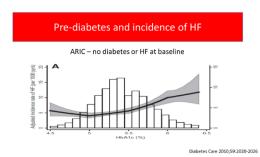




second part of his lecture, the speaker talked about the relationship between the impaired energy metabolism, poor muscle function and insulin resistance. More in particular Prof. Doehner presented very interesting data on the role played by the metabolic impairment and the inflammatory activation in the pathophysiology of HF and diabetes. In conclusion, the speaker pointed out that hyperglycemia and insulin resistance are casual, but the second one is very intrinsic to HF pathophysiology.

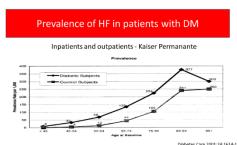
- What's about the interaction between diabetes and CHF, based on the data presented by the speaker?
- What is the pathophysiologic sequence of diabetes mellitus presented by the speaker?
- What are the pleiotropic effects of insulin beyond glucose control, based on the data presented by the speaker?
- What's about the relationship between insulin resistance and HF, from the speaker point of view?

#### Epidemiology and outcomes of heart failure and type 2 diabetes

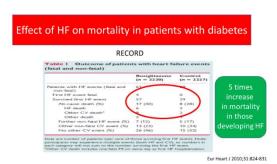


"Epidemiology and outcomes of heart failure and type 2 diabetes", was the topic of Prof. Petrie presentation. The speaker, coming from Glasgow (UK), talked about the so called "risky crossroad" characterized by the correlation between diabetes, coronary artery disease and HF. Going deeper in his lecture, Prof. Petrie presented very interesting data on diabetes

and HF incidence and prevalence and highlighted that both these to indices are increasing in men and women from 65 years old and over. In the main part of his lecture, the speaker presented very impressive data on the prevalence of diabetes in HF patients and on the effects of HF on mortality in diabetic patients and the ones due to diabetes in HF patients. The



speaker highlighted that mortality is almost doubled in these two populations. In the second



part of his lecture, Prof. Petrie talked about the effect of diabetes on the QoL in patients affected by HF, pointing to the very high incidence of hospitalization in these patients. In conclusion, the speaker pointed out that diabetes and HF are bed fellows and that it is time to understand the relationship between these two diseases and intervene with many trials of prevention and treatment.

- What's about the incidence and prevalence of the diabetic cardiomyopathy, based on the data presented by the speaker?
- What is the effect of pre-diabetes and the undiagnosed diabetes on mortality in HF patients, based on the data presented by the speaker?
- What's about mortality and other outcomes associated with diabetic cardiomyopathy, based on the data presented by the speaker?
- What is the effect of diabetes on HF hospitalizations in patients without HF presented by the speaker?

### Glucose abnormalities and coronary artery disease/heart failure: scope of the problem and diagnostic strategies

CV Death & Heart Failure requiring Hospitalization:
Diabetic vs. Non-Diabetic HF Patients
(CHARM-Program)

CHARM:
Iotal
10 7599 Pat.
NYHA II - V
Diabetes
n=2675 (28.5%)

Mex. Donati MR, Eur Heart J 2008; 28: 1224-1240

Prof. Standl coming from Munich (DE) spoke about "Glucose abnormalities and coronary artery disease/heart failure: scope of the problem and diagnostic strategies" and presented very interesting data on the correlation between hyperglycemia and

CAD in underdiagnosed patients. Going deeper in his lecture, the speaker talked about the impact of diabetes on

the outcomes of patients affected by HF and highlighted that the risk of heart failure increases a lot in the new diabetic patients. In the main part of his lecture, Prof. Standl presented a huge amount of data given from the main clinical trials

running in diabetic patients

UKPDS
Diabetes, Glucose, and CV
Disease

Diabetes (DM) is an established risk factor for CVD

In DM, higher glucose levels/HbA1c predict higher CV risk

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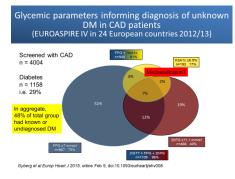
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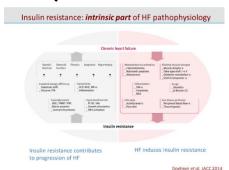
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affected by CVD. More in particular the speaker discussed the most important data on this topic published from the UKPDS, the SWEETHEART, the Euro Heart Survey diabetes studies and finally talked about the main diagnostic criteria for dysliglicemya and about the main glycemic parameters informing diagnosis of unknown diabetes in CAD patients. In conclusion, the speaker pointed out that CVD and DM are two sides of the same coin.

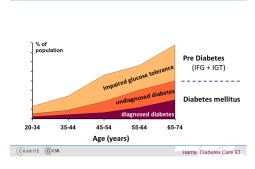
- What's about the correlation dysglycemia and coronary artery disease, based on the data presented by the speaker?
- What are the main diagnostic criteria for dysglycemia, from the speaker point of view?
- What are the main glycemic parameters informing diagnosis of unknown DM in CAD patients?
- What are the key topics of the Silent Diabetes Study, based on the data presented by the speaker?

