European
Renal & Cardiovascular
Medicine

EuReCa-M
CME course 2022

BOOK OF ABSTRACTS

EuReCa-M
European Renal
and Cardiovascular Medicine

Edited by:
prof. Francesca Mallamaci
prof. Robert Ekart

Published by:
ERA, Working Group EURECA-m
Univerzitetni klinični center Maribor
Ljubljanska ulica 5, Maribor, Slovenia

Print:
Dravski tisk, Maribor, Slovenia

Design:
Bojan Javornik

Year of issue:
2022

Circulation:
100 izvodov

CIP - Kataložni zapis o publikaciji
Univerzitetna knjižnica Maribor

616.1:616.61(082)

EURECA-M CME course (2022 ; Maribor)
Book of abstracts : EuReCa-M CME course 2022 : [Maribor, Slovenia, September 9-10, 2022] / [edited by Francesca Mallamaci, Robert Ekart]. - [Parma] : ERA, Working Group EURECA-m ; Maribor : Univerzitetni klinični center, 2022

ISBN 978-961-7039-64-1 (Univerzitetni klinični center)
COBISS.SI-ID 120026115

FACULTY:

Speakers:

Olga Balafa, Ioannina, Greece
Sebastjan Bevc, Maribor, Slovenia
Lucia Del Vecchio, Como, Italy
Robert Ekart, Maribor, Slovenia
Beatriz Fernandez Fernandez, Madrid, Spain
Charles J. Ferro, Birmingham, United Kingdom
Radovan Hojs, Maribor, Slovenia
Gerard London, Paris, France
Francesca Mallamaci, Reggio Calabria, Italy
Jolanta Malyszko, Warsaw, Poland
Patrick B. Mark, Glasgow, United Kingdom
Ziad A. Massy, Paris, France
Roberto Minutolo, Naples, Italy
Evangelia Ntounousi, Ioannina, Greece
Alberto Ortiz, Madrid, Spain
Pantelis Sarafidis, Thessaloniki, Greece
Claudia Torino, Reggio Calabria, Italy
Giovanni Tripepi, Reggio Calabria, Italy
Jose M. Valdivielso, Lleida, Spain
Marc G. Vervloet, Amsterdam, Netherlands
Carmine Zoccali, Reggio Calabria, Italy

Moderators, Chairs:

Sebastjan Bevc, Maribor, Slovenia
Robert Ekart, Maribor, Slovenia
Beatriz Fernandez Fernandez, Madrid, Spain
Charles J. Ferro, Birmingham, United Kingdom
Jolanta Malyszko, Warsaw, Poland
Patrick B. Mark, Glasgow, United Kingdom
Roberto Minutolo, Naples, Italy
Evangelia Ntounousi, Ioannina, Greece
Alberto Ortiz, Madrid, Spain
Claudia Torino, Reggio Calabria, Italy
Jose M. Valdivielso, Lleida, Spain
Marc G. Vervloet, Amsterdam, Netherlands
Carmine Zoccali, Reggio Calabria, Italy

BOARD MEMBERS EURECA-m:

Chair: **Francesca Mallamaci** (Italy)
Vice-Chair: **Charles J. Ferro** (United Kingdom)
Olga Balafa (Greece)
Lucia Del Vecchio (Italy)
Beatriz Fernandez Fernandez (Spain)
Robert Ekart (Slovenia)
Patrick Mark (United Kingdom)
Evangelia Ntounousi (Greece)
Patrick Rossignol (France)
José Manuel Valdivielso (Spain)

Local coordinator and organizer:

Robert Ekart
Professor of Internal Medicine, Nephrologist, University Medical Center Maribor, Clinic for Internal Medicine, Department of Dialysis, Maribor, Slovenia

Contents

"The EURECA-m CME course 2022, Maribor, Slovenia, 09/09/2022-10/09/2022 has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME®) with 9 European CME credits (ECMEC®s). Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity."

"Through an agreement between the Union Européenne des Médecins Spécialistes and the American Medical Association, physicians may convert EACCME® credits to an equivalent number of AMA PRA Category 1 CreditsTM. Information on the process to convert EACCME® credit to AMA credit can be found at www.ama-assn.org/education/earn-credit-participation-international-activities.

"Live educational activities, occurring outside of Canada, recognised by the UEMS-EACCME® for EC-MEC®s are deemed to be Accredited Group Learning Activities (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada."

Prof Francesca Mallamaci, MD, FERA - Chair Woman of the European Renal Association EURECA-m Working Group

Chief of the Department of Nephrology, Dialysis and TransplantationAzienda Ospedaliera "Bianchi-Melacrino-Morelli" & CNR-IFC, Institute of Clinical Physiology, Research Unit of Clinical Epidemiology and Physiopathology of Renal Diseases and Hypertension (European Society of Hypertension, ESH, Excellence Centre) of Reggio Calabria, Italy.

Introduction and highlights of the contents of the EURECAm meeting

Dear Colleagues, good morning.

First of all, Prof. Charlie Ferro, Vice-chairman of the EURECA-m working group, and I are delighted to extend our warmest welcome to all participants. I would like to thank Prof. Ekart for having strongly wanted this meeting of our working group despite all the difficulties caused by the Covid-19 pandemic over the past few years. The programme of this meeting came out in 2019 before Covid, so after almost 3 years or so, some changes were needed, and the programme was updated accordingly.

