ESC
European Society of Cardiology

GRAND COURSES 2017

THE CARDIOVASCULAR DISEASE CONTINUUM IN THE ERA OF EVIDENCE BASED MEDICINE

MAIN TOPICS

ARTERIAL HYPERTENSION
CORONARY ARTERY DISEASE
HEART FAILURE
ISCHAEMIC HEART DISEASE

RADISSON BLU LEOGRAND HOTEL

CHIŞINĂU CITY, MOLDOVA

10-11 NOVEMBER 2017

FINAL PROGRAMME

MENARINI group
BERLIN-CHEMIE MENARINI


CHIŞINĂU CITY
MOLDOVA

SCIENTIFIC PROGRAMME

10-11/11/2017

Supported by unrestricted
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WELCOME LETTER

Dear Colleagues,

We are extremely pleased to welcome you to the ESC / Moldavian Society of Cardiology jointly organised course with the general title "The Cardiovascular Disease Continuum in the Era of Evidence Based Medicine" on November 10th – 11th in Chişinău city, Moldova.

The European Society of Cardiology (ESC) is very focused on developing and implementing high standard guidelines, aimed at promoting evidence based medicine and eliminating existing healthcare gaps among the 56 ESC members' healthcare systems.

It is, indeed, the mission of the ESC to reduce the burden of Cardiovascular diseases and to fight inequalities and disparities of patient accessibility to modern medicine in its member countries.

The Moldavian Society of Cardiology, a significant member of ESC, works constantly on continuous medical education and ESC Guidelines implementation.

This course is a very good example of joint efforts for the good of our cardiovascular patients.

Professor
Jeroen Bax

President of the
European Society of Cardiology

Professor
Michail Popovici

President of the
Moldavian Society of Cardiology

FACULTY

CREA FILIPPO
Professor of Cardiology, Director, Institute of Cardiology, Catholic University of the Sacred Heart, Rome, Italy

PIEPOLI MASSIMO
Professor of Cardiology and Chief of Heart Failure Unit at Guglielmo da Saliceto Polichirurgico Hospital, Piacenza, Italy,

DOUMAS MICHAEL
Professor of Medicine, Aristotle University, Thessaloniki, Greece & GW University, Washington, DC

ROSENHEK RAPHAEL
Associate Professor and Director, Clinic for Valvular Heart Disease, Department of Cardiology, Medical University of Vienna, Austria

VARDAS PANOS
Professor of Cardiology and Head of Cardiology Department, University Hospital of Crete, Greece, Past President of the European Society of Cardiology

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CABAC-POGOREVICI IRINA
Ph.D Candidate, University Assistant at Cardiology Department State University of Medicine and Pharmacy "Nicolae Testemitanu", Chisinau, Republic of Moldova

CARAUSH ALEXANDRU
Professor, Chief of Arterial Hypertension Department, Institute of Cardiology, Chisinau, Republic of Moldova

GRIVENCO ALIONA
Cardiologist-Researcher, Heart Failure Department, Institute of Cardiology, Chisinau, Republic of Moldova

IVANOV VICTORIA
Professor, Chief of Ischemic Heart Disease Department, Institute of Cardiology, Chisinau, Republic of Moldova

POPOVICI MIHAIL
Professor, Academician of the Moldavian Academy of Science, President of Moldavian Society of Cardiology

REVENCO VALERIU
Professor, Chief of Cardiology Department State University of Medicine and Pharmacy Nicolae Testemitanu", Chisinau, Republic of Moldova"

VATAMAN ELEONORA
Professor, Chief of Heart Failure Department, Institute of Cardiology, Chisinau, Republic of Moldova

Friday, **10th November** 2017

14.00 – 14.30 **INTRODUCTORY PART**
THE AIM AND OBJECTIVES OF THE COURSE
Mihail Popovici (MD) – Panos Vardas (GR)

14.30 – 15.30 **DISTINGUISHED ESC TALKS**
Chairpersons: Mihail Popovici (MD) – Filippo Crea (IT)

- The cycle of research, education and medical practice
  Massimo Piepoli (IT)
- Cost and effectiveness. The basis of nowadays health care
  Panos Vardas (GR)

15.30 – 16.45 **CLINICAL SEMINAR I**
ESC GUIDELINES 2016, 2017
Chairpersons: Mihail Popovici (MD) – Panos Vardas (GR)

- 2016 European Guidelines on cardiovascular prevention in clinical practice
  Massimo Piepoli (IT)
- ESC Heart Failure Guidelines 2016
  Raphael Rosenhek (AT)
- What is new in the 2017 Guidelines on antiplatelet therapy in coronary artery disease
  Valeriu Revenco (MD)
- Management of Dyslipidaemias 2016 ESC/EAS, Guidelines
  Victoria Ivanov (MD)
- Discussion