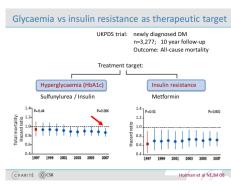
### Cardiovascular continuum: from insulin resistance to coronary artery disease/heart failure



Doehner from Berlin (DE), spoke "Cardiovascular continuum: from insulin resistance to coronary artery disease/heart failure" and presented very interesting data starting from the role played by insulin resistance as an intrinsic part of the HF pathophysiology. Going deeper in his lecture, the speaker talked about the prevalence of diabetic, non-diabetic and undiagnosed patients and presented very interesting data on the methods to be DM prevalence: diagnosed, undiagnosed and grey zone

applied for identifying patients affected by impaired glucose tolerance from those ones with undiagnosed diabetes. More in particular Prof. Doehner highlighted that all these insulin sensitive methods refer to glycemia only. In the main part of his lecture, the speaker presented very interesting data, demonstrating that insulin resistance is characterized by two different mechanisms in HFrEF and HFpEF patients. Speaking about hyperglycemia, Prof. Doehner presented very





interesting data on the value of HbA1c as risk marker in diabetic HF patients and highlighted that in many studies has been found an unclear association between HbA1c and mortality in CHF patients. Finally, Prof. Doehner talked about the role played by insulin resistance as therapeutic target and highlighted its role, by presenting very impressive data given by clinical trials running in diabetic HF populations. In conclusion, the speaker pointed out that the metabolic targets are the next frontier in HF therapy.

- What are the main insulin sensitivity assessment methods presented by the speaker?
- What's about the insulin resistance in HFrEF and HFpEF patients, based on the data presented by the speaker?
- What's about HbA1c as risk marker in diabetic HF patients, from the speaker point of view?
- What's about the empa-reg outcome study, based on the data presented by the speaker?
- What is the GLP2 inhibitor mode of action, based on the data presented by the speaker?

#### Pregnancy complications predict future cardiovascular disease and diabetes

Risk Factors for Cardiometabolic Disease in Women

- ▶ Hyperlipidemia
- ▶ Diabetes
- Obesity
- ▶ Cigarette smoking ▶ Physical inactivity ▶ Family history
- ▶ Hypertension ▶ Menopause
  - ▶ Hormonal contraceptives ▶ Hormone treatment
  - Reproductive life complicated by:
    - > PCOS
    - > Gestational diabetes > Hypertension in
    - pregnancy (preeclampsia)

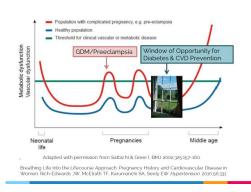
Prof. Seely from Boston (USA), spoke about "Pregnancy complications predict future cardiovascular disease and diabetes". More in particular, the speaker talked about the right time for obtaining a history to assess CVD risk in women. Going deeper in her lecture, the speaker presented very interesting data on the methods for recognizing pregnancy complications as cardiovascular risk factors and talked about the gestational diabetes in

pregnancy. ln the main part of her

lecture, Prof. Seely presented very interesting data on the recommendations for postpartum screening of women at high gestational diabetes risk. More in particular the speaker highlighted that gestational diabetes predicts risk for type 2 diabetes and CVD. In the second part of her lecture, Prof. Seely talked about preeclampsia and presented very interesting data given

Gestational Diabetes - After Pregnancy

- ▶ Resolves postpartum
- ▷Increases risk for future Type 2 DM (a CVR factor equivalent)
- ▷ May increase risk for CVD even independent of future DM

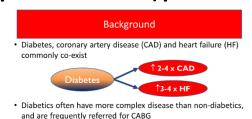


by many clinical trials, showing that this disease increases the risk of future cardiovascular disease. Finally, Prof. Seely, talked about the relationship between preeclampsia and future CVD death and presented very impressive data, demonstrating that women suffering from eclampsia within the 34 weeks of gestation are at higher risk of CVD death. In conclusion, the speaker pointed out that it is of high importance to screen women with prior GDM or preeclampsia for an effective prevention of type 2 diabetes and CVD.

- When obtaining a history to assess CVD in a woman, based on the data presented by the speaker?
- Can Type 2 DM be prevented in women with prior gestational diabetes, based on the data presented by the speaker?
- What are the main cardiometabolic prevention disease recommendations for women with prior GDM and preeclampsia, based on the data presented by the speaker?
- What's about the window of opportunity for diabetes and CVD prevention presented by the speaker?

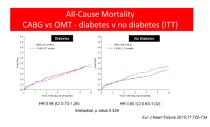
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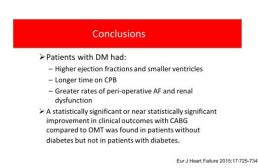
#### Coronary artery by-pass surgery as a treatment option in patients with type 2 diabetes



Prof. Petrie from Glasgow (UK), spoke about "Coronary artery by-pass surgery as a treatment option in patients with type 2 diabetes". More in particular, the speaker talked about the treatment options for CAD in patients affected by HF and diabetes. Going deeper in his lecture, the speaker talked about the pros and the cons of CABG in these patients and

presented very important and impressive data given from clinical studies like CASS, BARI 2D, FREEDOM and STICH trials. In the main part of his lecture, Prof. Petrie discussed the main data produced by these studies and more in particular he talked about the STICH trial and its subgroup composed by diabetic and HF patients. The data presented





by Prof. Petrie were very impressive, demonstrating that in people with diabetes CABG procedures compared to medical therapy did not present any benefit. In conclusion, the speaker pointed out that non-statistical significant effects have been found in diabetic patients underwent to CABG compared to medical therapy and that patients with diabetes do not have more to gain from CABG than patients with no diabetes