The first topic in our programme regards the **aim of the meeting and particularly what we expect from the Working Groups** and, in this case, what we expect from the EURECAm. The fundamental question is what is it best to focus on: a deep insight into specific topics, or educational role, or both? Generally speaking, Scientific **Working Groups are expected to encourage research, communication of knowledge, teaching, and maintaining strong relationships within the group and with other groups, planning common programmes, projects and sharing knowledge among groups. In few words, ERA is committed to increasing and enhancing the offer of Science and Education through its working groups. Therefore, the aim of EURECA-m is to promote collaboration between European centres pursuing research in the overlapping areas of cardiovascular and renal medicine and to improve knowledge in specialist areas** where research is scanty. In fact, very often in cardiovascular disease trials there is no information even on the kidney function of participant patients and the vast majority of these trials usually intentionally exclude patients with renal insufficiency. The result is that specifically designed research focusing on patients

with both chronic kidney disease and cardiovascular disease appears to be a priority issue, on both clinical and scientific grounds. Another important role of a Working Group is to create shared databases - a concrete example of fruitful collaboration which may address relevant clinical research questions. Several research groups in Europe collected, or are collecting, 24h ABPM recordings in patients with kidney diseases or with hypertension or heart diseases along with detailed clinical information and outcome data. The same applies to measures of vascular involvement like pulse wave velocity or to cardiac imaging techniques from echocardiography to Nuclear Magnetic Resonance. Large databases are a tremendous opportunity for generating or testing scientific hypotheses. With this in mind, EURECA-m will establish a special board of epidemiologists and biostatisticians that will be involved in collaborations of the kind, providing methodological input into study design, data collection/merging, and statistical analysis. Investigator-initiated trials embedded in clinical practice represent another new possibility for effective collaboration among research groups aimed at advancing knowledge on cardio-renal medicine. So far, EURECAm has been the most productive of the eight Working Groups of the ERA, having published many original, multicentre studies, metanalyses, and reviews in the most important fields of cardio-vascular complications in patients with CKD. Finally, this huge amount of knowledge is shared among the affiliates of EURECAm, and then with ERA members through webinars and face-to-face meetings such as those held during the annual congress. What is truly gratifying is the high attendance at these meetings, second only to the Immunology WG i.e Glomerulonephritis.

In conclusion, I think that a Working Group should:

a) reinforce relationships among colleagues with the same field of interest, aiming at building up cooperation among the WG members,

b) plan common projects and clinical trials in often neglected but still important fields of Cardio-vascular complications in CKD patients and

c) share new knowledge and boost interest of other colleagues through webinars and meetings with a strong educational focus.

The first session of this meeting starts with a lecture by **Prof. Charles J Ferro** entitled:

Sudden Cardiac Death in CKD Patients – What do we mean by this?

in which he will be highlighting the urgent need for research to investigate the pathophysiology of SCD in patients with CKD/ESRD and establish optimum management strategies, in order to prevent under- or over-reporting of SCD.

Another important topic is ***Dyslipidaemia in CKD – emerging treatments: an affordable improvement or just a privilege for few?*** where **Prof. José Manuel Valdivielso** will be talking about treatments for dyslipidaemia which have become very efficacious in decreasing cholesterol in non-uremic patients, but their impact in CKD-related atherosclerosis is unknown.

The first session is closed by a very intriguing lecture by **Prof. Carmine Zoccali** on the increasingly important topic: ***Artificial Intelligence in Cardiovascular and Renal Medicine.*** The talk, which includes discussion of the philosophical and social implications of AI in this field, will provide a guide for clinicians on relevant aspects of artificial intelligence and machine learning, illustrating selected applications of these methods in nephrology and cardiology to date, and identifying how cardiovascular and renal medicine could incorporate artificial intelligence, such as predictive modelling, in the future.

The second session deals with **Hypertension,** one of the most important traditional CV risk factors.

Prof. Radovan Hojs, MD, PhD will start us off by speaking about ***Hypertension as a risk factor on CKD progression.*** With a prevalence of up to 90% in later-stage CKD patients, hypertension is also a major contributor to CKD progression, but existing guidelines do not offer a consensus on optimal blood pressure targets in CKD patients. In this talk, Prof. Hojs will review existing evidence, and guidelines will be critically appraised.

The next speaker will be ***Prof. Pantelis Sarafidis*** who will be asking the question:

Hypertension in dialysis: Is there anything new? How to make diagnosis and which targets (if any)

In this talk, Prof. Sarafidis will be talking about how, after non-pharmacological measures are properly implemented, the introduction of drug treatment can further help in achieving the optimum BP i.e Blood Pressure which coincides with the lowest mortality.

We conclude the second session with a talk by **Prof. Olga Balafa**, entitled:

Hypertension in kidney transplant patients - where do we stand today?

where she will be talking about how various studies underline the fact that hypertension in KTRs is not adequately diagnosed and controlled by office BP measurement and current evidence which suggests that calcium channel blockers could be the preferred first-step antihypertensive agents.

The third session will be focussing on **Volume** and the first contribution comes from **Prof. Sebastjan Bevc**, with his talk:

Evolving concepts on volume control in haemodialysis: Bioimpedentiometry and B-Lines are complementary to each other or....

which will look at fluid volume management and new non-invasive tools which allow objective assessment of fluid status.

Prof. Robert Ekart will then speak about

Fluid volume overload and vascular stiffness in CKD patients

and will share what is already present in the literature regarding fluid overload and discuss their own results in their dialysis patients.

The fourth session deals with **methodological issues to study CKD progression** and the first lecture will be delivered by **Prof G. Tripepi** whose talk is entitled: ***Application of prognostic models in Nephrology***. Prof. Tripepi will speak about the importance of risk calculators and how, before being applied in clinical practice, risk prediction models should be properly validated by assessing their discrimination, calibration, explained variation, and risk reclassification.

