

Review Article

Cardio-renal-metabolic laboratory profile: an integrated strategy for the prevention and management of chronic non-communicable diseases

Luis Figueroa Montes^{1*}

¹Clinical Pathologist, Biochemistry Laboratory, Hospital III Suarez Angamos EsSalud, Lima, Peru

Article Info

*Corresponding Author:

Luis Figueroa Montes

E-mail: patologoclinico@gmail.com

Biochemistry Laboratory, Hospital III Suarez Angamos

EsSalud, Lima, Peru

Keywords

chronic kidney diseases of uncertain etiology, diabetes mellitus, obesity, cardiovascular diseases, metabolic syndrome

Abstract

Objective: This article emphasizes the need to integrate cardiovascular, renal, and metabolic assessments into routine clinical practice, with the aim of improving the prevention, diagnosis, and management of chronic non-communicable diseases (NCDs).

Methods: We conducted a comprehensive review of the current medical literature on cardio-renal-metabolic syndrome, alongside a critical analysis of traditional clinical profiles. Based on these findings, we propose a novel integrated laboratory profile that captures the interconnections between these systems, aiming to enhance diagnostic accuracy and patient management.

Results: Significant gaps in current fragmented assessments were identified, leading to the development of a profile that integrates key biomarkers from all three systems for a more comprehensive and accurate evaluation. This profile will be implemented according to the complexity of the care levels and according to the patient's stage of cardio-renal-metabolic syndrome.

Conclusion: Implementation of the new integrated cardiorenal-metabolic profile could likely optimize clinical care, reduce healthcare costs, and improve patient outcomes. However, its success will depend on the technical and logistical capabilities of clinical laboratory networks, as well as the stage of the patient's disease and the level of care at which it is implemented.

Introduction

The global rise in chronic non-communicable diseases (NCDs) - including cardiovascular, renal, and metabolic disorders - places an increasing strain on healthcare systems. These conditions share common pathophysiological mechanisms, such as chronic inflammation, oxidative stress, and insulin resistance, which drive their progression and interconnection [1].

Cardiovascular diseases (CVDs) are the leading cause of mortality worldwide, and their prevalence continues to increase due to population aging and unhealthy lifestyles, such as high-fat diet and sedentary lifestyle [2]. Furthermore, type 2 diabetes mellitus (DM) and obesity are key risk factors for the development of CVD, as well as for chronic kidney disease (CKD), which in turn exacerbates cardiovascular risk [3]. CKD, which affects 10% of the world's population and is associated with arterial hypertension and DM, underscores the importance of a comprehensive approach to the management of these conditions. Recent studies have shown that metabolic dysfunction, characterized by insulin resistance and hyperglycemia, not only drives the progression of CKD, but also increases the risk of adverse cardiovascular events [4].

In addition, the interconnection between these NCDs suggests the need for prevention and treatment strategies that address multiple conditions, with a focus on modifying common risk factors, such as diet, exercise, and glycemic control, but also with a comprehensive diagnosis from the clinical laboratory [5].

Traditional diagnostic profiles - such as lipid, renal, and metabolic panels - are typically ordered in isolation, which hinders a holistic understanding of NCD interconnections [1]. For example, the lipid profile, requested by the cardiologist, focuses on cardiovascular risk but does not evaluate markers of inflammation or endothelial dysfunction, which are key in the progression of renal and metabolic disease [6].

Similarly, the renal profile, ordered by the nephrologist, measures parameters such as creatinine and glomerular filtration rate (GFR), which does not include biomarkers of oxidative stress or insulin resistance, which are relevant for the assessment of cardiovascular and metabolic risk in patients with chronic kidney disease (CKD) [4].

On the other hand, the metabolic profile, ordered by the endocrinologist, focuses on glucose and lipids, but does not integrate markers of vascular or renal damage, which underestimates the risk of multi-organ complications in patients with DM [7].

These gaps highlight the urgent need for an integrated diagnostic laboratory profile that provides a more comprehensive assessment of NCDs. Traditional approaches that evaluate these conditions separately fail to account for their interconnections, resulting in fragmented patient care and

suboptimal outcomes. A novel, integrated approach is needed - one that reflects the pathophysiological complexity of these conditions and enables more effective, prevention-focused management.

Objective

To address these diagnostic gaps, we propose an integrated cardio-renal-metabolic laboratory profile that unifies risk assessment and management strategies for chronic non-communicable diseases.

Methodology

Central question: What are the limitations of current diagnostic laboratory profiles (lipid, renal, metabolic) and how can an integrated profile improve the evaluation and management of NCDs?

Medical Literature Search: A recent review of medical literature related to the topic using databases including PubMed, Scopus, Web of Science, and the Cochrane Library. Keywords used in the search included “diagnostic profile”, “chronic diseases”, “cardio-renal-metabolic interface”, “diabetes”, “chronic kidney disease” and “cardiovascular disease”, “cardiac injury”, “heart failure”, “metabolic syndrome”, “liver fibrosis”, “FIB-4”, “HOMA-IR”, “HOMA”, “troponin”, “high-sensitivity troponin”, “natriuretic peptides”.

Inclusion criteria: articles published from 2022 onwards.

Original studies, systematic reviews, meta-analyses and clinical guidelines were included.

Exclusion criteria: outdated, non-peer-reviewed or methodology-poor studies.

Literature selection and critical appraisal: titles and abstracts were reviewed to select relevant articles. All studies included in this review involving human subjects complied with the ethical principles for medical research involving human subjects, in accordance with the Declaration of Helsinki and published in peer-reviewed journals.

Key findings were identified, such as proposed biomarkers, limitations of current profiles and evidence on the pathophysiological interface of NCDs.