16.45 – 17.15 **Break**

17.15 – 18.15

CLINICAL SEMINAR II
ARTERIAL HYPERTENSION AS A SEVERE CHRONIC CARDIOVASCULAR DISEASE

Chairpersons: Valeriu Revenco (MD) – Raphael Rosenhek (AT)

- Pathophysiology of hypertension and pleiotropic effects of different classes of antihypertensives
  Michael Doumas (GR)
- Key determinants for arterial hypertension assessment
  Alexandru Caraus (MD)
- Arterial hypertension management before and after the SPRINT Trial
  Michael Doumas (GR)
- Discussion

18.15 – 18.45

LECTURE

Chairpersons: Victoria Ivanov (MD) – Massimo Piepoli (IT)

- Hyperuricaemia and Cardiovascular Disease
  Michael Doumas (GR)

18.45 – 19.45

CLINICAL SEMINAR III
ISCHAEMIC HEART DISEASE
Pathophysiology as the main axis of therapeutic decisions

Chairpersons: Alexandru Caraush (MD) – Raphael Rosenhek (AT)

- The many causes of transient myocardial ischaemia: clinical implications
  Filippo Crea (IT)
- Inflammation in acute myocardial infarction
  Mihail Popovici (MD)
- Angina management in real life. How to choose the right therapy for the right patient
  Panos Vardas (GR)
- Discussion

Saturday, **11th November** 2017

09.00 – 10.00 **CLINICAL SEMINAR IV**
THE ELDERLY CVD PATIENT. SPECIAL NEEDS AND CARE
Chairpersons: Victoria Ivanov (MD) – Michael Doumas (GR)

- Diabetes, Arterial Hypertension and CAD in the elderly
  Raphael Rosenhek (AT)
- The complexity of heart failure treatment in elderly patients
  Eleonora Vataman (MD)
- Discussion

10.00 – 10.30 **Break**

10.30 – 11:00 **A STATE OF THE ART LECTURE**
Chairpersons: Eleonora Vataman (MD) – Massimo Piepoli (IT)

- The future of Cardiovascular Medicine
  Panos Vardas (GR)

11.00 – 12.30 **CLINICAL SEMINAR V**
DAILY PRACTICE – CLINICAL CASES
Chairpersons: Eleonora Vataman (MD) – Michalis Doumas (GR)

- A 64-year-old female patient with a history of Myocardial Infraction (MI), Atrial Fibrillation (AF) and stable angina
  Filippo Crea (IT)
- A 76-year-old hypertensive patient with comorbidities
  Irina Cabac-Pogorevici (MD)
- A 72-year-old patient with post-AMI, dyslipidemia and heart failure with preserved ejection fraction
  Aliona Grivenco (MD)

12.30 – 12.45 **CLOSING REMARKS - END OF THE COURSE**

A 76-YEAR-OLD HYPERTENSIVE PATIENT WITH COMORBIDITIES

Irina Cabac-Pogorevici
Ph.D Candidate, University Assistant at Cardiology Department State University of Medicine and Pharmacy "Nicolae Testemitanu", Chisinau, Republic of Moldova

A 76-year-old hypertensive female presents to ambulance crew after emergency call on, complaining of constrictive chest pain episode, induced by small physical activity, shortness of breath at moderate exertion. Patient is known with, osteoarthritis of the knee joint (gonarthrosis) and grade II obesity. Levels of serum electrolytes, glucose, blood urea and creatinine and complete blood counts were normal, troponin negative and CK-MB normal, high level of blood lipids were noted. ECG showed sinus rhythm, right axis deviation, negative T waves II, III, aVF, V1- V6. The chest x-ray showed no evidence of active pleural or pulmonary parenchymal abnormality. Echocardiography revealed moderate left ventricular hypertrophy, moderate hypokinesia of the interventricular septum. The patient was discharged with recommendations for hospital admission to the Institute of Cardiology for coronary angiography. Three weeks later coronary angiography was performed and no significant lesions of the coronary arteries were revealed. The patient was discharged with the following diagnosis: Arterial hypertension grade III, very high risk - Idiopathic focal myocardial lesions of the anterior and inferior walls of the left ventricle - Mild pulmonary hypertension – Dyslipidaemia - Obesity grade II. Two weeks later, the patient was readmitted to the Institute of Cardiology complaining of extreme weakness at minimal exertion, dizziness and syncope at minimal exertion and acute dyspnea at minimal exertion. Physical examination revealed a diaphoretic and dyspneic patient without focal neurologic findings, the heart rate was regular but with tachycardia at 105 beats/minute, while her blood pressure was 100/65 mmHg. Transthoracic echo exam showed hypokinesia of the mid free wall and hyperkinetic motion at the apex of the right ventricle, paradoxical motion of the interventricular septum, moderately dilated right atrium and right ventricle and high probability of pulmonary hypertension (SPAP 85 mmHg). It was raised the suspicion of pulmonary embolism. D-dimer were positive and CTPA revealed thrombi in the main, segmental and subsegmental pulmonary arteries, indicating a high probability of a non-high risk pulmonary embolism. Thrombolytic treatment was not given - the patient received standard anticoagulation treatment with unfractionated heparin and an oral anticoagulant.