This talk will be followed by **Prof. Patrick Mark** who will give an insight into ***Which eGFR method is the best for cardiovascular risk prediction in CKD patients?*** and the controversy surrounding them.

Prof. Roberto Minutolo will further explore this topic with a presentation about ***Prediction of CKD progression among older patients***, how the prevalence of CKD is overestimated in older patients with slight eGFR decline and without albuminuria, how they should not be classified as having CKD, and the recently proposed age-adapted eGFR threshold for diagnosing CKD.

Another relatively new concept is ***Chronodisruption in CKD,*** which **Prof. Ortiz** will clarify for us by discussing evidence for chronodisruption in CKD, the impact of chronodisruption on CKD manifestations, potential chronodisruptors and their therapeutic implications, and current unanswered questions on this topic.

The 5th session sees a focus on **New therapies in Nephrology** and begins with **Prof. dr. Marc G. Vervloet** talking about ***Chronic kidney disease-mineral and bone disorder*** and how a rise in PTH over time, except for those with overt elevated levels, was associated with improved outcome.

The session continues with a talk about ***Chronic and acute hyperkalemia latest KDIGO Controversy Conference*** by **Prof. Jolanta Malysko,** addressing points from the Controversy Conference on potassium management in kidney disease.

The fifth session closes with **Prof. Lucia del Vecchio** speaking about ***the HIF factor and the cardiovascular system: possible strengths and weakness of HIF stabilizers***. She will discuss the safety of erythropoiesis stimulating agents (ESA) and the differences between ESA and HIF.

The sixth and final session is all about the **Heart and Vessels in CKD** and begins with **Prof. Gérard M London** talking about **aging and arteries in the General population and in uremic** patients in his talk entitled: ***"The age-stiffness relationships of elastic and muscular arteries in control population and ESRD patients"***

This will be followed by **Prof Ziad A. Massy** who will give ***"New insights on cardiovascular disease and calcification in CKD patients"*** and talk about how future interventional studies with multi-prolonged interventions focused on hard end-points (compared with classical and uncontrolled treatments) have the potential to generate higher-grade evidence.

Prof. Evangelia Ntounousi delivers the next session which will address the topic of *"Mechanisms of Renal Function deterioration in Heart Failure"*

including how the presence of a low cardiac output only partly explains the pathophysiology of kidney dysfunction and how, so far, specific mechanisms by which elevated central venous pressures in the context of HFpEF are almost unknown and are subjects of ongoing research.

Assoc. Prof. Beatriz Fernández Fernández will speak about ***renal stenosis*** which, according to latest reports is the cause of hypertension in 1% to 10% in some series. This session will highlight the cause, pathophysiology, presentation and related complications (CKD and ESRD) , and will review the role of the interprofessional team in its management.

Finally, the programme closes with a face-to-face educational session with questions and answers from experts in the field.

Prof Charles J Ferro, MD, FERA

Consultant Nephrologist, Department of Renal Medicine, Queen Elizabeth Hospital, Birmingham
Professor of Cardiovascular Science, University of Birmingham, United Kingdom.

Sudden Cardiac Death in CKD Patients – What do we mean by this?

Cardiovascular risk increases with declining renal function as is highest in patients on dialysis with 50% of all deaths attributed to a cardiovascular cause. Sudden Cardiac Death (SCD) accounts for 78% of cardiovascular deaths in dialysis patients.

The term SCD is applied to any unexpected death due to cardiac causes and is defined as a witnessed collapse occurring within an hour of a sudden change in clinical condition. This can therefore lead to both over and under reporting of the true incidence.

In the general population 50% of SCD are assigned to myocardial infarction with the rest to tachyarrhythmias. However, implantable loop recorder studies in dialysis patients have so far shown that 75% of SCD are due to bradyarrhythmias.

The incidence of risk factors for SCD in the general population such as ischaemic heart disease increases with declining renal function. In addition, there are unique features in patients with CKD related to the development of uraemic or CKD-associated cardiomyopathy, characterised by left ventricular hypertrophy, diastolic and systolic dysfunction and histologically by profound myocardial fibrosis. All these features provide the substrate for a vulnerable myocardium for SCD.

There is little evidence to guide the prevention of SCD with studies so far showing no benefit from implanted cardiac defibrillators in patients with an eGFR <35ml/min/1.73m2 nor in dialysis patients. High quality research is urgently required firstly to investigate the pathophysiology of SCD in patients with CKD/ESRD and then to establish optimum management strategies.

Prof José Manuel Valdivielso, MD, PhD

Vascular and Renal Translational Research Group, UDETMA, REDinREN del ISCIII, IRBLleida, Lleida, Spain.

Dyslipidaemia in CKD – emerging treatments: an affordable improvement or just a privilege for few?

Atherosclerosis represents the cause of the majority of the deaths worldwide. Dyslipidemia is the main cause of atherosclerosis, and very efficacious advances in its treatment have become recently available. Although cardiovascular events are the main cause of death in chronic kidney disease (CKD) patients, the contribution of atherosclerosis is still a matter for debate. Recent studies investigating the specific contribution of atheroma plaque to mortality in CKD have demonstrated that atherosclerosis is a risk factor very strongly associated with the incidence of cardiovascular events. Indeed, atherosclerosis seems to be accelerated in those patients. Furthermore, and although cholesterol levels are usually not elevated or even low in advanced stages of CKD, its early contribution to the progression of atherosclerosis is clear. Changes in lipidic profile in CKD also involve hypertriglyceridemia, which it has further shown to be a risk factor for higher atheromatosis in CKD. More subtle changes in the number, size and the composition of lipoproteins have been revealed to be involved in the high-risk profile of CKD patients. Therefore, it seems that treatments for dyslipidemia should have a clear effect in CKD patients. Among such treatments, inhibitors of PCSK9 have become a very efficacious way to decrease cholesterol. PCSK9 is a protein that binds to LDL receptor when is occupied with LDL and induces its intracellular degradation decreasing its surface levels. The treatments acts inhibiting the binding of PCSK9 to LDL receptor, increasing its recycling to the surface of the cell and the elimination of LDL particles from circulation. The possible impact of such treatments in CKD-related atherosclerosis is unknown.

