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Different Equations for Combined Chronic Kidney Disease and Cardiovascular Risk

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Abstract

Assessment of combined risk in chronic kidney disease and cardiovascular disease requires the use of multiple complementary tools, as no single model captures all relevant outcomes. Traditional cardiovascular risk scores, such as the Framingham Risk Score and the Atherosclerotic Cardiovascular Disease Risk Estimator, incorporate factors including age, sex, cholesterol levels, blood pressure, diabetes, and smoking. However, both have important limitations in chronic kidney disease, as kidney dysfunction is either not included or only indirectly considered, leading to underestimation of cardiovascular risk. The QRISK3 model represents a more suitable alternative for this population because it directly incorporates chronic kidney disease and proteinuria, along with additional variables such as body mass index and comorbidities, resulting in more accurate cardiovascular risk prediction. For renal outcomes, the Kidney Failure Risk Equation is the most widely validated tool, using demographic and laboratory parameters to estimate progression to end stage kidney disease, although it does not predict cardiovascular events. Combined models, such as those developed by the Chronic Kidney Disease Prognosis Consortium, integrate kidney function and albuminuria to predict both mortality and cardiovascular outcomes. Similarly, the Kidney Disease Improving Global Outcomes classification system provides a practical framework by combining estimated glomerular filtration rate and albuminuria to stratify risk of progression, cardiovascular events, and death. Biomarker-based approaches incorporating natriuretic peptides and troponin further enhance prediction, particularly for heart failure. Overall, optimal management requires an integrated approach combining cardiovascular and renal risk tools to improve prognostic accuracy and guide therapy.

Keywords: Albumin; Cardiovascular risk; Chronic kidney disease; Creatinine; Equations.

Abbreviation

ACR: Albumin-to-Creatinine Ratio

ASCVD: Atherosclerotic Cardiovascular Disease

CKD: Chronic Kidney Disease

EGFR: Estimated Glomerular Filtration Rate

KDIGO: Kidney Disease Improving Global Outcomes

KFRE: Kidney Failure Risk Equation

Introduction

When assessing combined risk in chronic kidney disease (CKD) and cardiovascular disease, several equations and scoring systems are used. These vary depending on whether the goal is predicting kidney progression, cardiovascular events, or both together. This paper aims at presenting a breakdown of the main approaches.

Cardiovascular risk assessment in patients with CKD requires careful consideration, as traditional models may not fully capture the increased risk associated with renal impairment. One commonly used tool is the Framingham Risk Score, which estimates the 10-year risk of cardiovascular disease. This score incorporates variables such as age, sex, total cholesterol levels, high-density lipoprotein (HDL) cholesterol, blood pressure, and the presence of smoking and diabetes (1).

Although widely utilized in clinical practice, this model has important limitations when applied to patients with CKD. Specifically, it tends to underestimate cardiovascular risk in this population, as CKD itself is not included as a variable in the risk calculation (2,3). Consequently, reliance solely on this score may lead to an underappreciation of the true cardiovascular risk in individuals with renal dysfunction.

Another widely used tool for cardiovascular risk assessment is the Atherosclerotic Cardiovascular Disease (ASCVD) Risk Estimator, which is recommended in the guidelines of the American College of Cardiology and the American Heart Association (4). This model estimates the risk of ASCVD based on variables such as age, sex, race, cholesterol levels, blood pressure, and the presence of diabetes and smoking.

In the context of CKD, this tool also presents limitations. Although CKD is recognized as an important clinical factor, it is not directly incorporated into the risk equation. Instead, it is considered a "risk enhancer," meaning that it should inform clinical judgment rather than quantitatively influence the calculated risk (4). As a result, the estimator may not fully reflect the increased cardiovascular risk observed in patients with renal dysfunction.

Another important tool for cardiovascular risk assessment is the QRISK3, which is considered one of the most appropriate models for patients with CKD. Unlike other traditional risk calculators, QRISK3 directly incorporates CKD - particularly stages 3 to 5 - as well as proteinuria, both of which are highly relevant factors in this population (5).

In addition to these variables, the model includes a broader range of clinical and demographic factors, such as body mass index, ethnicity, rheumatoid arthritis, and other comorbidities. By accounting for these elements, QRISK3 provides a more comprehensive and individualized estimation of cardiovascular risk (5). Consequently, it is regarded as more accurate for assessing risk in patients with CKD compared to other commonly used prediction tools.