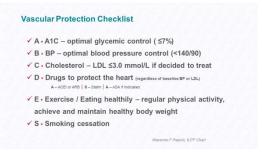
- What are the pros and the cons of CABG in DM and HF patients, based on the data presented by the speaker?
- Did the patients enrolled in these trials have diabetes and HF, from the speaker point of view?
- What's about CV mortality for CABG compared to medical therapy in diabetic and non-diabetic patients,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

### Coronary artery disease/heart failure risk assessment in patients with dysglycaemia

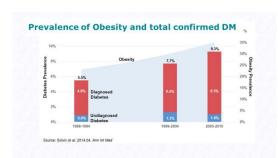


"Coronary artery disease/heart failure risk assessment in patients with dysglycaemia", was the topic discussed by Prof. Piepoli from Piacenza (IT), more in particular the speaker presented very interesting data on the total CV risk assessment. Going deeper in his lecture, Prof. Piepoli talked about the so called "key messages" like risk factor screening, total risk approach flexibility and risk estimation system. In

the main part of his lecture, the speaker presented very interesting data on the factors modifying score risks, through the discussion on main risk estimation charts. More in particular Prof. Piepoli talked about the risk factor goals and the target levels and about the vascular protection checklist. In the second part of his lecture, the speaker presented very interesting data on which patients should be tested for DM,



pointing to the ones with insulin resistance at cardiometabolic risk. More in particular Prof. Piepoli talked about the main criteria for testing DM in asymptomatic adult individuals and presented very interesting data on the main criteria for DM diagnosis. Finally, the speaker discussed about the use of blood glucose as the right screening method for identifying people



at risk of diabetes, pointing to the debate regarding whether the screening for fasting glucose is sufficient or whether an oral glucose tolerance test is needed and presented the main recommendations for the prevention of DM. In conclusion, Prof. Piepoli pointed out that for a very effective prevention a global approach, including the risk factor control, healthy life style and population level intervention are crucial.

- Who will benefit from prevention and when and how to assess risk and prioritize, based on the data presented by the speaker?
- Which patients should be tested for DM, from the speaker point of view?
- What's about the prevalence of obesity and total confirmed DM, based on the data presented by the speaker?
- How to assess the CV risk in DM patients, based on the data presented by the speaker?
- What are the main interventional strategies in patients affected by diabetes and CVD, from the speaker point of view?

#### Imaging screening in coronary artery disease/heart failure in type 2 diabetes

2. Stress echo for viability: how?

Rest Low-dose High-dose

Viable myocardium

Ischemic myocardium

Scar

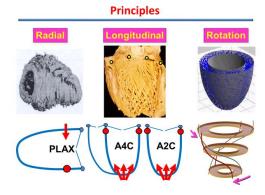
Viability = 3 (5) segments with "biphasic" response.

Sicari et al. Stress echo consensus. Eur Heart J 2009

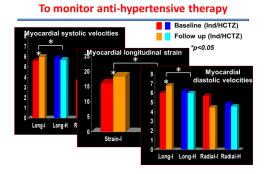
"Imaging screening in coronary artery disease/heart failure in type 2 diabetes" was the topic of Prof. Vinereanu presentation. The speaker, coming from Bucharest (RO), presented very interesting data starting from the main indications of echocardiography in type 2 diabetic patients with or without CAD. Going deeper in his lecture Prof. Vinereanu talked about the stress

echo application in DM patients, more in particular

on the choice between exercise or dobutamine. In the main part of his lecture, the speaker presented very interesting data on when why and how to perform stress echo for the diagnosis of ischemia. In the second part of his lecture, the speaker talked about the application of Echo in type 2 DM patients with or without subclinical LV dysfunction and presented very interesting data on the main mechanisms leading to LV



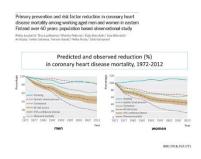
dysfunction and on the application of echocardiography in the early diagnosis and in



monitoring treatment. Talking about monitoring treatment the speaker presented very interesting data on a method characterized by the detection of the myocardial systolic and diastolic velocities and of the myocardial longitudinal strain, able to monitor an antihypertensive therapy. In conclusion, Prof. Vinereanu pointed out that these new techniques may be used for guiding and monitoring treatment in type 2 diabetic patients.

- When to use the dobutamine test for the screening of ischemia, from the speaker point of view?
- When and why stress echo should be used for viability, from the speaker point of view?
- What's about speckle tracking echocardiography, based on the data presented by the speaker?
- What are the main mechanisms leading to LV dysfunction starting from DM, based on the data presented by the speaker?
- What are the key points of the LV dysfunction early diagnosis by echocardiography, from the speaker point of view?