Prof Carmine Zoccali, MD, FASN, FERA

Renal Research Institute, New York USA, Istituto di Biologia molecoalare e genetica (BIOGEM), Ariano Irpino (Avellino) and Associazione Ipertensione Nefrologia e Trapianto Renale (IPNET), Reggio Calabria, Italy.

Artificial Intelligence in Cardiovascular and Renal Medicine

Artificial intelligence and machine learning already influence nearly every aspect of the human activities, and medicine in particular. Medical specialties like nephrology and cardiology are increasingly pervaded by this trend, from diagnosis to prognosis and therapy and prevention. This talk provides a guide for clinicians on relevant aspects of artificial intelligence and machine learning, illustrates selected applications of these methods in nephrology and cardiology to date, and identifies how cardiovascular and renal medicine could incorporate artificial intelligence in the future. In particular, predictive modeling concepts extracted from the current literature will be discussed in some depth. In closing, I will deal with the philosophical and social implications of artificial intelligence relevant to cardiology such as feature selection and frequent pitfalls such as improper dichotomization. Second, it discusses common algorithms used in supervised learning and reviews selected applications in cardiology and related disciplines.

Prof Radovan Hojs, MD, PhD

University Clinical Centre Maribor, Clinic for Internal medicine, Department of Nephrology
and
Faculty of Medicine, University of Maribor, Maribor, Slovenia.

Hypertension as a risk factor on CKD progression

Hypertension is very common worldwide, and the prevalence is already higher than 30% in many countries. Unfortunately, the prevalence of hypertension has increased in last decades, especially in low and middle-income countries. Hypertension is both a cause and consequence of chronic kidney disease (CKD). In patients with CKD, hypertension is present in up to 90%. Hypertension is also a major contributor of CKD progression. Control of hypertension is important in CKD patients as it leads to slowing of disease progression. Existing guidelines from hypertension, diabetes and renal societies do not offer a consensus on optimal blood pressure targets in patients with CKD. Non-pharmacological interventions are useful in reducing blood pressure but are rarely sufficient to control blood pressure in CKD patients. These patients will often require antihypertension medications, mostly combination of them, to control blood pressure adequately. Certain medications provide also additional blood pressure independent renoprotective action. In this review, existing evidence and guidelines will be critically appraised.

Prof Pantelis A. Sarafidis, MD, MSc, PhD

Associate Professor in Nephrology, School of Medicine, Aristotle University of Thessaloniki, Greece
Honorary Consultant in Nephrology, Department of Nephrology, Hippokration Hospital, Thessaloniki, Greece.

Hypertension in dialysis: Is there anything new? How to make diagnosis and which targets

The prevalence of hypertension in patients undergoing hemodialysis or peritoneal dialysis approaches 80-90% in studies with ambulatory blood pressure (BP) monitoring.

However, less than 30-35% of patients have adequate BP control. Pre- and postdialysis measurements are not valid estimates of interdialytic BP levels, and only home or ambulatory BP is associated with cardiovascular events and in hemodialysis patients. Thus, hypertension diagnosis and management should be based on home or ambulatory BP measurements. Sodium and water excess is the most important of several mechanisms involved in the complex pathophysiology of hypertension in dialysis; other mechanisms include increased arterial stiffness, endothelial dysfunction, activation of renin-angiotensin-aldosterone system and sympathetic-nervous-system. Treatment targets in patients on dialysis are not examined in proper randomized trials. As such, the current consensus is to try achieving intra- and interdialytic ambulatory BP levels that are not associated with increased cardiovascular risk in hemodialysis and the target levels recommended for patients with CKD in peritoneal dialysis. The primary goal in hypertension management in dialysis patients is achievement of patients' dry weight and avoidance of sodium gain. After non-pharmacological measures are properly implemented, the introduction of drug treatment can further help in achieving the optimum BP. All major antihypertensive classes, with the exception of diuretics, can be considered in hypertension management, as agents from most these classes were associated with reduced cardiovascular risk in previous trials.

The choice of a specific antihypertensive drug should be based on the co-morbid conditionsof the patient, and the pharmacologic characteristics of the agent, including dialyzability.

Olga Balafa, MD, PhD

Department of Nephrology, University Hospital of Ioannina, Ioannina, Greece.

Hypertension in kidney transplant patients- where we stand today?