KEY DETERMINANTS FOR ARTERIAL HYPERTENSION ASSESSMENT

Alexandru Caraush
Professor, Chief of Arterial Hypertension Department, Institute of Cardiology, Chisinau, Republic of Moldova

Hypertension is a highly prevalent cardiovascular risk factor underlying various pathological conditions such as heart failure, coronary artery disease, vascular disease, stroke or chronic kidney disease.
According to the most recent data from Europe, one in three to four males and one in four to five females had raised blood pressure. The prevalence data from the USA shows that approximately 34.5% of Americans are hypertensive.
Although the patients remain asymptomatic for relatively long time, the presence of hypertension

is associated with significantly increased risk for cardiovascular morbidity. The presence of hypertension is also associated with increased mortality. In Europe, for example, more than 50% of all deaths in 2015 were attributed to hypertension in both males and females. However, the risks associated with hypertension are largely reversible with adequate control of blood pressure. The initial evaluation of the patient with hypertension should: 1) confirm the diagnosis of hypertension 2) assess CV risk, asymptomatic organ damage and concomitant clinical conditions 3) detect causes of secondary hypertension. The characteristics of the basic groups of antihypertensive drugs are also elucidated. The presented data is based on 2013 ESH/ESC Guidelines for the management of arterial hypertension.

THE MANY CAUSES OF TRANSIENT MYOCARDIAL ISCHAEMIA: CLINICAL IMPLICATIONS

Filippo Crea
Professor of Cardiology, Director, Institute of Cardiology, Catholic University of the Sacred Heart, Rome, Italy

Chronic stable angina pectoris is the most prevalent symptomatic manifestation of ischaemic heart disease, and its management is a priority. The concept that chronic stable angina is caused by epicardial stenosis has been challenged on the basis of various observations. In a fraction of patients, myocardial ischaemia can persist or reoccur after having undergone successful complete coronary revascularization. Outcome analyses show little or no prognostic effect of elective angioplasty. Autopsy studies of patients with chronic stable angina suggest that coronary artery obstruction is not necessarily synonymous with myocardial ischaemia. Therefore, it seems that myocardial ischaemia can occur in the absence of obstructive epicardial and coronary atherosclerosis. In the majority of these cases, chronic stable angina is caused by coronary microvascular dysfunction while coronary artery spasm is the cause of ischemia in the remaining patients.
Current clinical guidelines recommend antianginal therapy to control symptoms, before considering coronary artery revascularization. Antianginal agents are approved by documenting that they improve total exercise duration, together with a reduction in daily frequency of chronic stable angina compared with placebo and/or equivalence to an active comparator. Cardiovascular outcomes, although highly advocated, are not a prerequisite for regulatory approval. None of the antianginal drugs has been proved to reduce cardiovascular mortality or the rate of myocardial infarction. When patients are optimally treated, mortality for chronic stable angina is low, which might explain why all trials designed to improve prognosis have been negative. Guidelines recommend a first-choice and a second-choice approach, based more on tradition and expert opinion, rather than evidence. This categorical approach has been questioned in the past couple of years. Newer antianginal drugs, which are classified as second choice, have more evidence-based clinical data that are more contemporary to support their use than is available for the traditional first choice drugs. Equally, the often-needed combination of double or triple therapy is based on expert opinion and not related to the underlying pathophysiology. What constitutes optimal antianginal treatment, therefore, varies considerably between countries, and the majority of doctors treat their patients according to their own preconceptions of the underlying physiopathology and comorbidities. A “diamond” approach might be more appropriate than current recommendations to guide clinicians in selecting the most suitable drug regimen, alone

or in combination, for an individual patient. As in hypertension, the idea of a diamond approach leaves treating physicians free to choose the most appropriate drugs, according to a patient's needs.