In addition to general cardiovascular risk models, kidney-specific tools have been developed to better

predict renal outcomes. One of the most widely used is the Kidney Failure Risk Equation (KFRE), which estimates the risk of progression to end-stage kidney disease in patients with CKD (6).

The four-variable version of the equation includes age, sex, estimated glomerular filtration rate (eGFR), and albumin-to-creatinine ratio (ACR), providing a practical and accessible method for routine clinical use. A more comprehensive eight-variable version expands this model by incorporating additional laboratory parameters such as serum calcium, phosphate, albumin, and bicarbonate, thereby improving risk stratification (6).

The KFRE has been extensively validated across diverse populations and is considered a reliable tool for predicting renal disease progression. However, it is important to recognize its limitations: despite its usefulness in nephrology, the equation does not predict cardiovascular outcomes and therefore should be used alongside cardiovascular risk assessment tools when managing patients with CKD (6).

Combined cardio-renal risk models have been developed to better capture the close interaction between kidney function and cardiovascular outcomes. One of the most prominent examples is the CKD Prognosis Consortium model, which integrates key markers of renal function, particularly eGFR and albuminuria, typically measured by the ACR (2).

This model is designed to predict clinically relevant outcomes, including cardiovascular mortality and all-cause mortality in patients with CKD. Its underlying principle is based on the strong and graded association between worsening kidney function and adverse outcomes. Specifically, the risk of mortality increases as eGFR declines and albuminuria rises, reflecting the combined impact of reduced filtration capacity and kidney damage (2,3).

By incorporating both functional and structural markers of kidney disease, this approach provides a more comprehensive assessment of risk, reinforcing the importance of evaluating eGFR and albuminuria together when stratifying patients with CKD.

Another relevant approach is the modified SCORE2, recommended in European guidelines, such as those from the European Society of Cardiology. This model is used to estimate cardiovascular risk in the general population but can be adapted in the context of CKD (7).

In this setting, CKD does not directly enter the equation as a variable; instead, it modifies the overall risk category. For instance, individuals with an eGFR below 60 mL/min/1.73 m² are automatically classified into a higher cardiovascular risk group. Additionally, this model is often used in combination with albuminuria staging, allowing for a more refined assessment of risk based on both kidney function and the degree of renal damage.

Risk models derived from the Angiotensin II Antagonist Losartan (RENAAL) study and the Irbesartan Diabetic Nephropathy Trial (IDNT) study have been specifically developed for patients with diabetic CKD populations. These models incorporate key clinical and laboratory variables, including proteinuria, blood pressure, and serum creatinine, which are central determinants of disease progression in this population.

By integrating these parameters, the models are able to predict both renal outcomes - such as progression to advanced kidney disease - and cardiovascular events. This dual predictive capacity makes them particularly valuable in diabetic patients, in whom renal dysfunction and cardiovascular risk are closely interconnected.

Biomarker-based cardiorenal risk equations have emerged as an important advancement in risk stratification, incorporating markers beyond those used in traditional models. These approaches typically include core measures such as eGFR and albuminuria, assessed by the ACR, along with cardiac biomarkers like N-terminal pro-B-type natriuretic peptide (NT-proBNP) and troponin.

In patients with CKD, the integration of these biomarkers allows for a more refined evaluation of both renal and cardiovascular risk. In particular, the addition of NT-proBNP and troponin enhances the ability to detect subclinical cardiac dysfunction and myocardial injury, which are common in this population. As a result, these models improve the prediction of clinically relevant outcomes, including heart failure and cardiovascular mortality, offering a more comprehensive assessment compared to conventional risk equations (2,3).

A practical and widely used approach for risk stratification in patients with CKD is the Kidney Disease Improving Global Outcomes (KDIGO) heat map. This model, proposed by the KDIGO initiative, provides a simple yet effective framework for assessing prognosis based on the combination of kidney function and kidney damage (7,8).

The system classifies patients according to eGFR categories, ranging from G1 to G5, and levels of albuminuria, categorized from A1 to A3. Conceptually, overall risk is determined by the interaction between these two variables - that is, the eGFR category and the ACR category.