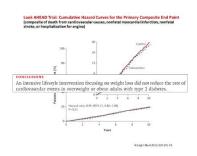
### Long-term intensive lifestyle interventions in coronary artery disease/heart failure in type 2 diabetes

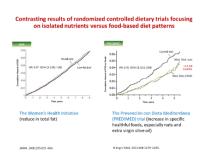


The main topic of Prof. Lalić presentation was "Long-term intensive lifestyle interventions in coronary artery disease/heart failure in type 2 diabetes". The speaker, coming from Belgrade (RS), presented very interesting data on the risk factors goals and target levels, by highlighting the role played by diet and physical

activity. Going deeper in her lecture, Prof. Lalić, talked about the main intervention strategies for

diabetes and hypertension management. In the main part of her lecture, the speaker presented very interesting data given from epidemiological studies on the primary prevention and risk factor in CHD patients and highlighted the role played by the LDL reduction in CHD mortality. In the second part of her lecture, Prof. Lalić, talked about the cardiovascular effects of an intensive





lifestyle intervention in type 2 diabetic patients and presented very interesting and impressive data on the effect of the body weight reduction without a particular attention to foods on the rate of death for CVD. Prof. Lalić, talked also about the importance of the right choice of the type of food for an effective CVD prevention. Finally, the speaker presented very impressive data given from the PURE study, where saturated fats showed to be not harmful for a well-established CVD prevention.

- What's about the contrasting results of randomized controlled dietary trials focusing on isolated nutrients versus food-based diet patterns, based on the data presented by the speaker?
- What's about the risk of mortality and major CVD by % energy from types of fat, based on the data presented by the speaker?
- What are the key topics of the comparison of the dietary effects of carbohydrate and fat on dysliproteinemia, from the speaker point of view?
- What's about the correlation between saturated fatty acids and the rate of CVD, based on the data presented by the speaker?

#### Glucose control and optimal glucose targets in patients with coronary artery disease/heart failure in type 2 diabetes



Prof. Standl from Munich (DE), spoke about "Glucose control and optimal glucose targets in patients with coronary artery disease/heart failure in type 2 diabetes" and presented very interesting data starting from the paradigm of the multifactorial management in diabetes. Going deeper in his lecture, the speaker highlighted that the glycemic control is only one of the components to be controlled for an effective management of the diabetic

patients. In the main part of his lecture, Prof. Standl talked about the cardiovascular targets and the related cardiovascular risks and presented a huge amount of data given from the main clinical trials running in diabetic patients on the CV outcomes. The speaker presented other very interesting data on the CV outcome trials in diabetes started since the 2012 and highlighted that a new era is coming, thanks to the new glucose lowering drugs coming on the market.

Glycaemic Control - Individualized Care

Less strict & wider range of HbA1c goals

• HbA1c <53 mmol/mol (7.0%)

• HbA1c 42—48 mmol/mol (6.0–6.5%)
in selected (UKPDS like) patients with

- short disease duration

- long life expectancy

- no significant cardiovascular disease

• HbA1c <58–64 mmol/mol (7.0-8.0%)
in elderly patients with

- long-standing and/or complicated disease

• All targets to be achieved without

- hypoglycaemia or other adverse effects

Care (EASC: UK)

Eur Heart 1/D33 34 (39): 3035-3087

More in particular Prof. Standl talked about the SUSTAIN 6, LEADR, CANVAS AND EXSCEL trials, their effects on the reduction of HbA1c and on the CV events. In the second part of his



relationship between hypoglycemia and cardiovascular risk, given by registry studies and clinical trials. Finally, Prof. Standl talked about therapy and presented very interesting data on the key classes of the glucose-lowering drugs for type 2 diabetic patients affected also by CVD and HF. In conclusion, Prof. Standl pointed out that in type 2 daibetic patients it is of high importance to promote a multifactorial therapy leading to the control of hypertension, dyslipidemia, abnormal blood platelet function and

lecture, the speaker presented very interesting data on the

hyperglycemia.

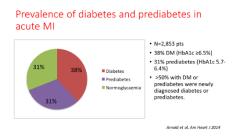
- What are the key points of the multifactorial managements of diabetic patients, for the speaker point of view?
- What are the effects of Canagliflozin on CV, Renal, Hospitalization, and Death Events, based on the data presented by the speaker?
- What are the key points of the individualized care in glycemic control presented by the speaker?
- What's about the correlation between Hypoglycaemia and Cardiovascular Risk, based on the data presented by the speaker?
- What are the 2017 ADA medical standards of medical care for diabetic patients presented by the speaker?

### Screening of glucose metabolism impairment in coronary artery disease/heart failure

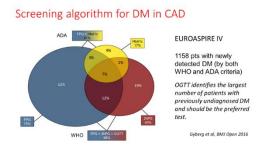


"Screening of glucose metabolism impairment in coronary artery disease/heart failure", was the topic discussed by Prof. Farmakis from Athens (GR). More in particular the speaker presented very interesting data starting from the key issue on the need for screening in diabetes mellitus patients. Going deeper in his lecture, Prof. Farmakis presented very impressive data on the burden of diabetes

due also to the difficult to perform an early diagnosis for the lack of symptoms at the beginning of this disease. In the main part of his lecture, the speaker talked about the correlation between diabetes and CVD disease and presented very interesting and impressive data on the prevalence of diabetes and prediabetes in acute MI and HF patients. Prof. Farmakis presented also other very



impressive data demonstrating that diabetes worsens the prognosis of CAD, HF and other CVDs. In the second part of his lecture, the speaker presented very interesting data on the methods to be applied for screening, like FPG, OGTT and HbA1c and the indications of the main international medical associations on diabetes for DM diagnosis. Prof. Farmakis pointed



out that the prevalence of the main glucometabolic disorders changes based on the test applied and presented the different screening algorithms proposed by the international medical societies on diabetes. In conclusion, Prof. Farmakis pointed out that screening for glucose metabolisms disorders in CAD and HF is important and if FPG and HbA1c are below the DM thresholds, OGTT should be used.

