

Table S1. Characteristics of Included Studies

First Author (Year)	Study Design	Population / Condition	Systems Involved	Primary Focus	Key Findings
Mutruc et al. (2025) [8]	Narrative review	CKM-related cardiometabolic multimorbidity	Cardiovascular; renal; metabolic	Pathophysiology, epidemiology, and staging of CKM syndrome	Identifies shared mechanisms linking cardiovascular disease, chronic kidney disease, obesity, and type 2 diabetes within a unified CKM framework.
Godoy-Matos et al. (2025) [9]	Narrative review	Metabolic syndrome, MASLD, cardiometabolic disease	Cardiovascular; renal; hepatic; pancreatic; adipose; vascular	CARDIAL-MS multisystem metabolic framework	Emphasizes adipose dysfunction, ectopic fat, and hepatokine imbalance as drivers of multisystem metabolic injury; proposes a four-stage CARDIAL-MS model.
Marassi & Fadini (2023) [10]	Narrative review	Adults with CKM syndrome	Cardiovascular; renal; metabolic; vascular	CKM staging and integrated risk framework	Demonstrates strong epidemiologic clustering of diabetes, cardiovascular disease, and CKD, with bidirectional risk amplification.
Targher et al. (2024) [13]	Narrative review	Adults with MASLD/MASH	Hepatic; cardiovascular; renal; metabolic; oncologic	Systemic complications of MASLD	MASLD independently associated with cardiovascular events, CKD, and extrahepatic cancers; risk increased with fibrosis severity.
Hutchison et al. (2023) [14]	Narrative review	Adults with MASLD/MASH	Hepatic; endocrine; metabolic	Endocrine regulation of MASLD	Hormonal axes modulate hepatic steatosis, fibrosis, and systemic insulin resistance, positioning MASLD as an endocrine–metabolic disorder.
Agustanti et al. (2023) [15]	Systematic review and meta-analysis	Adults with MAFLD	Metabolic; renal	MAFLD–CKD association	MAFLD associated with higher prevalent and incident CKD; renal risk increased with advanced hepatic fibrosis.
Zhou et al. (2023) [16]	Systematic review and meta-analysis	Adults with MAFLD	Hepatic; renal; metabolic	MAFLD and CKD risk	Fibrosis-based MAFLD phenotypes conferred greater CKD risk than steatosis alone.
Massy & Druke (2025) [17]	Narrative review	CKM syndrome framework	Cardiovascular; renal; metabolic; vascular	Integrated CKM staging and risk prediction	Shows that inclusion of eGFR and albuminuria improves adverse outcome prediction across CKM stages.
Sattar et al. (2021) [18]	Systematic review and meta-analysis of RCTs	Adults with type 2 diabetes	Cardiovascular; renal; metabolic; vascular	Cardiovascular and renal outcomes of GLP-1 receptor agonists	GLP-1 receptor agonists reduced major cardiovascular events, mortality, and kidney disease progression, indicating parallel cardio–renal benefit.
McGuire et al. (2021) [19]	Systematic review and meta-analysis of RCTs	Adults with type 2 diabetes	Cardiovascular; renal; metabolic	Cardio–renal effects of SGLT2 inhibitors	SGLT2 inhibitors reduced heart failure hospitalization and slowed CKD progression, independent of glycemic control.
Lincoff et al. (2023) [20]	Randomized controlled trial	Adults with obesity, no diabetes	Cardiovascular; renal; metabolic	Cardiovascular outcomes of semaglutide	Semaglutide reduced major cardiovascular events and mortality, with favorable renal signals.

Zou et al. (2025) [22]	Population-based prospective cohort	Adults with osteoarthritis	Cardiovascular; renal; metabolic	Osteoarthritis and CKM multimorbidity	Osteoarthritis associated with higher risk of dual and triple CKM multimorbidity and accelerated disease progression.
Ostrominski et al. (2023) [23]	Serial cross-sectional population study	U.S. adults (NHANES 1999–2020)	Cardiovascular; renal; metabolic	Population burden of multimorbidity	Over one quarter of adults had ≥ 1 cardiometabolic or renal condition; $\sim 8\%$ had triple-system involvement.
Lee (2025) [24]	Longitudinal cohort study	Adults with MASLD	Hepatic; cardiovascular; metabolic	Liver fibrosis and subclinical atherosclerosis	Time-updated FIB-4 independently predicted progression of coronary artery calcification.
Nzobokela et al. (2025) [25]	Narrative review	CRHM-related disorders	Cardiovascular; renal; hepatic; metabolic	Shared mechanisms and biomarkers	Identifies inflammation, oxidative stress, and insulin resistance as shared drivers; highlights suPAR, galectin-3, and GDF-15 as integrative biomarkers.
Daschner et al. (2025) [26]	Observational cohort study	Adults undergoing coronary angiography	Cardiovascular; renal	Protein carbamylation and vascular risk	Carbamylated albumin associated with arterial stiffness and increased cardiovascular and all-cause mortality.
Geertsema et al. (2024) [27]	Prospective population-based cohort	General population (PREVEND)	Renal; cardiovascular	Oxidative stress and CKD risk	Elevated serum peroxiredoxin-4 independently predicted incident CKD.
Zhou et al. (2025) [28]	Prospective cohort study	Adults with CKM stages 0–3	Cardiovascular; renal; metabolic	Adiposity-based metabolic risk indices	TyG-derived indices outperformed BMI in predicting cardiovascular and all-cause mortality.
Zhang et al. (2025) [29]	Systematic review and meta-analysis	Adults with and without NAFLD	Cardiovascular; hepatic; metabolic	Prognostic value of fibrosis scores	FIB-4 and NAFLD Fibrosis Score predicted cardiovascular events and mortality independent of NAFLD status.
Theodorakis & Nikolaou (2025) [30]	Narrative review	Adults with cardiometabolic disease across CKM and CRHM spectra	Cardiovascular; renal; hepatic; metabolic	Integrated management of CRHM syndrome and role of metabolic therapies	Extends CKM to a CRHM framework incorporating MASLD and highlights coordinated cardio-renal-hepatic benefits of contemporary metabolic therapies.