Towards a Cardiovascular-Kidney-Metabolic prevention approach

The European Renal Association (ERA) strongly welcomes the upcoming EU Cardiovascular Health Action Plan. Recognising that cardiovascular disease (CVD) serves both as a leading health burden in itself and as a critical risk factor for chronic kidney disease (CKD) and other metabolic conditions, we fully support the EU's coordinated efforts to curb CVD morbidity and mortality.

The prevalence of CKD is rising rapidly (850 million people worldwide[1], 100 million in Europe). As highlighted by the WHO[2], CKD is among the fastest-growing causes of death, projected to be the **third leading cause of death in high-income countries by 2050**[3]. Most of the increased mortality risk observed in patients with CKD is due to CVD[4 5].

Indeed, CKD is a potent and independent risk factor for CVD. Individuals with CKD face elevated risks of developing CV death, coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral vascular disease and sudden cardiac death[6 7 8].

Increased CV risk begins with even low levels of renal impairment and in people with normal kidney function and mildly increased albuminuria. The risk then increases exponentially with both worsening renal function and increasing albuminuria with the highest risk in those with both[4 5]. There is a biological plausibility underlying a cause-and-effect relationship between CKD and CVD, supported by clinical trials[9 10 11 12 13].

Among patients with advanced CKD (stages 4–5), the prevalence of CVD is ~50%, with CV causes accounting for 40–50% of total mortality, compared with 26% in the general population[14].

Thus, CKD should be regarded both as a likely consequence of CVD and as a crucial contributor to the overall CVD burden.

This has been recognised by the European Society of Cardiology and 12 European Scientific Societies, which identified CKD, along with diabetes and familial hypercholesterolaemia, as three conditions requiring targeted primary prevention to reduce CVD risk[15 16]. Moreover, the American Heart Association conceptualised the **Cardiovascular-Kidney-Metabolic (CKM) syndrome** to emphasise the close links between overweight-obesity, type 2 diabetes mellitus, kidney health and CV health[17].

It is imperative that CVD, CKD and diabetes be addressed in an integrated manner —as **CKM syndrome**— to effectively tackle the shared and interrelated drivers of CV and related conditions, as recommended by cardiology[15 17], diabetes and renal[6 16] scientific associations, the Council[7] and the WHO[2].

The ERA has recently developed the ABCDE framework for the holistic assessment of CKM health, that can be adapted to the different national health care systems.

ABCDE stands for

- Albuminuria
- Blood pressure
- Cholesterol
- Diabetes (i.e., glycemia)
- Estimated glomerular filtration rate[4 5 16 18]

i.e., for one urine test, one physical examination feature, and three blood analytes that allow to correctly fit individuals into major categories in the CKM spectrum requiring specific drug interventions for the primary prevention of CVD, according to the 2021 ESC guidelines[15]. It summarises the CKM assessments that should be provided by the healthcare system, as other key elements to assess CKM health can be self-assessed such as the body mass index, the smoking status and lifestyle.

In conclusion:

1. All patients at risk of CKD should be screened for CKM health using the ABCDE approach:
   - Albuminuria: readily quantifiable from a spot urine sample as the urinary albumin:creatinine ratio (uACR)
   - Blood pressure: measured as per national or international guidelines (eg ESC BP Guidelines)
   - Cholesterol: lipid profile (total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides)
   - Diabetes: random and/or fasting plasma glucose in addition to a HbA1c measured in a blood test
   - Estimated glomerular filtration rate; calculated from a serum creatinine using a validated equation
2. Evidence shows that screening for CKD using albuminuria is cost-effective, at least in those aged >45[19].

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