Selecting laboratory tests for the new profile

The American Heart Association (AHA) in 2023, published “Cardiovascular, Renal, and Metabolic Health: An AHA Presidential Notice”, which addresses the importance of integrating the assessment of cardiovascular, renal, and metabolic health due to the interconnection of these systems in the development of chronic diseases. Thus, the concept of cardio-renal-metabolic syndrome (CKM) is introduced, as a condition that reflects the interrelationship between these three areas and their impact on overall health [8].

CKM syndrome is classified into different stages, ranging from stage 0 (no risk factors) to stage 4 (established cardiovascular disease with renal or metabolic complications). The AHA emphasizes the need to identify and treat this syndrome early to prevent serious complications, such as heart failure, chronic kidney disease, and diabetes [8].

Different laboratory tests are recommended depending on the stage of CKM syndrome, specific laboratory tests to assess the risk and progression of the disease. These are:

- Cardiovascular markers: lipid profile (total cholesterol, LDL, HDL, triglycerides), high-sensitivity C-reactive protein (CRP) and natriuretic peptides (BNP/NT-proBNP).
- Renal markers: serum creatinine (GFR) and albuminuria (urine albumin-creatinine ratio).
- Metabolic markers: fasting plasma glucose, glycated hemoglobin (HbA1c), and insulin.
- Other markers: liver function tests, platelet count.

In addition, there are other non-laboratory variables that are measured, such as: coronary calcium concentration, ejection fraction, weight, BMI, others. Based on this evidence, I propose a new integrated cardio-renal-metabolic laboratory profile [8]. Profiles that exist to address NCDs in a disintegrated way. Currently, different specialties request laboratory test profiles to see in a disintegrated way the patient's clinical condition. In this part I will explain the different profiles used to see specific topics.

Lipid profile

The lipid profile (PL), is a blood test that measures the levels of specific lipids to assess cardiovascular risk and guide the treatment of dyslipidemia. Its main components include: total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglycerides. From these measurements, non-HDL cholesterol and very low-density lipoprotein (VLDL) can also be calculated [9,10].

PL is crucial for assessing a patient's lipid status, which plays an important role in the primary and secondary prevention of cardiovascular diseases (9,11). Currently, the therapeutic goal in the management of dyslipidemia is to reduce LDL cholesterol to levels appropriate for the patient's cardiovascular risk, through lifestyle changes and lipid-lowering drugs [9].

Renal Profile

Currently, the renal profile consists of two parts: the estimation of the glomerular filtration rate (eGFR) by measuring serum creatinine and the urine albumin/creatinine ratio (ACR) by measuring creatinine and albumin in random urine. The GFR assesses kidney function and the ACR assesses kidney damage. Let's look at both components.

Estimating the Glomerular Filtration Rate (GFR)

The eGFR is a fundamental component for assessing kidney function and is usually calculated using serum creatinine

levels through validated equations. The most commonly used equation is the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, which has been updated to exclude race as a variable to promote health equity [12].

This equation is recommended for use in all US laboratories and is considered more accurate [13]. It should be noted that cystatin C is another marker used to estimate eGFR. Combining creatinine and cystatin C in eGFR may improve accuracy and support better clinical decision making compared to using either marker alone. The KDIGO 2024 guidelines suggest using either cystatin C-based eGFR (cys-based eGFR) or a combined creatinine and cystatin C-based eGFR (cr-cys-based eGFR) [12,14].

In pediatric patients, specific equations have been developed to account for age and sex differences, such as those proposed by the Chronic Kidney Disease in Children (CKiD) study. These equations are designed to reduce bias and improve accuracy in children and young adults [15,16].

Albumin-to-creatinine ratio (ACR)

The ACR is used to assess albuminuria, a marker of kidney damage and a predictor of cardiovascular risk. The ACR is calculated from a urine sample (preferably random) and provides a reliable estimate of daily albumin excretion, which is crucial for diagnosing and monitoring chronic kidney disease (CKD) and assessing cardiovascular risk, particularly in patients with diabetes [12,17].

The ACR has three levels: normal to mildly increased albuminuria (<30 mg/g), moderately increased (30-299 mg/g), and severely increased (≥ 300 mg/g) [14,18].

In patients with diabetes mellitus (DM), an elevated ACR is associated with an increased risk of major adverse cardiovascular events (MACE) and overall mortality, even when the ACR is within the normal range. Including the ACR in risk models improves the prediction of these outcomes [19,20]. Guidelines recommend annual ACR testing in adults with DM, with more frequent monitoring if eGFR is less than 60 mL/min/1.73 m² or if albuminuria exceeds 30 mg/g [18].

Metabolic profile

To understand more broadly, I will detail all the tests that allow us to have knowledge of the patient's metabolic homeostasis.

Diagnostic tests for diabetes mellitus (DM)

The diagnosis of DM is based on measuring plasma glucose levels and hemoglobin A1c (HbA1c or glycated hemoglobin). According to the American Diabetes Association (ADA) and other guidelines from societies and experts, they recommend the following tests to diagnose DM [18,21,22]:

- Fasting plasma glucose (FPG): measures blood glucose after an overnight fast of at least 8 hours. A glucose level ≥ 126 mg/dL (7.0 mmol/l) is diagnostic of diabetes.
- 2-hour plasma glucose (2hPG): During a 75-g oral glucose tolerance test (OGTT), blood glucose is measured 2 hours after ingesting a 75-gram anhydrous glucose solution. A

2hPG level ≥ 200 mg/dL (11.1 mmol/L) is diagnostic of diabetes.