By integrating these parameters, the KDIGO heat map allows clinicians to stratify patients according to their likelihood of CKD progression, as well as their risk of cardiovascular events and overall mortality. This combined approach highlights the importance of evaluating both functional decline and structural kidney damage when assessing prognosis in CKD.

In clinical practice, cardiorenal risk is often understood as the result of multiple interacting factors rather than a single determinant. A simplified conceptual framework suggests that total risk arises from the combination of traditional cardiovascular risk factors - such as hypertension, dyslipidemia, diabetes, and smoking - together with the degree of kidney dysfunction and systemic processes associated with renal disease (8,9).

In patients with CKD, this means that overall risk increases as eGFR declines and albuminuria worsens, reflecting both reduced kidney function and structural damage (2,8). In addition, chronic inflammation, which is commonly present in this population, further amplifies cardiovascular risk.

Thus, total cardiorenal risk can be conceptually viewed as the cumulative effect of traditional cardiovascular risk factors, declining eGFR, increasing albuminuria, and underlying inflammatory activity. This integrated perspective reinforces the need for a comprehensive and multifactorial approach to risk assessment and management in patients with CKD (Table 1).

Table 1. Practical comparison.

Model	Predicts Cardiovascular Risk	Predicts Chronic Kidney Disease Progression	Includes Chronic Kidney Disease Variables
Framingham	✓	✕	✕
Atherosclerotic Cardiovascular Disease	✓	✕	Partial
QRISK3	✓	✕	✓
Kidney Failure Risk Equation	✕	✓	✓
Kidney Disease Improving Global Outcomes Grid	✓	✓	✓
Chronic Kidney Disease-Prognosis Consortium Models	✓	✓	✓

Discussion: the integration of renal and cardiovascular risk tools is essential due to the bidirectional relationship between CKD and cardiovascular disease. Traditional models such as Framingham underestimate risk in CKD populations, whereas QRISK3 incorporates renal variables directly (5). KFRE provides robust prediction of kidney failure but must be complemented with cardiovascular assessment (6). The KDIGO classification remains central, linking albuminuria and eGFR to both renal and cardiovascular outcomes (8).

Conclusion: in clinical practice, different tools are recommended for specific aspects of risk assessment in patients with CKD. Among cardiovascular risk calculators, the QRISK3 is considered one of the most appropriate options for this population, as it incorporates variables directly related to kidney disease and provides a more accurate estimation of cardiovascular risk.

For predicting renal disease progression, the KFRE remains the most reliable and widely validated tool, offering robust risk stratification for progression to advanced kidney disease.

However, the most effective strategy in routine care is a combined approach. This typically involves the use of the KDIGO heat map to assess kidney-related risk alongside a cardiovascular risk calculator, such as the ASCVD Risk Estimator or QRISK3. By integrating these tools (Figure 1), clinicians can achieve a more comprehensive evaluation of both renal and cardiovascular risk, ultimately improving patient management and outcomes.

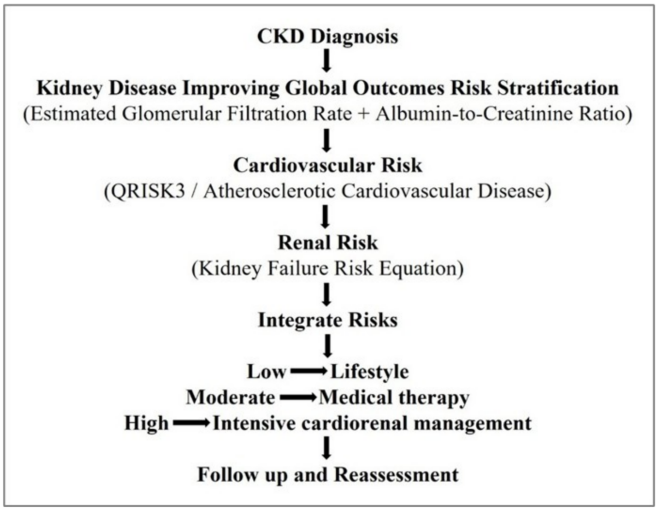

Figure 1. Visual flow (Text diagram).

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Conflicts of interest

No conflict of interest.

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