- Why do we need screening, based on the data presented by the speaker?
- What method should we use for screening, from the speaker point of view?
- What is the main problem of diabetes from the prevention point of view, based on the data presented by the speaker?
- What are the effects of the diabetes therapy on HF, based on the data presented by the speaker?
- What's about the screening algorithm for patients affected by diabetes and CAD, based on the data presented by the speaker?

### Diagnostic aspects of coronary artery disease/heart failure in type 2 diabetes



Prof. Khandheria from Milwaukee (USA), spoke about "Diagnostic aspects of coronary artery disease/heart failure in type 2 diabetes". More in particular, the speaker started his lecture with the presentation of two clinical cases, the first one a 72-year-old female affected by DM and chest pain

with some abnormalities in contraction but with normal EF and global cardiac function. Prof.

Khandheria pointed out that even those patients with apparently well controlled diabetes tend to worsen their cardiac functions and the new imaging techniques like strain and strain rate imaging are able to detect these preliminary findings. The second patient was a 62-year-male, affected





by type 2 diabetes, in treatment with an oral agent and with a HbA1c of 6.8, but with reduced ejection fraction, dilated atrium and global ventricular dysfunction. The speaker highlighted that global longitudinal strain is very effective in detecting systolic dysfunction, more in particular in those diabetic patients with albuminuria. Finally, the speaker talked about stress echocardiography, by highlighting that it is a very effective test for the prediction of mortality in patients with diabetes and known or suspected coronary artery disease.

- What's about multiple imaging modalities for diabetes and heart disease diagnosis, from the speaker point of view?
- What are the predictive factors of the diastolic function deterioration in type 2 diabetic patients, based on the data presented by the speaker?
- What's about the cure, from the speaker point of view?
- What's about the use of stress echocardiography to predict mortality in diabetic patients with CHD, based on the data presented by the speaker?

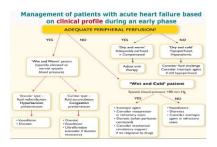
#### Acute coronary syndrome/acute heart failure in type 2 diabetes



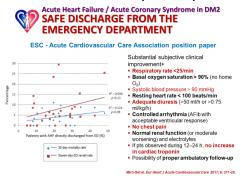
"Acute coronary syndrome/acute heart failure in type 2 diabetes", was the topic discussed by Prof. Ristić from Belgrade (RS), more in particular the speaker talked about the main factors triggering acute heart failure. Going deeper in his lecture, Prof. Ristić presented very interesting data on the role played by acute hyperglycemia on the inhibition of the

endothelial function. In the main part of his lecture, the speaker talked about the

atypical symptoms referred by many diabetic patients, mostly women, responsible for the onset of acute heart failure or acute coronary syndrome and presented very interesting clinical and imaging data given from such patients. In the second part of his lecture, the speaker talked about the acute heart failure management and on one of the worse complications like the



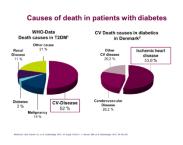
cardiac arrest. The speaker presented also very interesting data on the antithrombotic therapy



before performing PCI and on the fibrinolytic therapy. In the last part of his lecture, Prof. Ristić talked about the management of hyperglycemia in symptomatic HFrEF patients, more in particular he presented very interesting data on the management of oral therapy and on the safe discharge from the emergency department. In conclusion, Prof. Ristić pointed out that time is essential in the management of acute coronary patients but also of the ones affected by acute heart failure.

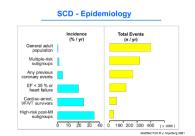
- Why there is a very high mortality for acute heart failure and acute coronary syndrome in DM2 patients, based on the data presented by the speaker?
- What are the main symptoms based on the data presented by the speaker?
- What are the main predictors of mortality for patients affected by acute heart failure, presented by the speaker?
- What's about the recommendations on pharmacotherapy for the management of patients with acute heart failure, from the speaker point of view?

#### Arrhythmias/sudden cardiac death in coronary artery disease and heart failure in type 2 diabetes



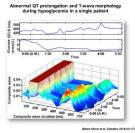
Prof. Mitrović from Bad Neuheim (DE), presented very interesting data on "Arrhythmias/sudden cardiac death in coronary artery disease and heart failure in type 2 diabetes". Going deeper in his lecture, the speaker talked about the

epidemiology of diabetes and highlighted that this disease is suspected to be a high-risk condition for SCD. In the main part of his



lecture, Prof. Mitrović presented very interesting data on SCD definition, magnitude of the problem and causes. In the second part of his lecture, the speaker talked about the relationship between HF, diabetes and SCD and presented very impressive

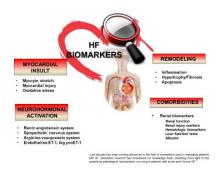
data on the arrythmogenic causes of SCD. More in particular Prof. Mitrović presented very



interesting data on the main mechanisms of arrhythmia leading to SCD in diabetic patients. Finally, the speaker talked about the main ECG alterations in diabetic patients and presented very interesting data on the QT-interval alterations, like the long QT-interval, one of the main causes of SCD. In conclusion, Prof. Mitrović pointed out that diabetes is associated with an increased risk of arrhythmias and SCD.