- Hemoglobin A1c (HbA1c): This test reflects average glucose levels over the past 2 to 3 months. An HbA1c level $\geq 6.5\%$ (48 mmol/mol) is diagnostic of DM. It is important that the HbA1c test be performed using a method certified by the National Glycohemoglobin Standardization Program (NGSP) and standardized according to the Diabetes Control and Complications Trial (DCCT).
- Random plasma glucose: In the presence of classic symptoms of hyperglycemia (polyuria, polydipsia, and unexplained weight loss) or a hyperglycemic crisis, a random glucose level ≥ 200 mg/dL (11.1 mmol/L) can be used to diagnose DM.

In the absence of unequivocal hyperglycemia, it is recommended that the diagnosis of diabetes is confirmed by repeat testing on a different day. In addition, if two different tests (e.g., FPG and HbA1c) are above their respective diagnostic thresholds, the diagnosis can be confirmed without repeat testing [21].

Diagnosis of metabolic syndrome (MS)

The diagnosis of MS involves identifying patients with at least three of five specific components. These components are elevated waist circumference, elevated serum triglycerides, reduced HDL cholesterol, elevated blood pressure, and elevated fasting plasma glucose. This diagnostic criterion is widely accepted and is based on the harmonized definition proposed by an international consortium of cardiovascular and DM organizations [23,24].

- Elevated waist circumference: This is a marker of abdominal obesity and is a critical component of MS. Specific cutoff values for waist circumference may vary based on ethnic and regional considerations. For example, the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) suggests a waist circumference >102 cm for men and >88 cm for women, while the International Diabetes Federation (IDF) provides ethnicity-specific cutoffs.
- Elevated triglycerides: A triglyceride level of ≥ 150 mg/dL is considered elevated.
- Reduced HDL: Low values <40 mg/dL for men and <50 mg/dL for women, contributing to the diagnosis of metabolic syndrome.
- Elevated blood pressure: Blood pressure is considered elevated if the systolic blood pressure is ≥ 130 mmHg or the diastolic blood pressure is ≥ 85 mmHg.
- Elevated fasting plasma glucose: A level ≥ 100 mg/dL is used as a threshold for this component (prediabetes).

The diagnosis of MS is important because it is associated with an increased risk of cardiovascular disease and type 2 DM. The

prevalence of MS is increasing worldwide, driven by factors such as urbanization, sedentary lifestyles, and dietary changes [25].

Liver fibrosis profile

Liver fibrosis is a pathological process characterized by excessive accumulation of extracellular matrix (ECM) proteins in the liver, which occurs in response to chronic liver injury. This condition is a common consequence of several chronic liver diseases, including viral hepatitis, alcoholic liver disease, and nonalcoholic steatohepatitis (NASH) [26].

NASH is an inflammatory liver condition that is part of the spectrum of nonalcoholic fatty liver disease. It is a major clinical concern because it can progress to cirrhosis, liver failure, and hepatocellular carcinoma, and is a leading cause of liver transplantation in the United States [27,28,29].

The pathogenesis of NASH involves multiple factors, including lipotoxicity, oxidative stress, mitochondrial dysfunction, and inflammation. NASH is associated with MS, obesity, type 2 DM, and dyslipidemia, and its prevalence is increasing worldwide [30].

In order to assess the possibility of a patient having some degree of liver fibrosis, there is an easily calculated FIB-4 score. This is a non-invasive tool used to assess liver fibrosis, especially in patients with diseases such as NASH. The FIB-4 score is calculated using the following formula: $[\text{Age (years)} \times \text{AST (IU/L)}] / [\text{PLT (109/L)} \times \text{ALT } 1/2 \text{ (IU/L)}]$ AST= aspartate transaminase enzyme, ALT= alanine transaminase enzyme, PLT= platelet count

On the interpretation of the FIB-4 score we have that [31,32]:

- The FIB-4 index is valued for its simplicity and cost-effectiveness, making it a useful initial screening tool, in primary care as well as in specialist settings [33].

Non-ischemic cardiac injury profile

The relationship between non-ischemic cardiac injury and high-sensitivity troponin is based on the ability of high-sensitivity troponin assays to detect very low levels of cardiac troponins, which are biomarkers of myocardial injury. Cardiac troponins, such as troponin I and T, are proteins that are released when myocardial injury occurs, such as in the case of a myocardial infarction (MI) or other forms of cardiac stress [34].

High-sensitivity troponin assays have improved analytical performance compared to previous generation assays. These assays can detect troponin levels in most healthy individuals, helping to identify even minor myocardial injuries that might not be detected with conventional assays [35].

The ability to detect small changes in troponin levels over time is crucial to distinguish between acute myocardial infarction and other causes of troponin elevation, as serial measurements can provide information on the kinetics of troponin release [34].

Heart failure profile

Natriuretic peptides (NPs), including atrial natriuretic peptide (ANP), B-type natriuretic peptide (BNP), and N-terminal pro-BNP (NT-pro-BNP), play a crucial role in the diagnosis, treatment, and pathophysiology of heart failure (HF). These peptides are produced by cardiomyocytes and are involved in the regulation of blood volume and sodium concentration, exerting effects such as natriuresis, diuresis, vasodilation, and inhibition of the renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system [36,37,38,39].

Elevated levels of BNP and NT-pro-BNP indicate increased cardiac stress and are used to diagnose HF, assess its severity, and predict prognosis. The FIB-4 score of <1.3 suggests a low risk of advanced fibrosis (F3-F4) and usually does not require immediate further investigation.

- A score between 1.3 and 2.67 is considered indeterminate and further evaluation is recommended, often using additional noninvasive tests such as measurement of liver stiffness, by transient elastography or enhanced liver fibrosis testing.