Hypertension is a highly prevalent complication in kidney transplant recipients (KTRs) and is associated with cardiovascular morbidity and graft failure. Pathogenesis is multifactorial involving a) traditional risk factors b) chronic kidney disease related factors (mainly volume-overload) and c) kidney transplant specific factors like donor-associated variables and immunosuppressant medication (corticosteroids and calcineurin inhibitors). Despite the clinical impact of hypertension in KTRs, we still have not established the optimal blood pressure (BP) goal or the optimal antihypertensive medication as randomized controlled (RCT) studies are missing. Recent KDIGO guidelines (2021) recommend a target BP <130/80 mmHg using standardized office BP measurement, mainly based on CKD population studies. However various studies underline the fact that hypertension in KTRs is not adequately diagnosed and controlled by office BP measurement, as 30% of these measurements misclassify hypertension. A recent meta-analysis demonstrated the importance of ABPM, since KRTs present a high prevalence of masked and uncontrolled hypertension (26 and 56% respectively) and a lesser white coat effect (10%). Current evidence suggests calcium channel blockers could be the preferred first-step antihypertensive agents, as they improve graft function and reduce graft loss. Nevertheless, KDIGO guidelines recommend CCB or renin-angiotensin system inhibitor as first line-therapy in KRTs according to physician judgment and familiarity with these agents. In any case no RCT has evaluated cardiovascular and kidney effects of these medications in KRTS so far.

Prof Sebastjan Bevc, MD, PhD

Department of Nephrology, University Medical Center Maribor
and
Faculty of Medicine, University of Maribor, Slovenia.

Evolving concepts on volume control in haemodialysis: Bioimpedentiometry and B-Lines are complementary each other or....

Fluid volume management is an important goal of dialysis treatment. Volume overload is directly associated with hypertension, increased arterial stiffness, left ventricular hypertrophy, heart failure, and higher rates of mortality and morbidity of patients on dialysis.

Optimal hydration control and the accurate assessment of fluid status in dialysis patients remain a challenge for clinical nephrologists.

In recent years, new non-invasive bedside tools such as bioelectrical impedance assessment (BIA) and ultrasound of lung (LUS) have been developed and accepted to allow objective assessment of fluid status. BIA predicts body composition, including total body water (TBW), intracellular water (ICW), and extracellular water (ECW), and can successfully quantify hydration in dialysis patients. LUS is a technique that subjectively quantifies the interstitial fluid accumulation, defined by "B lines" or "lung comets" as reverberating artefacts arising from the pleural line due to thickened subpleural interlobular septa by oedema. BIA and LUS can be used to determine the optimal dry weight, adjust fluid removal, and drug therapies during haemodialysis. In addition, both methods can have an impact on patient's outcome.

This presentation focuses on both non-invasive tools and addresses their use for the diagnosis, prognosis, and treatment of volume overload in haemodialysis patients.

Prof Robert Ekart, MD, PhD

University Medical Centre Maribor, Clinic for Internal Medicine, Department of Dialysis, Maribor, Slovenia and
University of Maribor, Medical Faculty, Maribor, Slovenia.

Fluid volume overload and vascular stiffness in CKD patients

The kidneys play a critical role in regulating extracellular fluid volume (ECFV). Expansion of ECFV increases with declining renal function and is common in patients with chronic kidney disease (CKD). The prevalence of volume overload in the early stages of CKD and its significance are still unclear. Clinical assessment of fluid status in earlier stages of CKD is relatively difficult because physical signs of edema are of limited value. Volume overload is associated with cardiovascular disease and is a predictor of outcome in hemodialysis and peritoneal dialysis patients. Many fluid status studies have been performed in dialysis patients, but only a limited number of studies have been performed in CKD patients who are not yet on dialysis.

Another effect of CKD is arterial stiffening, which can be characterized by increased augmentation index (AIx) or carotid-femoral pulse wave velocity (cfPWV). Arterial stiffening has been positively associated with the rate of decline in renal function in CKD patients. In addition, ECFV expansion may increase arterial wall stress, leading to structural (arterial wall thickness) and functional (distensibility) changes in the arterial wall, resulting in arterial stiffening. Arterial stiffness has long been considered a complication of hypertension. However, there is a bidirectional interaction between arterial stiffness and hypertension. Among the various factors involved in the pathogenesis of arterial hypertension in CKD patients is fluid overload. It is still unclear whether fluid overload itself can increase blood pressure. The purpose of this presentation is to discuss published work in this area and to present our own results in our dialysis patients.

Prof Giovanni Tripepi

IFC-CNR & Nephrology, Dialysis and Transplantation Unit, Reggio Calabria, Italy.

Application of prognostic models in Nephrology

Prognosis, together with diagnosis and treatment, is one of the three decisional processes of clinical medicine. Prognosis aims at quantifying the risk of a certain event (e.g. death) occurring in a given patient over a predefined time period in probabilistic terms. Prognostic estimates for the risk of such an event are provided by risk prediction models, i.e. mathematical tools that provide prognostication of relevant clinical outcomes in terms of absolute risk. Risk calculators are considered as important in clinical medicine because they inform the patient to be aware of the future course of his/her disease and to guide clinicians to start or to tailor a specific therapy. Before to be applied in clinical practice, risk prediction models should be properly validated by assessing their discrimination, calibration, explained variation, and risk reclassification, this latter being a tool to evaluate the gain in risk prediction by using a new model compared with an established one. I will discuss the concepts of developing and validating risk prediction models by means of two examples, the Framingham risk calculator for prediction of coronary heart disease (CHD), and the recently published Renal Risk Score to predict progression of chronic kidney disease (CKD).

Prof Patrick Mark, MB ChB, PhD

School of Cardiovascular and Metabolic Health, University of Glasgow, Glasgow, United Kingdom.

Which eGFR method is the best for cardiovascular risk prediction in CKD patients?

It is well established the chronic kidney disease, indicated by a reduction in glomerular filtration rate is a risk factor for premature cardiovascular disease. A number of eGFR formulae (MDRD, CKD-EPI 2009 and 2021) to calculate estimated GFR (eGFR) based on serum creatinine have been developed and updated. Further cystatin based eGFR formulae have also been generated.