A 64-YEAR-OLD FEMALE PATIENT WITH A HISTORY OF MYOCARDIAL INFARCTION, ATRIAL FIBRILLATION AND STABLE ANGINA

Filippo Crea
Professor of Cardiology, Director, Institute of Cardiology, Catholic University of the Sacred Heart, Rome, Italy

The case of a 64-year-old female patient with several risk factors including smoking, hypertension, diabetes and obesity and a history of inferior STEMI in 2013 will be presented. The recent medical history was characterized by typical effort-related angina. On examination, she presented a mild systolic murmur on the mitral area. The ECG showed pathologic Q waves in inferior leads. 2D-echo showed moderate eccentric mitral regurgitation, slight enlargement of the left atrium, preserved ejection fraction and inferior hypokinesia.
The following topics will be interactively discussed:
- Diagnostic criteria
- Risk stratification
- Therapeutic options

One month after discharge the patient was admitted to the hospital with TIA confirmed at MRI. The diagnostic approach to embolic stroke of unknown source (ESUS) will be discussed.
The diagnostic work up showed that the cause of TIA was asymptomatic atrial fibrillation. The therapeutic approach to atrial fibrillation with regard to:
- Antithrombotic treatment
- Anti-arrhythmic strategy

will be discussed as well.

PATHOPHYSIOLOGY OF HYPERTENSION AND PLEIOTROPIC EFFECTS OF DIFFERENT CLASSES OF ANTIHYPERTENSIVES

Michael Doumas
Professor of Medicine, Aristotle University, Thessaloniki, Greece & GW University, Washington, DC

More than 60 years ago, Page proposed the "mosaic" theory, suggesting that arterial hypertension is a multifactorial disease. Accumulating evidence strongly indicates that several mechanisms contribute to blood pressure elevation through either increased peripheral vascular resistance or increased cardiac volume. The renin-angiotensinaldosterone system and the sympathetic nervous system play a seminal role in blood pressure homeostasis and their activation increases blood pressure levels. However, many other mechanisms are implicated in the pathogenesis of hypertension, including structural and functional alterations of the large and small vessels, natriuretic peptides, vasoactive peptides, endothelial dysfunction, subclinical

inflammation, oxidative stress, abnormalities in coagulation and fibrinolysis. Last but not least, the kidneys have a central role in blood pressure homeostasis through a variety of mechanisms contributing in the genesis and maintenance of blood pressure elevation. Three aspects need to be highlighted: a) the contribution of each mechanism is different in each individual, b) there exists a strong crosstalk between several of these mechanisms, and c) attenuation of one mechanism might be associated with counter-regulatory activation of other mechanisms.
The advent of antihypertensive therapy has been associated with impressive cardiovascular benefits. Antihypertensive therapy results in significant reduction of myocardial infraction, heart failure, stroke, transient ischaemic attack, end-stage renal disease, and cardiovascular mortality. Up to now, more than 100 agents belonging in 10 categories of hypertensive drugs are available in the market for the adequate lowering of elevated blood pressure. The dogma that the benefits of antihypertensive therapy are ought to blood pressure reduction per se and lowering the elevated blood pressure is all that matters prevailed for years.
However, data from large clinical trials performed the previous decade (LIFE, ASCOT, ACCOMPLISH, ONTARGET) point towards significant differences between the various classes of antihypertensive drugs, suggesting beneficial effects beyond blood pressure reduction, and rendering the pleiotropic effects of some categories at the epicenter of cardiovascular research. The term “pleiotropic effects” includes cardioprotection, nephroprotection and cerebral protection, protection from or reversal of target organ damage, beneficial effects on other mechanisms implicated in the pathogenesis of blood pressure elevation, and beneficial effects on other cardiovascular risk factors. Inhibitors of the renin-angiotensin system (ACE-inhibitors, angiotensin receptor blockers), calcium antagonists, and nebivolol (a third-generation beta blocker with vasodilatory properties through increased nitric oxide bioavailability) are currently considered antihypertensive drugs that exert pleiotropic actions, and thus provide benefit in more than one of the aforementioned aspects beyond
blood pressure reduction.