A score >2.67 indicates a high likelihood of advanced fibrosis, warranting referral to a hepatologist for further evaluation, which may include measurement of liver stiffness or liver biopsy to confirm the stage of fibrosis. These biomarkers have a high negative predictive value, allowing to rule out HF in both emergency and outpatient settings when levels are below certain thresholds (e.g., BNP < 100 pg/ml, NT-proBNP < 300 pg/ml in emergency settings) [40,41].

Overall, NPs are central to the treatment of HF, providing diagnostic, prognostic, and therapeutic benefits, while highlighting the complex interplay of neurohormonal systems in cardiovascular homeostasis and disease progression [40,41].

Insulin resistance profile

Table 1: List of laboratory tests by level of care for the Cardio-Renal-Metabolic Profile.

Level of complexity of the health system	Proposed laboratory tests for the integrated Cardio-Renal-Metabolic Profile
First level of care	Cholesterol, HDL and triglycerides Glucose Serum creatinine (GFR) AST, ALT and platelet count (FIB-4)
Second level of care	Cholesterol, HDL and triglycerides Glucose, oral glucose tolerance test, glycated hemoglobin Serum creatinine (GFR) Albumin and creatinine in urine (ACR) AST, ALT and platelet count (FIB-4)

The homeostatic model assessment index (HOMA) is a method used to estimate insulin resistance (HOMA-IR) and indirectly beta cell function from fasting plasma glucose and insulin levels. It is used in clinical and epidemiological studies due to its simplicity, with the minimal requirement of a single fasting blood sample for plasma glucose and insulin measurements [42].

The HOMA-IR index is calculated using the formula [43]:

$$\text{HOMA-IR} = (\text{insulin} \times \text{glucose}) / 22.5^*$$

(*) When glucose concentration is expressed in mmol/L, or:

$$\text{HOMA-IR} = (\text{insulin} \times \text{glucose}) / 405^{**}$$

(**) When glucose glycemia is expressed in mg/dL. In both cases, insulin is in mU/L.

This index provides an estimate of insulin resistance, which is a key feature in the pathophysiology of type 2 DM and MS. The HOMA-IR index has been validated against more complex methods of assessing insulin resistance and is frequently used in large-scale studies to assess the prevalence and risk factors associated with insulin resistance [44]. However, it is important to note that cut-off values for HOMA-IR may vary depending on the population and the specific clinical context [45].

Results

A list of laboratory tests is proposed that will comprehensively address cardio-renal-metabolic syndrome in patients. This list of laboratory tests can be requested according to the complexity of the health system and its work in laboratory networks, where priority is given to sending the sample and not the physical referral of the patient to the higher level of the health system. Table 1 details the list of laboratory tests by level of care for the Cardio-Renal-Metabolic Profile and Table 2 details the list of laboratory tests by stage of CKM syndrome.

Third level of care	Cholesterol, HDL and triglycerides Glucose, oral glucose tolerance test, glycated hemoglobin Serum creatinine (GFR) Albumin and creatinine in urine (ACR) AST, ALT and platelet count (FIB-4) Insulin (HOMA index) High-sensitivity troponin Natriuretic peptides High-sensitivity CRP Lipoprotein(a) -Lp(a) Other tests
----------------------------	--

This tablet shows the different laboratory tests that must be implemented by level of complexity according to the health system.

Table 2: List of laboratory tests by stage of CKM syndrome for the Cardio-Renal-Metabolic Profile

Stage of cardio-renal-metabolic syndrome	Types of laboratory tests for the integrated Cardio-Renal-Metabolic Profile	Patient's clinical condition or risks	Findings
Stage 0 – Patients without risk factors	Perform laboratory tests according to age	Healthy patient	Normal BMI Normal ICC Fasting plasma glucose, 2-hour plasma glucose, HbA1c in normal values
Stage 1 – Excess adipose tissue dysfunction and dysglycemia	Glucose Hb A1c Oral glucose tolerance test	Overweight Obesity Prediabetes	Increased BMI Increased ICC Fasting plasma glucose, 2-hour plasma glucose, HbA1c in prediabetes values
Stage 2 – Metabolic risk factors (Metabolic syndrome)	Glucose Hb A1c Oral glucose tolerance test Cholesterol, HDL and triglycerides Serum creatinine (GFR) Urine albumin and creatinine (ACR)	Overweight Obesity Diabetes Dyslipidemia CKD	Increased BMI Increased WHR Fasting plasma glucose, 2-hour plasma glucose, HbA1c in diabetes values Hypertriglyceridemia Low HDL Hypertension CKD stage 3
Stage 3 – With subclinical atherosclerosis (Cardiovascular disease)	Glucose Hb A1c Oral glucose tolerance test Cholesterol, HDL and triglycerides Serum creatinine (GFR) Albumin and creatinine in urine (ACR) Insulin (HOMA index) AST, ALT and platelet count (FIB-4) High-sensitivity troponin Natriuretic peptides High-sensitivity CRP	Overweight Obesity Diabetes Dyslipidemia CKD Atherosclerosis in coronary arteries Decreased cardiac ejection fraction	Increased BMI Increased ICC Fasting plasma glucose, 2-hour plasma glucose, HbA1c in diabetes values Dyslipidemia Hypertension CKD stage 3

<p>Stage 4 – With established cardio-renal-metabolic syndrome</p>	<p>Glucose Hb A1c Oral glucose tolerance test Cholesterol, HDL and triglycerides Serum creatinine (GFR) Albumin and creatinine in urine (ACR) Insulin (HOMA index) AST, ALT and platelet count (FIB-4) High-sensitivity troponin Natriuretic peptides High-sensitivity CRP Lipoprotein(a) -Lp(a) Other tests</p>	<p>Overweight Obesity Diabetes Dyslipidemia CKD Myocardial infarction Stroke Peripheral arterial disease Heart failure Atrial fibrillation</p>	<p>Increased BMI Increased ICC Fasting plasma glucose, 2-hour plasma glucose, HbA1c in diabetes values Dyslipidemia Hypertension CKD stage 4</p>
--	--	--	--

This table details the type of laboratory tests that should be requested according to the stage of cardio-renal-metabolic syndrome and the clinical details presented at each stage.