The goals of using eGFR formulae are both to accurately classify kidney function and additionally to indicate patients at higher risk of clinical events, most importantly kidney failure and cardiovascular disease so that preventative therapy can be instigated. Cystatin based eGFR generally is more accurate and performs better at predicting clinical outcomes but is not widely available in routine practice.

Controversy exists as some experts have suggested that eGFR formulae may label some older people with small reductions in eGFR as inappropriately having CKD and have called for 'age adapted' eGFR thresholds. However, conversely this approach may lead to people at higher risk of adverse events not being identified and offered therapies to mitigate cardiorenal risk.

In this session, I will discuss the implications of using creatinine or cystatin based eGFR to predict clinical outcomes by using large epidemiological datasets. I will make suggestions as to which approaches should be used in current practice and highlight research priorities in this area.

Prof Roberto Minutolo, MD, PhD

Division of Nephrology
University of Campania Luigi Vanvitelli, Naples, Italy.

Prediction of CKD progression among older patients

With increasing age, there are alterations in the function of the kidney accompanied by both macroscopic and microscopic changes resulting in an increased susceptibility to diverse insults. In healthy elderly population eGFR declines with age. This physiologic phenomenon has as immediate consequence the fact that by using KDIGO classification, the prevalence of CKD is inflated by those older patients with slight eGFR decline and without albuminuria. However, if this would be merely due to kidney senescence, these patients should not be classified as having CKD. For that raison, it has been recently proposed an age-adapted eGFR threshold (75, 60, and 45 mL/min/1.73m2 for age $<$40, 40-64, and $\geq$65 years) for diagnosing CKD. It has been recently demonstrated that $>$40% of patients identified as CKD using KDIGO definition were older than 65 y, with eGFR 45-59 mL/min/1.73m2 and normal UACR and therefore were not classified as CKD with age-adapted definition. More important, these patients had a renal risk similar to non-CKD elderly population (age $>$65 y and eGFR $>$60 mL/min/1.73m2). It is well known that eGFR decline in older CKD patients is slower as compared with youngers likely because higher prevalence of nephroangiosclerosis and lower albuminuria in elderly. Therefore, older CKD patients are exposed to a lower risk of ESKD and to an increased risk of death. In terms of treatment, since CVD is highly prevalent in CKD population, especially in older, withdrawal of ACEi/ARB therapy may expose these patients to an increased CV and mortality risk. Treatment with SGLT2 inhibitors seems equally effective in younger and older CKD population.

Prof Alberto Ortiz, MD, PhD

School of Medicine, IIS-Fundacion Jimenez Diaz, University Autonoma of Madrid, Friat and Redinren, Madrid, Spain.

Chronodisruption in CKD

Multiple physiological variables change over time in a predictable and repetitive manner, guided by molecular clocks that respond to external and internal clues and are coordinated by a central clock. The kidney is the site of one of the most active peripheral clocks. Biological rhythms, of which the best known are circadian rhythms, are required for normal physiology of the kidneys and other organs. They impact ton health and disease. In a recent example, the metastatic spread of cancer is achieved by the haematogenous dissemination of circulating tumour cells (CTC) was shown to depend on the awake-sleep cycle: breast cancer CTCs generated during sleep are highly prone to metastasize, whereas CTCs generated during the active phase are devoid of metastatic ability.

Chronodisruption refers to the chronic disruption of circadian rhythms leading to disease. While there is evidence that circadian rhythms may be altered in kidney disease and that altered circadian rhythms may accelerate chronic kidney disease (CKD) progression, there is no comprehensive review on chronodisruption and chronodisruptors in CKD and its manifestations. Indeed, the term chronodisruption has been rarely applied to CKD despite chronodisruptors being potential therapeutic targets in CKD patients. We now discuss evidence for chronodisruption in CKD and the impact of chronodisruption on CKD manifestations, identify potential chronodisruptors, some of them uremic toxins, and their therapeutic implications, and discuss current unanswered questions on this topic.

Key references:

1. Carriazo S, Ramos AM, Sanz AB, Sanchez-Niño MD, Kanbay M, Ortiz A. Chronodisruption: A Poorly Recognized Feature of CKD. Toxins (Basel). 2020;12(3):151.
2. Diamantopoulou Z, Castro-Giner F, Schwab FD, et al. The metastatic spread of breast cancer accelerates during sleep. Nature. 2022;607(7917):156-162

Prof. dr. Marc G. Vervloet, MD, PhD, Internist-nephrologist

Amsterdam Cardiovascular Sciences; Department of Nephrology
Amsterdam University Medical Center, The Netherlands.

Chronic kidney disease-mineral and bone disorder: changing insights form changing parameters?

Many studies have demonstrated associations of single time point concentration of calcium, phosphate and PTH with clinical outcomes such as mortality, especially so in people treated by dialysis. Most of these associations are U-shaped with an optimal range, which dictates target ranges in treatment guidelines.

Values over time of these laboratory markers of CKD-MBD may provide additional information. Recent data suggest that persistence of hyperphosphatemia for instance, reflecting prolonged exposure to this specific uremic toxin, underscores current practice, that aims to lower its concentration. In addition, changes of these parameters over time may reflect the natural history of MBD in end stage kidney disease or may reflect the success or failure of treatments employed. This is supported by data for changing phosphate categories, showing that improvement of hypophosphatemia into the normal range is associated with improved outcome. Remarkably not all studies did demonstrate benefit of reduced phosphate when hyperphosphatemia was present at baseline, and that important differences exist between man and woman. However, a most recent large observational study did observe that the higher baseline phosphate concentration was, the greater the benefit of more phosphate reduction, in terms of mortality risk. Remarkably, this benefit was more pronounced for short term (3 months) as compared to long term risk. With regards to PTH, it was found that the proportion with low PTH, below the optimal range, is relatively high. In general, a rise in PTH over time, except for those with overt elevated levels, was associated with improved outcome.

