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Although the mutually harmful relationships between metabolic diseases, chronic kidney disease, and cardiovascular diseases are well recognized, there are differing views on the extent to which these conditions together constitute a syndrome. In a recent American Heart Association (AHA) presidential advisory, published in *Circulation*, the adverse interplay among these diseases is referred to as cardiovascular-kidney-metabolic (CKM) syndrome. AHA presidential advisory defines cardiovascular-kidney-metabolic syndrome and guides how to better detect, prevent, and manage it.



About the AHA presidential advisory

Metabolic diseases, such as obesity and type 2 diabetes, as well as chronic kidney diseases, can cause damage to nearly all major organ systems. Furthermore, they increase the risk of cardiovascular diseases, such as heart failure, atrial fibrillation, coronary artery disease, stroke, and peripheral artery diseases. Health and mortality risks increase by having more than one of these conditions, especially due to cardiovascular diseases.

The advisory defines CKM syndrome as a health disorder attributable to connections among obesity, diabetes, chronic kidney diseases, and cardiovascular diseases, including heart failure, atrial fibrillation, coronary heart disease, stroke, and peripheral artery disease. CKM



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syndrome includes those at risk for cardiovascular diseases and those with existing cardiovascular diseases.

This syndrome increases the risk of developing and progression of cardiovascular diseases. Inflammation, dyslipidemia, hypertension, and insulin resistance from CKM syndrome seem to accelerate atherosclerotic cardiovascular disease. Nonetheless, the connection between CKM syndrome and heart failure and arrhythmias, as well as between cardiovascular disease and an increased risk of later kidney disease, remains under-researched.

The advisory guides how to stage CKM syndrome, predict its cardiovascular outcomes, and manage, prevent, and even reverse it in adults and children. In recognition of the importance of these concepts, this advisory proposes a novel model that classifies cardiovascular-kidney-metabolic syndrome into stages :

stage 0: no cardiovascular-kidney-metabolic risk factors present (absence of excess/dysfunctional adiposity, metabolic risk factors, chronic kidney disease);

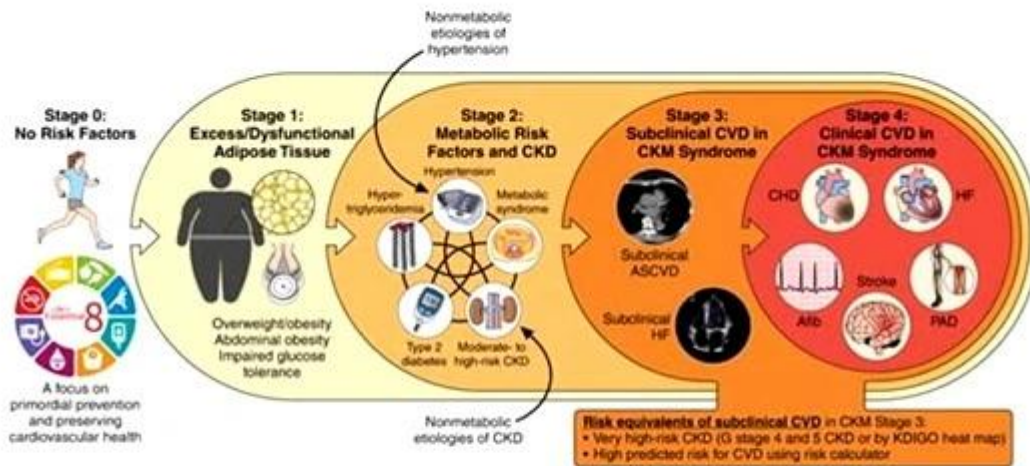
stage 1: excess adiposity, dysfunctional adiposity, or both, with dysfunctional adiposity defined as hyperglycemia or prediabetes;

stage 2: metabolic risk factors, moderate- to high-risk chronic kidney disease, or both;

stage 3: subclinical cardiovascular disease overlapping with cardiovascular-kidney-metabolic risk factors, very high-risk chronic kidney disease, or high predicted cardiovascular disease risk;

stage 4: clinical cardiovascular disease overlapping with cardiovascular-kidney-metabolic risk factors. Stage 4 is further divided into stages 4a (without kidney failure) and 4b (with kidney failure).

Stages of Cardiovascular-Kidney-Metabolic Syndrome



Abbreviations: Afb indicates atrial fibrillation; ASCVD, atherosclerotic cardiovascular disease; CHD, coronary heart disease; CKD, chronic kidney disease; CKM, cardiovascular-kidney-metabolic; CVD, cardiovascular disease; HF, heart failure; KDIGO, Kidney Disease Improving Global Outcomes; and PAD, peripheral artery disease.

Blumenthal, C. E., et al., Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association, 2023, *Circulation*.



Original illustration from Ndumele et al. *Circulation*. 2023

The designations of moderate-, high- and very high-risk chronic kidney disease are defined by the Kidney Disease Improving Global Outcomes (KDIGO) Heat Map, which creates categories based on combinations of estimated glomerular filtration rate and albuminuria. The KDIGO classifications of moderate-, high- and very high-risk chronic kidney disease reflect increasing risk for kidney failure, cardiovascular disease, and all-cause mortality.

The CKM staging model emphasizes the progressive pathophysiology of CKM syndrome and the significance of early detection of CKM-related changes to support prevention efforts. It highlights the stepwise increase in absolute risk for cardiovascular diseases associated with later stages.

According to the advisory, screening for risk factors should begin early in life and increase in frequency if CKM syndrome stages progress. Notably, gender-related physiological and pathophysiological differences in the presentation and progression of CKM syndrome are not well understood. Neither are the influences of genetic risk factors. Also, the risk of CKM



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syndrome varies significantly among racial, ethnic, and social groups.

Conclusion

CKM health reflects the intricate interrelationships between metabolic risk factors, chronic kidney disease, and the cardiovascular system. Poor CKM health has significant implications for adverse clinical outcomes, most notably cardiovascular morbidity, and premature mortality. However, there is a growing array of therapies and healthcare strategies that have a great potential to improve outcomes for patients with CKM syndrome.

This article was published in *Circulation*.

Journal References

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