Discussion

The proposed integrated Cardio-Renal-Metabolic Profile synergistically addresses the pathophysiological interconnection between cardiovascular, renal, and metabolic diseases. This unified approach improves the ability to identify cardio-renal-metabolic syndrome (CKM) early, facilitating risk stratification and personalization of clinical management [8]. An integrated healthcare approach coordinates multiple services to enhance patient outcomes, efficiency, and resource utilization [46].

For this reason, this approach is beneficial in the management of complex and chronic diseases, where patients often require services from multiple health care providers. Unlike the current fragmented approach, where lipid, renal, and metabolic profiles are ordered separately, this integrated profile provides a comprehensive analysis, capturing interactions between these systems. For example, the addition of biomarkers such as natriuretic peptides and high-sensitivity troponin at advanced levels provides an accurate assessment of cardiac stress and myocardial damage, which is not possible with traditional profiles that ignore these biomarkers [8].

In current models, the different profiles do not consider the coexistence and cross-impact between conditions such as DM and CKD on overall cardiovascular risk. This results in partial

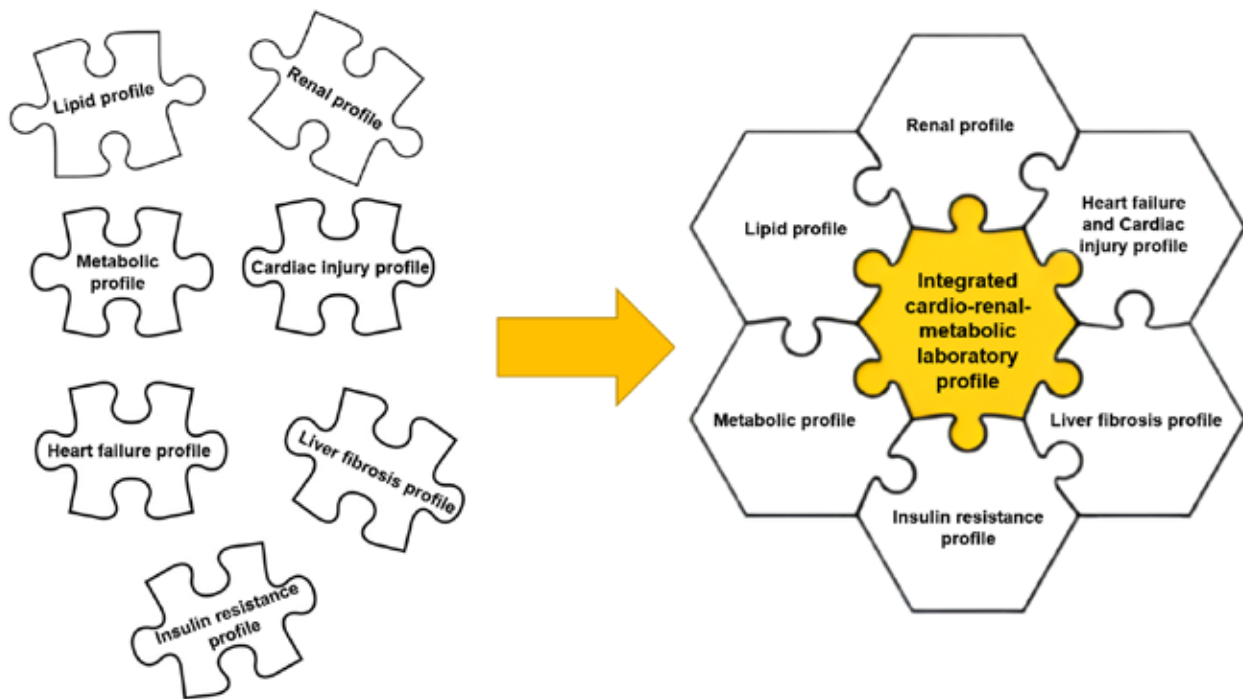
diagnoses and suboptimal therapeutic management. In addition, the duplication of tests generates an unnecessary increase in health care costs. Excessive laboratory testing negatively impacts patients and healthcare systems. The excessive use of medical tests is a recognized problem that can have physical, psychological and social consequences [47,48,49].

In contrast, an integrated profile not only optimizes resources, but also facilitates clinical adherence by avoiding multiple requests and repetitions of redundant tests. This proposal is adaptable to various healthcare settings in different health contexts. For example, in high-income countries, the profile can be integrated into advanced digital systems for automated analysis and continuous monitoring of CKM, with predictive analytics using artificial intelligence [5].

In low- and middle-income countries, the tiered design of the profile by level of care (first, second, and third level) ensures that basic tests such as serum creatinine and lipid profile are implemented at primary levels, while more complex biomarkers, such as high-sensitivity troponin and natriuretic peptides, are restricted to higher levels [50].

The possibility of scalability and customization of the implementation of the profile allows it to be adjusted according to the specific needs of the patient and the resources available in each health care setting, maintaining diagnostic quality in various health systems [50]. This new integrated profile is shown in the following figure.

Figure 1: New integrated Cardio-Renal-Metabolic Profile.



In this Figure we can observe how different laboratory profiles that are requested by different medical specialties could be integrated into a single CKM profile, well supported, seeking the timely prevention of this syndrome.