A 72-YEAR-OLD PATIENT WITH POST-AMI, DYSLIPIDEMIA AND HEART FAILURE WITH PRESERVED EJECTION FRACTION

Aliona Grivenco
Cardiologist-Researcher, Heart Failure Department, Institute of Cardiology, Chisinau, Republic of Moldova

Introduction: The high incidence of Heart Failure with preserved ejection fraction and inconclusive information on effective therapy present in clinical practice difficulties by providing rationale treatment. During the clinical case that will be presented the choice of the treatment strategies in accordance to current guidelines, will be discussed.
Case Presentation: Patient P., 72-year-old man, ex-smoker, hospitalized in the Institute of Cardiology with the following complaints: breathlessness, paroxysmal nocturnal dyspnea, intermittent palpitations, reduced exercise tolerance, fatigue, tiredness, ankle swelling, loss of appetite. Medical history. Patient P. is hypertensive since 1998 (maximum blood pressure (BP) > TA 200/100 mmHg). Episodic hypotensive treatment with Lisinopril 10 mg. In 2014, he suffered a Myocardial Infarction with left ventricular aneurysm and thrombosis and diagnosed with Type 2 Diabetes Mellitus. In 2015, he underwent myocardial revascularization by coronary artery bypass grafting, aneurysm repair and thrombectomy. Postoperative period: persistent atrial fibrillation, frequent ventricular extrasystoles, treating Amiodaron. He participated in a cardiac rehabilitation

program. From 2015 to 2017, he feels satisfactory and takes medication: Valsartan 80 mg, Bisoprolol 2,5 mg, Indapamide 1,5 mg, Rivaroxaban 20 mg, Aspirin 75 mg, Metformin 500 mg x 2 (twice a day), Atorvastatin 10 mg (non-regular). The last 3-4 months, there were the above complaints.

Physical examination. Body mass index = 32,8 kg/m2, heart rate (HR) 80 bpm, BP=160/80 mmHg, moderate ankle oedema. Bilateral respiratory sounds decreased, bilateral fine crepitations. Paraclinic investigations: The electrocardiogram (ECG) revealed normal sinus rhythm, antero-lateral Q waves with old infarction. Transthoracic echocardiography showed the left ventricle (LV) with normal diameters and volumes, global left ventricular systolic function normal (EF = 57%), akinesis of the apex. LV wall thicknesses = 15 mm. LV mass 194 gr, LV myocardial index – 98 g/ m2, Left atrial volume index = 50 ml/m2. A 24-hour Holter ECG recording normal sinus rhythm (average HR – 68 bpm), total ventricular extrasystoles beats=229. Chest X-ray examination showed pulmonary congestion. Laboratory parameters: NT pro BNP 790 pg/ml, fasting glucose -9,5 mmol/l, HbA1C -8,4%, Cholesterol - 4,95 mmol/l, Low density lipoprotein - 2,88 mmol/l, High density lipoprotein - 1,26 mmol/l, triglycerides - 1,75 mmol/l. Other results without abnormalities. Score Charlson index of comorbidity = 8.

Discussion: The clinical dilemma in this case was the choice of treatment tactics:

- Continue treatment with angiotensin receptor blocker (Valsartan) or indicated angiotensin-converting enzyme inhibitor?
- Add loop diuretics to treatment?
- What b-blokers are better for this patient?
- Treatment with anticoagulants (score CHA2DS2VASc – 5 p and HAS-BLED -2 p)?
- Continue therapy with aspirin?
- Does the patient need statin therapy?
- What treatment is recommended for diabetes?

MANAGEMENT OF DYSLIPIDAEMIAS, 2016 ESC/EAS GUIDELINES

Victoria Ivanov
Professor, Chief of Ischemic Heart Disease Department, Institute of Cardiology, Chisinau, Republic of Moldova

Management of dyslipidaemias as an important part of CVD prevention. Screening for lipid abnormalities, including the lipid profile, may be considered in adult men ≥40 years of age, and in women ≥50 years of age or post-menopausal, particularly in the presence of other risk factors. In addition, all subjects with evidence of atherosclerosis in any vascular bed or with type 2 diabetes, irrespective of age, are regarded as being at high risk; it is recommended to assess their lipid profile. Total cholesterol (TC) is recommended to be used to estimate total CV risk by means of the SCORE system. Patients with established CVD, diabetes, renal impairment or very high levels of individual risk factors are at high to very high risk. LDL-C is recommended to be used as a primary lipid analysis for screening, risk estimation and management. LDL-C remains the primary target of therapy in most strategies of dyslipidaemia management. Intensity of LDL-C reduction according to the level of the total CV risk. For patients with very high CV risk, the treatment target for LDL-C is less than 1.8 mmol/L or a ≥50% reduction from baseline LDL-C. Target level of LDL-C for subjects at high risk is < 2.5 mmol/L. For subjects at moderate risk, an LDL-C target of 3 mmol/L should be considered. Lifestyle interventions will have an important long-term impact on health. Statins are among the most studied drugs

in CV prevention. Statins substantially reduce CV morbidity and mortality in both primary and secondary prevention, they also been shown to slow the progression or even promote regression of coronary atherosclerosis. Statins should be prescribed on highest tolerable dose to reach the goal. The following scheme is proposed prior the statin initiation: evaluate the total CV risk of the subject, involve the patient with decisions on CV risk management, identify the LDL-C target for that risk level, calculate the percentage reduction of LDL-C required to achieve that goal, choose a statin and dose that, on average, can provide this reduction. Response to statin treatment is variable, up-titration to reach target is mandatory, if the highest tolerated statin dose cannot reach the goal, consider drug combinations.