- What's about the main causes of death in patients with diabetes, based on the data presented by the speaker?
- What are the main arrhythmogenic causes of sudden cardiac death, based on the data presented by the speaker?
- What are the major ECG-changes in Diabetes, presented by the speaker?

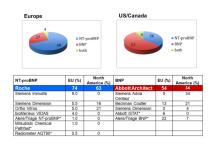
#### Old and new biomarkers in the diagnosis of heart failure



Prof. Stanković from Belgrade (RS), spoke about "Old and new biomarkers in the diagnosis of heart failure" and presented very interesting data on prevalence and incidence of HF around the world. Going deeper in her lecture, Prof. Stanković pointed out that survival remains poor and very similar to that one of cancer. In the main part of her lecture, the speaker presented very interesting data on the expected

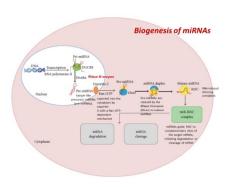
increase of its burden, due to the increase in incidence

of diabetes and hypertension. More in particular Prof. Stanković talked about diagnosis, pointing to the difficult to perform a right and early diagnosis due to the very high complexity of this disease, and presented very interesting data on the main biomarkers connected to HF. The speaker presented other very interesting data on their utility starting from the Natriuretic Peptides and their application in Europe, USA and Canada, pointing to the differences



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between pro-BNP, BNP and NTpro-BNP. Prof. Stanković talked also about the interactions



of other organs like the kidney, who can modify the NP values as well as their variations due to the EF levels. In the second part of her lecture, the speaker presented other very interesting data on new markers like the MMp-4, MMp-8 and 9, mainly connected with the atherosclerotic processes and more suitable for the detection of the diastolic alterations. Finally, Prof. Stanković, talked about the microRNAs associated with myocardial fibrosis in HFpEF patients and presented very interesting data on their biogenesis.

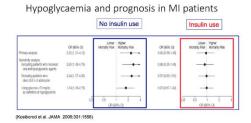
- What biomarkers are good for, based on the data presented by the speaker?
- What is the role of biomarkers in the HF prevention, based on the data presented by the speaker?
- What is the correlation between MMPs and diastolic function, based on the data presented by the speaker?
- What are the main characteristics of the mRNAs as biomarkers for the early detection of HFpEF, presented by the speaker?

## Antihyperglycemic treatment in acute coronary syndrome/optimal medical treatment of chronic coronary disease in type 2 diabetes

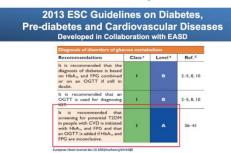
"Antihyperglycemic treatment in acute coronary syndrome/optimal medical treatment of chronic coronary disease in type 2 diabetes", was the topic discussed by Prof. Rosano from London (UK), more in particular the speaker talked about acute coronary syndromes and Post-ACS. Going deeper in his lecture, Prof. Rosano presented very interesting data on the differences in glucose

handling, that represents a problem for the very high number of variables for the right glucose levels detection. In the main part of his lecture, the speaker highlighted that the poor

prognosis of ACS patients with diabetes is basically related to two main issues, the first one about the low intervention rate of these patients compared to the non-diabetics and the second one about the bed outcome also in case of intervention. Prof. Rosano, pointed to the importance of hyperglycemia but also of hypoglycaemia for the worse outcome of ACS, diabetic patients. In the second part of his lecture, the speaker



presented very interesting data given from the DIGAMI 1 and 2 studies, with the intention to well define the hypoglycaemic treatment in the ACS setting. Prof. Rosano talked also about



the right cardiovascular treatments for such these patients, like the aldosterone blockers and about the newer hypoglycaemic medications like lixisenatide and DPP4 inhibitors. In conclusion, Prof. Rosano pointed out that the intense glucose control by insulin lowers mortality in patients with high HbA1c levels and that OGTT can reveal a high proportion of patients with glucose abnormalities at risk for new events.

- What's about mortality in patients with ACS, based on the data presented by the speaker?
- What's about admission glucose as risk factor after MI from the speaker point of view?
- What's about the relationship between hypoglycaemia and prognosis in MI patients, based on the data presented by the speaker?
- What are the main results of the DIGAMI 1 study presented by the speaker?
- Is Infusion or long-term insulin important, based on the data presented by the speaker?

#### Percutaneous interventions in the treatment of coronary artery disease in type 2 diabetes



Prof. Allaqaband from Milwaukee (USA), spoke about "Percutaneous interventions in the treatment of coronary artery disease in type 2 diabetes" and presented very interesting data starting from the evolving landscape of diabetes and the rise in the risk of cardiovascular death in diabetic patients. Going deeper in his lecture, Prof. Allaqband, pointed out that diabetic patients with prior MI have the highest

and presented very interesting data on the risk of cardiovascular events and death due to diabetes. In the main part of his lecture, the speaker talked about the pathophysiology of atherosclerosis in diabetic patients and presented very interesting data on the coronary revascularization in these patients. More in particular Prof. Allagband, starting from the data

Diabetes adversely effects various biochemical processes leading to dysregulation of nici coste biology, increased levels of one-sethifted largh acids, changes in ploporotion relations, increase in advanced glycation end products, increase in systemic inflammation, aberrari leucocyte-endothelial interactions and increased propensity for thrombosts among others.

Endothelial Dysfunction

Diabetic Dyslipidemia

Prothrombotic Milleu

How does Diabetes alter the Presentation of Coronary Artery Disease?