The implementation of improvements in health systems often faces a variety of barriers, which can be broadly classified into organizational, financial, human resources and technological areas [51]. Within their limitations, we can address some barriers, focused on initial and infrastructure costs, such as the acquisition of equipment and reagents for specialized laboratory tests, in clinical laboratories in countries with limited resources.

Another limitation would be that specialist physicians continue with disintegrated requests, as they are accustomed to requesting classic profiles and may show resistance in adopting this integrated approach [52]. It is important to highlight the need for validation in real conditions, with multicenter pilot studies being essential to evaluate their effectiveness, economic impact and operational viability in different scenarios [53]. Finally, the logistical work of laboratory networks, especially in countries with limited infrastructure, to ensure the adequate transport of samples for more complex tests at a higher care level.

One study shows an age-adjusted prevalence according to stages: stage 0 (11.2%), stage 1 (28.1%), stage 2 (47.4%), stage 3 (5.3%) and stage 4 (8.1%). The highest proportion of stage 4 was among adults ≥ 60 years old. Advanced stages 3 and 4 were associated with lower educational level, income and employment and higher mortality with a crude mortality rate of

188.8 per 1.000 person-years [54].

A cross-sectional study conducted in 29.722 American adults showed that unemployment, low family income, food insecurity and having 2 or more adverse social determinants of health were associated with a higher probability of advanced stages of CKM [55]. Other studies show that the higher the stage of CKM syndrome, the higher the risk of cardiovascular mortality, hence the importance of its early detection and stratification [56,57].

In conclusion, the proposal for an integrated cardio-renal-metabolic laboratory profile represents a paradigmatic advance in the diagnosis and management of NCDs. Its ability to offer a comprehensive and personalized assessment improves clinical decision-making, risk stratification, and health outcomes. Despite challenges related to cost, logistics, and healthcare infrastructure, the potential benefits strongly support adopting this profile as a standard of care. Validation through pilot studies will be crucial to establish its impact on different health systems, especially in low- and middle-income countries, where the burden of disease is greater and health budgets are strained. This profile not only reflects technical progress, but also an opportunity to transform laboratory medicine into a driver of prevention and health equity.

Author contribution

The author declares that he participated from the conception of the idea, drafting of the article, final editing, and approval of the final content.

Source of funding

Self-funded.

Conflicts of interest

The author declares that he has no conflict of interest related to this research study.

Acknowledgments

The author expresses his gratitude to Dr. Luis Fernando Hinojosa Baltierra of Mexico for his accurate and professional English translation, which ensured the clarity and intent of the original scientific text.

References

1. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396(10258):1204-1222. [http://doi:10.1016/S0140-6736\(20\)30925-9](http://doi:10.1016/S0140-6736(20)30925-9).
2. Roth GA, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. *J Am Coll Cardiol*. 2020;76(25):2982-3021. <http://doi:10.1016/j.jacc.2020.11.010>.
3. Alicic RZ, Rooney MT, Tuttle KR. Diabetic Kidney Disease: Challenges, Progress, and Possibilities. *Clin J Am Soc Nephrol*. 2017;12(12):2032-2045. <http://doi:10.2215/CJN.11491116>
4. Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases. *Kidney Int*. 2019;96(5):1048-1050. <http://doi:10.1016/j.kint.2019.07.012>
5. WHO (Internet). WHO Discussion Paper on the development of an implementation roadmap 2023-2030 for the WHO Global Action Plan for the Prevention and Control of NCDs 2023-2030 (accessed:28/01/2025). Enlace web: <https://www.who.int/publications/m/item/implementation-roadmap-2023-2030-for-the-who-global-action-plan-for-the-prevention-and-control-of-ncds-2023-2030>
6. Arnett DK, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140(11):e596-e646. <http://doi:10.1161/CIR.0000000000000678>
7. Ruiz-Ortega M, Rodrigues-Diez RR, Lavozy C, et al. Special Issue "Diabetic Nephropathy: Diagnosis, Prevention and Treatment". *J Clin Med*. 2023; 12(4): 1456. <https://doi.org/10.1007/s11655-022-3591-y>
8. Ndumele CE, et al; American Heart Association. Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. *Circulation*. 2023;148(20):1606-1635. <http://doi:10.1161/CIR.0000000000001184>
9. Parhofer KG, Laufs U. Lipid Profile and Lipoprotein(a) Testing. *Dtsch Arztebl Int*. 2023;120(35-36):582-588. <http://doi:10.3238/arztebl.m2023.0150>
10. Jacobson TA, et al; NLA Expert Panel. National Lipid Association Recommendations for Patient-Centered Management of Dyslipidemia: Part 2. *J Clin Lipidol*. 2015;9(6 Suppl):S1-S122.e1. <http://doi:10.1016/j.jacl.2015.09.002>.
11. De Vries M, Klop B, Castro Cabezas M. The use of the non-fasting lipid profile for lipid-lowering therapy in clinical practice - point of view. *Atherosclerosis*. 2014;234(2):473-475. <http://doi:10.1016/j.atherosclerosis.2014.03.024>
12. American Diabetes Association Professional Practice Committee. 11. Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S219-S230. <http://doi:10.2337/dc24-S011>
13. Finelli A, et al. Management of Small Renal Masses: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol*. 2017;35(6):668-680. <http://doi:10.1200/JCO.2016.69.9645>.
14. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. 2024;105(4S):S117-S314. <http://doi:10.1016/j.kint.2023.10.018>
15. Pierce CB, Muñoz A, Ng DK, Warady BA, Furth SL, Schwartz GJ. Age- and sex-dependent clinical equations to estimate glomerular filtration rates in children and young adults with chronic kidney disease. *Kidney Int*. 2021;99(4):948-956. <http://doi:10.1016/j.kint.2020.10.047>
16. Miller WG. Perspective on New Equations for Estimating Glomerular Filtration Rate. *Clin Chem*. 2021;67(6):820-822. <http://doi:10.1093/clinchem/hvab029>.
17. Seegmiller JC, Bachmann LM. Urine Albumin Measurements in Clinical Diagnostics. *Clin Chem*. 2024;70(2):382-391. <http://doi:10.1093/clinchem/hvad174>.
18. Sacks DB, Arnold M, Bakris GL, Bruns DE, Horvath AR, Lernmark Å, Metzger BE, Nathan DM, Kirkman MS. Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus. *Diabetes Care*. 2023;46(10):e151-e199. <http://doi:10.2337/dc23-0036>.
19. Zeng C, Liu M, Zhang Y, Deng S, Xin Y, Hu X. Association of Urine Albumin to Creatinine Ratio With Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus. *J Clin Endocrinol Metab*. 2024;109(4):1080-1093. <http://doi:10.1210/clinem/dgad645>
20. Hwang SW, Lee T, Uh Y, Lee JY. Urinary albumin creatinine ratio is associated with lipid profile. *Sci Rep*.

