

Cardiovascular–Kidney–Metabolic Syndrome: A Paradigm Shift in Chronic Disease Care

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Cardiovascular–Kidney–Metabolic (CKM) syndrome is a systemic health disorder characterized by the pathophysiological interactions among metabolic risk factors (such as obesity and diabetes), chronic kidney disease (CKD), and the cardiovascular system. It is not considered a single disease but rather a framework to describe how these interconnected problems can lead to multi organ dysfunction and a high rate of adverse cardiovascular outcomes.

CKM Staging Construct

The syndrome is classified into five stages that reflect its progressive nature and the stepwise increase in absolute cardiovascular disease (CVD) risk.

- **Stage 0:** No CKM risk factors are present; the primary focus is on primordial prevention and maintaining ideal cardiovascular health.
- **Stage 1: Excess or dysfunctional adiposity** is present, defined by overweight, abdominal obesity, or impaired glucose tolerance (prediabetes) without other metabolic factors or CKD.
- **Stage 2:** Presence of **established metabolic risk factors** (such as hypertension, type 2 diabetes, hypertriglyceridemia, or metabolic syndrome) or **moderate-to-high risk CKD**.
- **Stage 3: Subclinical CVD** is identified in the setting of other CKM risk factors (e.g., elevated cardiac biomarkers like NT-Pro BNP or abnormal imaging), or the patient has risk equivalents like very high-risk CKD or high predicted 10-year CVD risk.
- **Stage 4: Clinical CVD** (such as heart failure, stroke, coronary heart disease, or peripheral artery disease) in the presence of CKM risk factors. This stage is further divided into **Stage 4a** (without kidney failure) and **Stage 4b** (with kidney failure).

Screening and Diagnosis

Screening is recommended across the life course,

beginning as early as age 3 for blood pressure and obesity. For adults, diagnostic evaluations include:

- **Anthropometric measurements:** Annual checks of BMI and waist circumference.
- **Laboratory tests:** Fasting blood glucose or HbA1c, lipid panels (including triglycerides), and renal function markers like eGFR and uACR.
- **Advanced diagnostics:** For Stage 3, cardiac biomarkers (BNP/NT-Pro BNP, high-sensitivity troponin) or imaging (EKG/ECG, echocardiogram, or coronary artery calcium screening) may be used to identify heart stress or subclinical atherosclerosis.

Management and Treatment

The goal of management is to delay or halt the progression of the syndrome and prevent clinical CVD events.

- **Lifestyle Interventions:** Fundamental components include a heart-healthy diet (limiting salt, sugary drinks, and processed foods), at least 30 minutes of physical activity most days, stress management, and tobacco cessation.
- **Pharmacotherapy:** Cardioprotective agents such as **SGLT2 inhibitors** and **GLP-1 receptor agonists** are prioritized, particularly for patients with diabetes and CKD. Other essential medications may include **ACE inhibitors** or **ARBs** for blood pressure control and Finerenone for kidney protection.
- **Holistic Care Model:** An interdisciplinary team approach involving primary care, cardiology, nephrology and endocrinology is emphasized to reduce fragmented care. Additionally, clinicians must systematically screen for **social determinants of health (SDOH)**, such as food or housing insecurity, and integrate these findings into the care plan.

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