Prof Jolanta Malyszko, MD, PhD

Department of Nephrology, Dialysis and Internal Medicine, Warsaw Medical University, Poland.

Chronic and acute hyperkalemia latest KDIGO Controversy Conference

Hyperkalemia is a common electrolyte disorder observed in the clinical practice. Hyperkalemia is uncommon when glomerular filtration rate (GFR) is greater than 60 ml/min per 1.73 m2 and increases in prevalence with lower GFR. It is often associated with underlying predisposing conditions, such as moderate or severe kidney disease, heart failure, diabetes mellitus, or significant tissue trauma. Additionally, medications, such as inhibitors of the renin-angiotensin-aldosterone system, potassium-sparing diuretics, nonsteroidal anti- inflammatory drugs, succinylcholine, and digitalis, are associated with hyperkalemia. Kidney Disease: Improving Global Outcomes (KDIGO) convened a controversy conference to identify evidence and address controversies on potassium management in kidney disease. The toxic effects of hyperkalemia on the cardiac conduction system are potentially lethal. The ECG is a mainstay in managing hyperkalemia. Membrane stabilization by calcium salts and potassium-shifting agents, such as insulin and salbutamol, is the cornerstone in the acute management of hyperkalemia. However, only dialysis, potassium-binding agents, and loop diuretics remove potassium from the body. Frequent reevaluation of potassium concentrations is recommended to assess treatment success and to monitor for recurrence of hyperkalemia.

Prof Lucia del Vecchio, MD, PhD

Department of Nephrology and Dialysis, Sant'Anna Hospital, ASST Lariana, Como, Italy.

The HIF factor and the cardiovascular system: possible strengths and weakness of HIF stabilizers

Anaemia is a common complication of chronic kidney disease; it has been consistently associated with poor outcome. Despite general effectiveness and relatively good tolerability, in recent years the safety of erythropoiesis stimulating agents (ESA) has been a matter of debate. In particular, ESA use at high doses and when aiming at near to normal haemoglobin levels has been related to increased risk of mortality, cardiovascular events and thrombosis. The physiological mechanisms involved in the regulation of the body to hypoxia have been investigated in depth; the hypoxia inducible factors (HIF) were identified having a central role. Among the pathways controlled by the system, HIF activation stimulate the synthesis of erythropoietin and increase iron availability. New molecules were then developed that take advantage of this mechanism. They inhibit the prolyl hydroxylase enzymes (PH) and increase the activity of the hypoxia-inducible factors (HIF). It follows increased erythropoiesis and a decrease in serum hepcidin also in inflamed patients.

Several HIF=PH inhibitors have undergone clinical development; some of them have already entered clinical use. Differing from ESA, they are administered orally. Overall, they effectively correct anaemia in non-dialysis and dialysis patients.

Even if HIF-PH inhibitors expose patients to lower erythropoietin levels than ESA, this does not translate into a better safety profile. For this reason, they should be considered a valid alternative to current ESAs. HIF-PHIs seem more effective in subjects who are hypo-responsive to ESAs; if confirmed, this may be one circumstance when these drugs may be the agent of choice.

Prof Gérard M London, MD, PhD

FCRIN INI-CRCT Cardiovascular and Renal Clinical Trialists, Manhes Hospital, Paris, France.

The age-stiffness relationships of elastic and muscular arteries in control population and ESRD patients

Aging is a powerfull and independent risk factor for vascular disorders and heart failure. The aorta and large central arteries became stiffer with advancing age with less or absent relationship of stiffness to age in the peripheral muscular conduit arteries, The consequences are leading to the disappearance or inversion of the arterial stiffness gradient and less protection of the microcirculation from high arterial pressure transmission. These changes have a double impact: on the heart/upstream, with left ventricular hypertrophy and decreased coronary perfusion; and, downstream, on renal and brain microcirculation (decrease in glomerular filtration and cognitive functions). Cardiovascular disease is an important cause of morbidity and mortality in patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD). All epidemiological studies have clearly shown that accelerated arterial and cardiac aging is characteristic of these populations. These conclusions are primarily based on age/aortic pulse wave velocity correlation characterized by significantly higher slope (beta coefficient) of the relationship. The influence of age-peripheral conduit relationships on stiffness gradient in ESRD are less described with conflicting results. The analyses of age to aortic and peripheral arteries stiffness and stiffness gradients in different populations of ESRD - diabetics and non-diabetics and eventual therapeutical interventions will be presented.

Prof Ziad A. Massy, MD, PhD

Service de néphrologie, CHU Ambroise Paré, APHP, 92104 Boulogne-Billancourt/Paris, and Centre de recherche en épidémiologie et santé des populations (CESP), Université Paris-Saclay, Versailles Saint-Quentin, INSERM UMRS 1018, 94807 Villejuif, France.

New insights on cardiovascular disease and calcification in CKD patients

The prevalence of cardiovascular morbidity and mortality is higher in patients with chronic kidney disease (CKD)-especially those with end-stage kidney disease-than in the general population. The contribution of atherosclerosis to cardiovascular disease in patients with CKD although present in CKD patients is partial. Recent reports favor the involvement of additional cardiovascular disease, such as arteriosclerosis (characterized by vascular stiffening), vascular calcification, congestive cardiomyopathy, and sudden cardiac death. The cardiovascular events associated with atherosclerosis are more often fatal in patients with CKD than in individuals without CKD.