- 2024;14(1):14870. <http://doi:10.1038/s41598-024-65037-w>
21. American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2025. *Diabetes Care*. 2025;48(Supplement_1):S27-S49. <http://doi:10.2337/dc25-S002>
 22. Sacks DB, Arnold M, Bakris GL, Bruns DE, Horvath AR, Lernmark Å, Metzger BE, Nathan DM, Kirkman MS. Executive Summary: Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus. *Diabetes Care*. 2023;46(10):1740-1746. <http://doi:10.2337/dc23-0048>
 23. Grundy SM, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2019;73(24):e285-e350. <http://doi:10.1016/j.jacc.2018.11.003>.
 24. Meschia JF, et al; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Functional Genomics and Translational Biology; Council on Hypertension. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45(12):3754-832. <http://doi:10.1161/STR.0000000000000046>
 25. Neeland IJ, Lim S, Tchernof A, Gastaldelli A, Rangaswami J, Ndumele CE, Powell-Wiley TM, Després JP. Metabolic syndrome. *Nat Rev Dis Primers*. 2024;10(1):77. <http://doi:10.1038/s41572-024-00563-5>
 26. Akkız H, Gieseler RK, Canbay A. Liver Fibrosis: From Basic Science towards Clinical Progress, Focusing on the Central Role of Hepatic Stellate Cells. *Int J Mol Sci*. 2024;25(14):7873. <http://doi:10.3390/ijms25147873>
 27. Sheka AC, Adeyi O, Thompson J, Hameed B, Crawford PA, Ikramuddin S. Nonalcoholic Steatohepatitis: A Review. *JAMA*. 2020;323(12):1175-1183. <http://doi:10.1001/jama.2020.2298>
 28. American Diabetes Association Professional Practice Committee. 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S52-S76. <http://doi:10.2337/dc24-S004>
 29. Giashuddin S, Alawad M. Histopathological Diagnosis of Nonalcoholic Steatohepatitis (NASH). *Methods Mol Biol*. 2022;2455:1-18. http://doi:10.1007/978-1-0716-2128-8_1
 30. Santos JPMD, et al. Non-Alcoholic Steatohepatitis (NASH) and Organokines: What Is Now and What Will Be in the Future. *Int J Mol Sci*. 2022;23(1):498. <http://doi:10.3390/ijms23010498>
 31. Ouzan D, et al. Using the FIB-4, automatically calculated, followed by the ELF test in second line to screen primary care patients for liver disease. *Sci Rep*. 2024;14(1):12198. <http://doi:10.1038/s41598-024-62549-3>
 32. Mignot V, et al. Early screening for chronic liver disease: impact of a FIB-4 first integrated care pathway to identify patients with significant fibrosis. *Sci Rep*. 2024;14(1):20720. <http://doi:10.1038/s41598-024-66210-x>.
 33. Roh YH, Kang BK, Jun DW, Lee CM, Kim M. Role of FIB-4 for reassessment of hepatic fibrosis burden in referral center. *Sci Rep*. 2021;11(1):13616. <http://doi:10.1038/s41598-021-93038-6>.
 34. Writing Committee; Kontos MC, de Lemos JA, Deitelzweig SB, Diercks DB, Gore MO, Hess EP, McCarthy CP, McCord JK, Musey PI Jr, Villines TC, Wright LJ. 2022 ACC Expert Consensus Decision Pathway on the Evaluation and Disposition of Acute Chest Pain in the Emergency Department: A Report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2022;80(20):1925-1960. <http://doi:10.1016/j.jacc.2022.08.750>
 35. Park KC, Gaze DC, Collinson PO, Marber MS. Cardiac troponins: from myocardial infarction to chronic disease. *Cardiovasc Res*. 2017;113(14):1708-1718. <http://doi:10.1093/cvr/cvx183>
 36. Tsutsui H, et al. Natriuretic Peptides: Role in the Diagnosis and Management of Heart Failure: A Scientific Statement From the Heart Failure Association of the European Society of Cardiology, Heart Failure Society of America and Japanese Heart Failure Society. *J Card Fail*. 2023;29(5):787-804. <http://doi:10.1016/j.cardfail.2023.02.009>
 37. Volpe M, Gallo G, Rubattu S. Endocrine functions of the heart: from bench to bedside. *Eur Heart J*. 2023;44(8):643-655. <http://doi:10.1093/eurheartj/ehac759>
 38. Gallo G, Rubattu S, Autore C, Volpe M. Natriuretic Peptides: It Is Time for Guided Therapeutic Strategies Based on Their Molecular Mechanisms. *Int J Mol Sci*. 2023;24(6):5131. <http://doi:10.3390/ijms24065131>
 39. Sangaralingham SJ, Kuhn M, Cannone V, Chen HH, Burnett JC. Natriuretic peptide pathways in heart failure: further therapeutic possibilities. *Cardiovasc Res*. 2023;118(18):3416-3433. <http://doi:10.1093/cvr/cvac125>.
 40. Eltayeb M, Squire I, Sze S. Biomarkers in heart failure: a focus on natriuretic peptides. *Heart*. 2024;110(11):809-818. <http://doi:10.1136/heartjnl-2020-318553>
 41. Vergani M, Cannistraci R, Perseghin G, Ciardullo S. The Role of Natriuretic Peptides in the Management of Heart Failure with a Focus on the Patient with Diabetes. *J Clin Med*. 2024;13(20):6225. <http://doi:10.3390/jcm13206225>
 42. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. *Diabetes Care*. 2004;27(6):1487-1495. <http://doi:10.2337/diacare.27.6.1487>
 43. Matli B, et al. Distribution of HOMA-IR in a population-