More oxtensive atherosclerosis and diffuse multivessel disease.

More total occlusions and longer lesions with greater plaque burden Higher incidence of left main disease

Silent is chemialMi

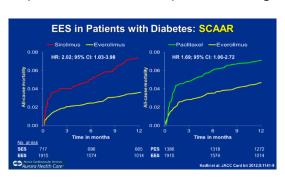
Accelerated disease progression

Worse outcomes despite revascularization

of the BARI

CHD

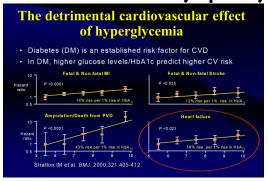
risk



study, till the FREEDOM trial, presented a huge amount of data related to the comparison between diabetic and non-diabetic patients who underwent to revascularization. Finally, he pointed out that most patients affected by diabetes can undergo stenting with favourable outcomes and that CABG should be reserved for very complex anatomy, in patients in otherwise good health.

- How does diabetes alter the presentation of CAD, based on the data presented by the speaker?
- What's about Cardiovascular Deaths due to Obesity & Diabetes, based on the data presented by the speaker?
- What is the CHD Risk following a Myocardial Infarction in diabetic patients, based on the data presented by the speaker?
- What's about PCI vs CABG in diabetic patients, based on the data of the BARI study presented by the speaker?

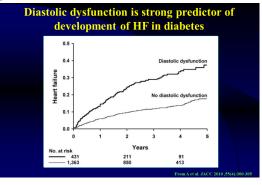
Diabetic cardiomyopathy



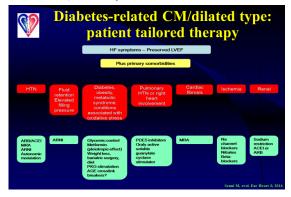
"Diabetic cardiomyopathy" was the topic discusses by Prof. Seferović. The speaker, chairman of the symposium, presented very interesting data on the detrimental cardiovascular effect of hyperglycemia and on CAD presentation in diabetics characterized by a multivessel diffuse and several findings. Going deeper in his lecture, Prof. Seferović talked about the coronary microcirculation in diabetics and about prevalence and incidence of HF in these patients. The speaker presented very interesting data on the so

called "cardiovascular continuum", pointing to the tight correlation between diabetes and

the microvascular complications like in the diabetic cardiomyopathy. In the main part of his lecture, Prof. Seferović talked about the relationship between the left ventricular diastolic dysfunction and the progression of diabetes and presented very impressive data on its role as strong predictor of the development of HF in diabetic patients. In the second part of his lecture, the speaker presented very interesting data on the diabetic cardiomyopathy and on its mechanisms leading to the myocardial



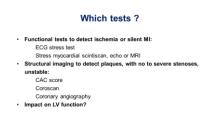
remodelling and dysfunction affecting these patients. Prof. Seferović talked also about pathophysiology and presented very interesting data on the pathophysiological mechanisms affecting the diabetic patients with cardiomyopathy and HF with preserved but also reduced EF. Finally, the speaker talked about the clinical presentation of the diabetic cardiomyopathy



and about therapy, tailored on the specific characteristics of any patient. More in particular the speaker presented very interesting data given from the main clinical trials running in diabetic patients treated with the newer drugs. In conclusion, Prof. Seferović, pointed out that diabetic cardiomyopathy is a very complex disease and in order to improve the outcome of these patients it is necessary more cooperation among physicians of different specialities.

- What is the detrimental cardiovascular effect of hyperglycemia, based on the data presented by the speaker?
- What are the main characteristics of the coronary microcirculation in diabetes, presented by the speaker?
- Is there a correlation between LV diastolic dysfunction and mortality in diabetes, from the speaker point of view?
- What are the mechanisms contributing to myocardial remodeling and dysfunction in diabetic cardiomyopathy, presented by the speaker?

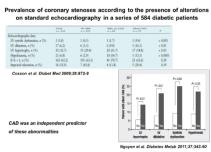
### Silent ischemia in coronary artery disease/heart failure in type 2 diabetes: frequent and ominous



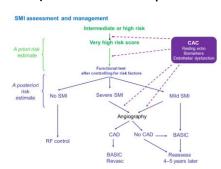
Prof. Valensi from Paris (FR), spoke about "Silent ischemia in coronary artery disease/heart failure in type 2 diabetes: frequent and ominous". More in particular, the speaker talked about the prevalence of the silent coronary ischemia, its predictive value, its relationship with heart failure and finally about which patients should be screened for silent ischemia and how. Going deeper in his lecture, Prof. Valensi talked also about the main points characterizing the coronary status, like

the possible presence of any

atheroma and stable or unstable plaques and presented very interesting data on the main tests able to detect these features. More in particular the speaker presented many data on the myocardial perfusion scintigraphy application in diabetic patients referred for CAD evaluation and on the use of CT scan for the same purpose. In the main part of his lecture Prof. Valensi talked about the predictive value of the silent coronary disease and presented very interesting



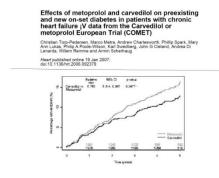
data given from the French multicentre study, showing that the patients with the highest CV event rate were those ones affected by silent coronary stenosis. Talking about the relationship between silent coronary disease and HF, the speaker presented very interesting data given from many clinical trials and highlighted that silent CAD may account for several cases of HF. Finally, Prof. Valensi presented other very interesting data, pointing to the people to be



screened for silent ischemia and on the tests to be performed. More in particular the speaker talked about the guideline recommendations on the patients to be screened for and about the SMI assessment and management, by highlighting the role played by CAC score in this setting. In conclusion, Prof. Valensi pointed out that the SMI screening should be concentrated on patients at very high risk and that these patients should be treated more aggressively for their risk factors.