Based on clinical and experimental findings, we hypothesized the following: the initial cardiovascular abnormalities in the CKD setting include arteriosclerosis, left ventricular diastolic dysfunction, and left ventricular hypertrophy, abnormalities that, in adult patients, are often accompanied and/or associated with atherosclerosis. The prevalence of atherosclerosis and vascular calcification increases with age, and CKD is considered of a model of accelerating ageing. Atherosclerosis and vascular calcification are aggravated by CKD. However, atherosclerosis in the opposite of vascular calcification is not specifically induce by CKD.

Uremic toxins constitute nontraditional CKD-specific cardiovascular risk factors that alter the endothelial functions by inducing inflammation an oxidative stress, and then later on worsen clinical outcomes. The interactions between uremic toxins make the pathophysiology of cardiovascular complications even more complex. Currently, studies of the respective individual effects of diet, binders, sorbents, and hemodialysis on clinical outcomes are limited. Future interventional studies with multi-prolonged interventions focused on hard end-points compared with classical and uncontrolled treatments have the potential to generate higher-grade evidence.

Dr. Claudia Torino, MSc, PhD

Researcher - Clinical Epidemiology and Pathophysiology of Renal Diseases and Hypertension
Laboratory of Bioinformatics
CNR-IFC, Reggio Calabria Unit, Reggio Calabria, Italy

The Lust 2 trial: where are we now?

Heart failure (HF), a high-risk condition, is frequent among CKD patients, with an incidence of 17% - 21% (JASN 2007;18:1307–1315). Lung congestion measured by ultrasound (US) is a strong risk factor for decompensated heart failure in patients with HF (ESC Heart Fail. 2020; 7:2621–2628) and for death and cardiovascular events in HD patients (JASN 2013; 24:639-46). Two randomized trials (Eur J Heart Fail. 2019; 21:1605-1613; Heart 2020; 0:1–6), adopting lung US as a guide to treatment in patients with HF, registered a remarkable risk reduction in acute decompensated HF recurrence in these patients. Furthermore, secondary analyses in the LUST study documented a 63% reduction of the rate ratio of repeated episodes of decompensated HF in HD patients.

We designed a randomized trial in stage 3b-5 CKD patients with decompensated HF to test the efficacy of a treatment strategy guided by lung water as measured by lung US. In the LUST2 trial, patients randomised in the active arm will have diuretic treatment guided by lung US performed by the attending nephrologist; in the control arm, diuretic treatment will be guided by standard clinical criteria. Visits will be scheduled at baseline, 2, 4, 6, 9, 12 months. The primary study endpoint is the incidence rate of decompensated heart failure episodes requiring hospitalization or all-cause death over 1 year follow up.

The LUST2 trial, involving 14 European centres, will clarify if the systematic application of lung US has potential for limiting recurrence of decompensated HF in patients with advanced CKD and HF.

Prof Evangelia Ntounousi, MD, PhD

Nephrology Department, School of Health Sciences, University of Ioannina,Ioannina.

Mechanisms of renal function deterioration in heart failure

Abundant experimental and clinical evidence is showing that kidney dysfunction is a frequent occurrence in all phenotypes of heart failure (HF), involving complex, intertwined pathophysiological mechanisms. Reduced renal perfusion and venous congestion have been traditionally considered as the classical culprits responsible for kidney function impairment in HF. The reduced renal blood flow in the setting of a low-flow state induces activation of the renin-angiotensin and sympathetic nervous system, vasopressin secretion, further perpetuating the vicious circle. Accordingly, the augmented activation of the neurohumoral axis results in preglomerular vasoconstriction and decreased intraglomerular pressures on the one hand, as well as increased proximal tubular sodium and water reabsorption in order to maintain effective plasma volumes. Eventually, reduction of the GFR, tubular injury and a worsened congestive state ensue whereas glomerulosclerosis and interstitial fibrosis develop in the long term. Furthermore, the low-resistance characteristics of the renal vasculature together with low oxygen tension in the outer medulla render the kidneys sensitive to hypotension-related injury. Notably, the presence of a low cardiac output only partly explains the pathophysiology of kidney dysfunction. The specific mechanisms by which elevated central venous pressures in the context of HFpEF, result in renal venous hypertension, increased renal resistance, and ultimately diminished intrarenal blood flow are a subject of ongoing research.

Between the failing heart and the kidneys, several other pathological mechanisms have come to the spotlight, including an inflammatory state, altered immune responses, endothelial dysfunction and amplified oxidative stress. In addition, the presence of shared risk factors for cardiovascular and kidney disease, metabolic and nutritional changes, development of anemia and iron deficiency status might further exacerbate renal function in the setting of HF. Finally, the possible nephrotoxic effects of medications prescribed in HF, should be kept in mind.

Assoc. Prof. Beatriz Fernández Fernández, MD, PhD

Nephrology Department, Fundación Jimenez Díaz, Madrid, Spain
Universidad Autónoma de Madrid, Spain.

Notes on renal artery stenosis

Renal artery stenosis (RAS) is one of the major causes of hypertension and according to latest reports is the cause of hypertension in 1% to 10% in some series. Atherosclerosis or fibromuscular dysplasia are the most frequent causes of RAS. In this session we will highlight the cause, pathophysiology, presentation and related complications (CKD and ESRD) , and will review on the role of the interprofessional team in its management.

Sponsors

ERA - EUROPEAN RENAL ASSOCIATION

FRESENIUS MEDICAL CARE SLOVENIJA

AMGEN

ASTELLAS

BAXTER

LEK


EuReCa-M
European Renal
and Cardiovascular Medicine