- based cohort and proposal for reference intervals. *Clin Chem Lab Med.* 2021;59(11):1844-1851. <http://doi:10.1515/cclm-2021-0643>
44. Diniz MFHS, et al. Homeostasis model assessment of insulin resistance (HOMA-IR) and metabolic syndrome at baseline of a multicentric Brazilian cohort: ELSA-Brasil study. *Cad Saude Publica.* 2020;36(8):e00072120. <http://doi:10.1590/0102-311X00072120>
45. Toin T, Reynaud Q, Denis A, Durieu I, Mainguy C, Llerena C, Pin I, Touzet S, Reix P. HOMA indices as screening tests for cystic fibrosis-related diabetes. *J Cyst Fibros.* 2022;21(1):123-128. <http://doi:10.1016/j.jcf.2021.05.010>
46. Foo C, et al. Integrating tuberculosis and noncommunicable diseases care in low- and middle-income countries (LMICs): A systematic review. *PLoS Med.* 2022;19(1):e1003899. <http://doi:10.1371/journal.pmed.1003899>
47. Korenstein D, Chimonas S, Barrow B, Keyhani S, Troy A, Lipitz-Snyderman A. Development of a Conceptual Map of Negative Consequences for Patients of Overuse of Medical Tests and Treatments. *JAMA Intern Med.* 2018;178(10):1401-1407. <http://doi:10.1001/jamainternmed.2018.3573>
48. Pennestri F, Tomaiuolo R, Banfi G, Dolci A. Blood over-testing: impact, ethical issues and mitigating actions. *Clin Chem Lab Med.* 2024;62(7):1283-1287. <http://doi:10.1515/cclm-2023-1227>
49. Beriault DR, Gilmour JA, Hicks LK. Overutilization in laboratory medicine: tackling the problem with quality improvement science. *Crit Rev Clin Lab Sci.* 2021;58(6):430-446. <http://doi:10.1080/10408363.2021.1893642>
50. Fleming KA, et al. The Lancet Commission on diagnostics: transforming access to diagnostics. *Lancet.* 2021;398(10315):1997-2050. [http://doi:10.1016/S0140-6736\(21\)00673-5](http://doi:10.1016/S0140-6736(21)00673-5)
51. Durojaiye C, et al. Barriers and facilitators to high-volume evidence-based innovation and implementation in a large, community-based learning health system. *BMC Health Serv Res.* 2024;24(1):1446. <http://doi:10.1186/s12913-024-11803-5>
52. Deng W, Yang T, Deng J, Liu R, Sun X, Li G, Wen X. Investigating Factors Influencing Medical Practitioners' Resistance to and Adoption of Internet Hospitals in China: Mixed Methods Study. *J Med Internet Res.* 2023;25:e46621. <http://doi:10.2196/46621>
53. Pfeiffer RM, Chen Y, Gail MH, Ankerst DP. Accommodating population differences when validating risk prediction models. *Stat Med.* 2022;41(24):4756-4780. <http://doi:10.1002/sim.9447>
54. Kim JE, Joo J, Kuku KO, Downie C, Hashemian M, Powell-Wiley TM, Shearer JJ, Roger VL. Prevalence, Disparities, and Mortality of Cardiovascular-Kidney-Metabolic Syndrome in US Adults, 2011-2018. *Am J Med.* 2025 Feb 3:S0002-9343(25)00063-4. <http://doi:10.1016/j.amjmed.2025.01.031>
55. Zhu R, Wang R, He J, Wang L, Chen H, Niu X, Sun Y, Guan Y, Gong Y, Zhang L, An P, Li K, Ren F, Xu W, Guo J. Prevalence of Cardiovascular-Kidney-Metabolic Syndrome Stages by Social Determinants of Health. *JAMA Netw Open.* 2024;7(11):e2445309. <http://doi:10.1001/jamanetworkopen.2024.45309>
56. Claudel SE, Schmidt IM, Waikar SS, Verma A. Cumulative Incidence of Mortality Associated with Cardiovascular-Kidney-Metabolic Syndrome. *J Am Soc Nephrol.* 2025 Feb 11. <http://doi:10.1681/ASN.0000000637>
57. Li N, Li Y, Cui L, Shu R, Song H, Wang J, Chen S, Liu B, Shi H, Gao H, Huang T, Gao X, Geng T, Wu S. Association between different stages of cardiovascular-kidney-metabolic syndrome and the risk of all-cause mortality. *Atherosclerosis.* 2024;397:118585. <http://doi:10.1016/j.atherosclerosis.2024.118585>