- Which patients should we screen for silent ischemia and how, based on the data presented by the speaker?
- which patients should we screen and using which tests, from the speaker point of view?
- What is the predictive value of the silent myocardial ischemia, based on the data presented by the speaker?
- Is there any correlation between silent coronary disease and HF, based on the data presented by the speaker?
- Is there a correlation between the problematic use of internet and the suicidal behaviour, based on the data presented by the speaker?

#### Pharmacological management of heart failure in type 2 diabetes



"Pharmacological management of heart failure in type 2 diabetes", was the topic discussed by Prof. Metra from Brescia (IT), more in particular the speaker talked about diabetic cardiomyopathy and HF. Going deeper in his

lecture, Prof. Metra presented very interesting data on the increasing risk of HF in the patients affected by diabetes. In the

Combined AT<sub>1</sub> Receptor Neprilysin Inhibition (ARNI) for the treatment of Heart Failure

LCZ696

Sacubitril valsartan

Natriuretic peptides
BK, ADM, Subst.P,
VIP, CGRP

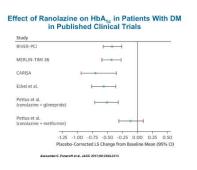
Vasodilation
Diuresis – natriuresis Inhibition of hypertrophy fibrosis
Pogradation
Products
Neprilysin

Vasoconstriction
Sodium-water retention
Products
Neprilysin

Neprilysin

Vasoconstriction
Sodium-water retention
Products

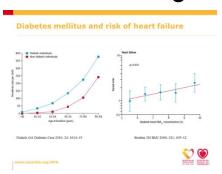
main part of his lecture, the speaker talked about the therapeutic algorithm for diabetic patients affected by symptomatic HF, more in particular the one with reduced EF and presented very interesting data on beta-blockers,



mineralocorticoid antagonists, renin-angiotensin antagonists and finally on metabolic therapy. Prof. Metra presented a huge amount of data given from the major clinical trials running in diabetic patients affected by HF. In conclusion, the speaker pointed out that the use of beta-blockers can increase the rate of hypoglycaemia, the AT1 receptors neprilysin inhibitors have shown a better metabolic control and that the metabolic therapy with ranolazine can be useful in patients with concomitant angina.

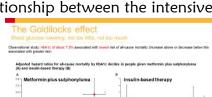
- What is the event rates in diabetic patients with heart failure, based on the data presented by the speaker?
- What are the key points of the therapeutic algorithm for a patient with symptomatic HFrEF, presented by the speaker?
- What's about the main effects of beta-blockers in the diabetic patients affected by HF, based on the data presented by the speaker?
- What are the mortality/morbidity outcomes in patients with worsening chronic HFrEF receiving eplerenone or different doses of finerenone, based on the data presented by the speaker?
- What's about the efficacy of the renin-angiotensin antagonists in nondiabetic versus diabetic patients with heart failure, based on the data presented by the speaker?
- Why can ARNI improve the glycaemic control, from the speaker point of view?
- What's about the effect of ranolazine on HbA1c in patients with diabetes in the published Clinical Trials, presented by the speaker?

#### Glucose lowering treatment in patients with heart failure



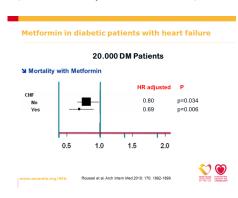
Prof. Rosano from London (UK), presented very interesting data on "Glucose lowering treatment in patients with heart failure". More in particular the speaker presented very interesting data starting from the worse prognosis of diabetic patients affected by HF. Going deeper in his lecture, Prof. Rosano talked about the relationship between the intensive

glucose control and mortality and presented very interesting data on the



right balance between glucose lowering therapy and the need for glucose intake in the heart, in order to better perform its functions. In the main part of his lecture, the speaker talked about the main drugs to be used in diabetic patients affected by HF and presented very interesting data on metformin,

glitazones, GLP1 therapy,
DPP4 inhibitors, empagliflozin and on dapaglifozin. Prof.
Rosano discussed the main topics raised from the main
clinical trials running in diabetic patients affected by HF
and treated with all these drugs and highlighted that the
management of heart failure in diabetic patients should
not differ to that of non-diabetic ones and that the
cardiovascular safety of the novel anti diabetic agents
regarding the heart failure events need to be carefully



• What is the relationship between diabetes mellitus and the risk of heart failure, based on the data presented by the speaker?

evaluated.

- What's about the prognosis in patients with heart failure and diabetes, based on the data presented by the speaker?
- What's about the effect of metformin in diabetic patients affected by HF, based on the data presented by the speaker?
- What is the effect of the DPP4 inhibitors on the HF hospitalisations, based on the data presented by the speaker?
- What is the effect of Dapagliflozin on new onset heart failure in diabetics, based on the data presented by the speaker?



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.