INFLAMMATION IN ACUTE MYOCARDIAL INFARCTION

Mihail Popovici
Professor, Academician of the Moldavian Academy of Science, President of Moldavian Society of Cardiology

Growing evidences emphasize the close relation of inflammation and acute myocardial infarction. The inflammatory response triggered by myocardial necrosis in the first hours after insult comprises a series of interdependent processes influencing post-infarction myocardial remodeling. Pro-inflammatory cytokines derived from neutrophils that accumulate mostly after 24 hours and macrophages type 1 (top accumulation after 72 hours) and counteracting anti-inflammatory interleukins released by macrophages type 2 (top accumulation at 7th day) are the most important factors activating extracellular matrix collagenolysis and oxidative stress, which in their turn are regarded as main determinants of post-infarction remodeling pattern: either adaptive or pathological.

Thus, the anti-inflammatory treatment appears to be an additional arguable part of secondary prophylaxis in the evolution of the post-infarction period. One of the treatment's target will be the modulation of the extracellular matrix proteinases activity that will blunt collagenolysis and intercept post-pathological remodeling left ventricle dilation. Although experimental aftermaths demonstrated anti-inflammatory treatment relevance and promising results, clinical trials have mostly failed to do so. Nevertheless, the CANTOS trial results are encouraging by showing benefits of anti-IL1beta treatment concerning the decrease of both hsCRP and post-infarction MACE rate. However, CANTOS encompasses patients with hsCRP >2,0 mg/L, this cohort being very large, and on the other with no refer to acute phase of infarction.

In this regard, our study was aimed at the daily evaluation of the circulating levels of pro- and anti-inflammatory markers in 2 groups of patients during the first 7 days after STEMI revascularization (the average necrosis zone size was similar, 25-28%) who after 4-6 months developed either adaptive (n=56) or pathological (n=57) myocardial remodeling. Remarkably, the weekly dynamics of serum concentration of the main pro-inflammatory markers (hsCRP, IL-1, IL-6, TNF-alpha) was the same in both groups: top elevation at 3rd day after revascularization followed by a decline in the last 4 days. In contrast, the dynamics of anti-inflammatory markers (Il-4 and IL-10) was conspicuously linked to the remodeling pattern. In the group of patients with adaptive remodeling these markers rose from starting on the 3rd day up to 7th day by 52-55% which is in accordance with the time of anti-inflammatory macrophages expression boost, while in patients with pathological remodeling no increase in these markers was established.

Accordingly, our findings could represent an appropriate tool for post-infarction remodeling pattern prediction and selection of patients for anti-inflammatory therapy.

WHAT IS NEW IN THE 2017 GUIDELINES ON ANTIPLATELET THERAPY IN CORONARY ARTERY DISEASE

Valeriu Revenco
Professor, Chief of Cardiology Department State University of Medicine and Pharmacy Nicolae Testemitanu", Chisinau, Republic of Moldova"

The estimated number of patients requiring dual antiplatelet therapy (DAPT), consisting of the combination of aspirin and an oral inhibitor of the platelet P2Y receptor for adenosine 5'-diphosphate (ADP), is considerable and has increased over time in Europe. Based on population estimates from 2015, in the region of 1.400.000 and 2.200.000 patients per year may have an indication for DAPT after coronary intervention or myocardial infarction (MI), respectively. Given the trade-off between ischaemic vs. bleeding risks for any given DAPT duration, the use of scores might prove useful to tailor DAPT duration in order to maximize ischaemic protection and minimize bleeding risks in the individual patient. Compared with OAC therapy alone, the addition of DAPT to OAC therapy results in at least a two- to three-fold increase in bleeding complications. The duration of triple therapy should be limited up to a maximum of 6 months or omitted after hospital discharge, taking into account the ischaemic (e.g. complexity of treated CAD, amount of disease left untreated, technical considerations regarding stent implantation techniques and results) as well as the bleeding risk. The use of ticagrelor or prasugrel in this setting is not recommended. Differences in the pharmacology of P2Y12 receptor inhibitors with regard to their binding site, half-life, and speed of onset and offset of action are important factors that might lead to drug interactions when switching from one agent to another and registry data indicate that switching is not infrequent in practice so switching algorithms based on pharmacodynamic studies are provided. A multidisciplinary expert team should be considered for pre-operative evaluation of patients with an indication for DAPT before elective surgery. Scheduled surgery requiring discontinuation of the P2Y12 inhibitor should be considered after at least 1 month, irrespective of the stent type, if aspirin can be maintained throughout the perioperative period. If both oral antiplatelet agents have to be discontinued perioperatively, a bridging strategy with cangrelor, tirofiban, or eptifibatide may be considered, especially if surgery has to be performed within 1 month after stent implantation. DAPT remains a highly effective preventive treatment for stent thrombosis across the board; however, the risks of late and (even more) very late stent thrombosis have declined considerably since the advent of newer- generation DESs. Hence, after 21 years of research, DAPT has moved from a local (i.e. stent-related) to a systemic treatment strategy (i.e. capable of preventing thrombosis).

COST AND EFFECTIVENESS. THE BASIS OF NOWADAYS HEALTH CARE

Panos Vardas
Professor of Cardiology and Head of Cardiology Department, University Hospital of Crete, Greece, Past President of the European Society of Cardiology

It is becoming a worldwide reality that health care cost, for most of the countries and especially for those with aging population, increases exponentially and menaces the sustainability and affordability of the Health Care Systems.

During the last twenty years, well-organized countries use increasingly regularly methods for the assessment of cost and effectiveness of various drugs and implanted medical devices, such as pacemakers, defibrillators, stents and heart valves.
The base of this evaluation is focused on cost per QALY (Quality Adjusted Life Year). The latter is a generic measure of disease burden including both the quality and the quantity of life lived under a certain treatment. It is used in economic evaluation to assess the value for money of medical interventions. One QALY equates to one year in very good health.
Several Health Institutes, like NICE (National Institute for Health and Clinical Excellence) in Great Britain, use QALY when assessing the various applied treatments. The number of extra QALYs associated with a new medicine (compared with what is already happening in the NHS) is combined with the extra cost of that medicine, which produces an "incremental cost per QALY" ratio.
For example, if a drug costs € 50,000 more than the alternative and only gave the patient six months more of life in good health, it would cost € 100,000 per QALY gained. NICE generally considers that interventions costing to the NHS € 23.000 per QALY gained are cost effective and those costing up to € 34.000 per QALY gained might, with certain conditions satisfied, be considered cost effective.

THE FUTURE OF CARDIOVASCULAR MEDICINE

Panos Vardas
Professor of Cardiology and Head of Cardiology Department, University Hospital of Crete, Greece, Past President of the European Society of Cardiology

The Cardiovascular Medicine closely monitors the socio-economic conditions of each era and is being developed according to their evolution.
A couple of centuries ago, in the time of famine and lack of antibiotics, the rheumatic fever, an inflammatory disease, which infected mainly children and teenagers, prevailed. Later on, in their middle age, the victims of rheumatic fever developed valvulopathies of the mitral and aortic valves mostly.
During the last fifty years, the rheumatic fever disappeared, in most countries, along with the relevant valvulopathies. Unfortunately, at the same time, during the last 50 years, as the life model changed and prosperity offered more possibilities to the population of industrial states, the scourge of coronary disease along with its complications (sudden death, heart failure, acute myocardial infraction, stable angina) showed up. Fortunately, in many countries, morbidity and mortality, due to coronary artery disease, are reduced, because of the change in the model of life.
Therefore, what the main subject of cardiology of the future will be? Without doubt the degenerative heart diseases, such as degenerative valvulopathies, heart failure and arrhythmias. Based on the above assumption, we will try to summarize the expected developments, as follows:
1. Interventional, non-surgical therapeutic techniques
2. Digital Health
   2.1. Bedless Hospitals, paperless Units, Big Data and analytics
   2.2. Telemedicine

3. Tissue Engineering
   3.1 Stem cells

All above will be gradually developed and will surely dominate in the clinical practice during the coming twenty years.

THE INCREASED COMPLEXITY OF THE HEART FAILURE TREATMENT IN THE ELDERLY PATIENTS

Eleonora Vataman
Professor, Chief of Heart Failure Department, Institute of Cardiology, Chisinau, Republic of Moldova

Heart failure (HF) is a leading cause of morbidity, hospitalization and mortality in older patients. More than 80% of patients with HF are older than 65 years. World prevalence of HF will rise substantially over the next 20-30 years. Patients often have co-existing multi-morbid illness, cognitive impairment, functional deficit, frailty and need polypharmacy. The commonest cause of HF is coronary artery disease followed by other causes of myocardial damage, abnormal loading conditions or arrhythmias. The concomitant diseases, such as diabetes, chronic kidney disease, anemia, chronic obstructive pulmonary disease, depression, arthritis, sensory impairment and cognitive dysfunction substantially add to the complexity of HF care. HF with preserved ejection fraction is the most common phenotype. Preclinical HF is four times more common than symptomatic but it is difficult to be recognized at the earlier stage. The basic investigations for HF do not significantly differ in comparison to a younger patient.

The treatment goals are to alleviate symptoms, to prevent progression of disease and repetitive hospitalizations. Older HF patients are under-represented in clinical trials and most therapies recommended in the guidelines have not been adequately tested in elderly patients. Carefully pharmacology selection is imposed by physiological age-related changes in body composition, which first results in higher plasma concentrations of hydrophilic drugs versus tendency to decreasing of lipophilic drugs. Second, multiple co-morbidities increase the risk of drug side effects (liver or renal dysfunction, orthostatic hypotension). Patients with chronic HF on average take 10 medications with significant risk for adverse reactions caused by drug-drug interactions. Third, when choosing a management plan we need also to take into account the presence of social and economic issues, frailty and caregiver burden.

Revascularization is recommended in patients with coronary artery disease and active ischemia contributing to HF symptoms. Other management strategies are developing: HF multidisciplinary clinics with a significant role of the clinic nurse; home-based care with visiting nurses; interactive telecommunication for rural areas. Devices: implantable cardiac defibrillator (ICD) is less beneficial for elderly patients; cardiac resynchronization (CRT) does improve patient quality of life. Tele-home monitoring improves outcomes such as reduction in hospitalization and mortality. A palliative care approach is appropriate and is relevant to the elderly with advanced disease. End-of-life care discussion must be initiated by the patient`s physician or health care team.

CHIȘINĂU, Republic of Moldova

Chișinău is the capital and largest city of the Republic of Moldova. The city is Moldova's main industrial and commercial center, and is located in the middle of the country, on the river Bîc. Chișinău, as capital of Republic of Moldova, consists of city itself and nearby suburbs tightly interconnected, together making up the municipality of Chișinău. Chișinău is the most economically prosperous locality in Moldova and its largest transportation hub.

Chișinău's growth plan was developed in the 19th century. In 1836 the construction of the Kishinev Cathedral and its belfry was finished. The belfry was demolished in Soviet times and was rebuilt in 1997. Chișinău also displays a tremendous number of orthodox churches and 19th century buildings around the city such as Ciuflea Monastery or the Transfiguration Church. Much of the city is made from limestone dug from Cricova, leaving a famous wine cellar there.

Many modern-style buildings have been built in the city since 1991. There are many office and shopping complexes that are modern, renovated or newly built, including Kentford, SkyTower, and Union Fenosa headquarters. However, the old Soviet-style clusters of living blocks are still an extensive feature of the cityscape.

The city is home to 12 public and 11 private universities, the Academy of Sciences of Moldova, a number of institutions offering high school and 1-2 years of college education. In Chișinău there are several museums. The three national museums are The National Museum of Ethnography & Natural History, the National Museum of Arts and the National Museum of Archaeology & History.

- **TIME ZONE:**
  UTC/GMT + 2 hours
- **CURRENCY:**
  Moldovan leu (MDL)
- **WEATHER IN NOVEMBER:**
  6° C to 11° C
- **COURSE VENUE**
  Radisson Blu Leogrand Hotel
  Mitropolit Varlaam St 77, Chisinau 2012, Moldova
  https://www.radissonblu.com/en/hotel-chisinau
- **MAIN MEETING ROOM**
  Raut & Prut
- **SPEAKERS BRIEFING**
  Friday, November 10th 2017 →
  10:00-12:00
  Loft Lounge
- **WI-FI:** WiFi access will be provided free of charge in the Course Venue. Password will be provided onsite
- **COFFEE BREAKS**
  All Coffee Breaks will take place at the Main Foyer of Radisson Blu Leogrand Hotel
- **LUNCHES**
  Lunches will take place in Nistru Ballroom of Radisson Blu Leogrand Hotel as follows
  10.11.2017 → 13:00-14:00
  11.11.2017 → 13:00-14:00
- **COURSE DINNER**
  Friday, November 11th 2017 →
  20.00
  Ambassador Restaurant, Radisson Blu Leogrand Hotel

"The Grand Courses 2017, Chişinău City, Moldova, 10/11/2017-11/11/2017 has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME®) with **7** European CME credits (ECMEC®s). Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity."

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