



Detection of Chronic Kidney Disease at Early Stage Prevents Kidney and Heart Failure

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Abstract

The early detection of chronic kidney disease can prevent damage of kidney as well as myocardial infarction. There are several report which confirm the inter relationship between kidney failure and heart attack. The present paper describes a crucial relationship between kidney glomerular filtration rate and cardiovascular disease risk factors. There are several reported markers and methods for detection of kidney failure are available but all these methods still have some limitations. Biosensors are emerging technology which can predict damage at early stage using electrochemical aptamer technique in which protein binds with specific marker and resulting signals are electrochemically detected as changes in current with respect to control.

Keywords: Chronic kidney disease; Cardiovascular disease; Glomerular filtration; Heart failure

Short Communication

There are many traditional and non-tradition factors which are account for the risk for cardiovascular disease (CVD) in chronic kidney disease (CKD) condition. Traditional CVD risk factors are hypertension, hyperlipidemia and diabetes which do not report for the high cardiovascular risk in CKD patients. The standard clinical interventions for managing CVD, flourishing in the general population, are ineffective to lower the death rate in CKD patients. Non-traditional factors, related to disturbed mineral and vitamin D metabolism were able to provide some account in terms of vascular calcification for the increased risk of CVD in CKD patients [1]. CVD is the leading cause of death is mostly due to cardiac metabolic risk and CKD. CVD and kidney disease are closely interrelated and disease of one organ causes dysfunction of the other, ultimately leading to the failure of both organs (Figure 1) and this is often referred as cardio renal syndrome (CRS). In CKD patients, heart failure (HF) is the major cardiovascular problem which increases with declining kidney function [1,2]. CKD, diagnosed mainly by reduced estimated glomerular filtration rate (eGFR <60 ml/min/1.73 m²) and albuminuria/proteinuria (>30 mg/24 h or albumin/creatinine ratio >30 mg/g or >1 on specific dipstick) is considered an independent cardiovascular risk factor and, therefore, diagnosis of CKD implies a very high cardiovascular risk [3,4]. Traditional CVD risk factors do not account for the high cardiovascular risk in CKD patients and also standard clinical interventions for managing CVD that are winning in the general population, are ineffective in CKD patients [4]. Non-traditional factors were able to give some account in terms of vascular thickening and calcification, for the increased risk of CVD in CKD patients [5]. People at every stage of CKD are at increased risk of CVD (Figure 2). The national kidney foundation 'Kidney Disease and Quality Outcomes Initiative' (KDQOI) classification system for CKD is based largely on the estimated glomerular filtration rate [6]. The five stages of CKD are summarized in Table 1. The National Kidney Disease Education Program [7] has recommended the routine use of the eGFR instead of the serum creatinine alone to more accurately assess kidney function in adults over the age of 18. The eGFR can be calculated using a version of the modification of diet in renal disease (MDRD) equation. A modified version of this equation can calculate the eGFR using the variables of serum creatinine, age, sex and mussels mass. This equation less accurately correlates with measured glomerular filtration rate (GFR) in individuals with an eGFR 460 ml/min/1.73 m² and is often reported as 460 ml/min/1.73 m² [8]. As a result, it is difficult to clinically differentiate between stage 1 and 2 chronic kidney disease (CKD) leading to a proposal for a modified staging system [9]. Automatic eGFR reporting along with the serum creatinine has been endorsed by a number of subspecialty societies including the American Society of Nephrology, the American Diabetes Association, the American Association of Clinical Chemistry, the College of American Pathologists,

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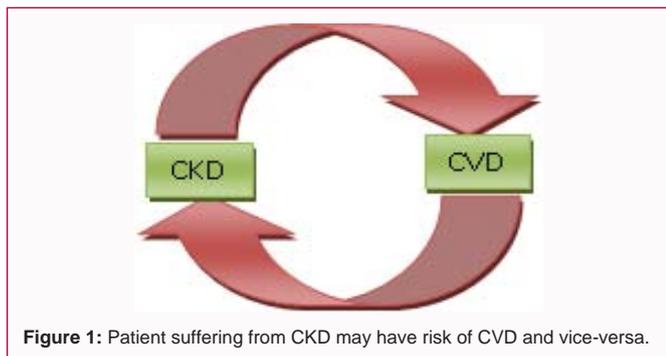


Figure 1: Patient suffering from CKD may have risk of CVD and vice-versa.

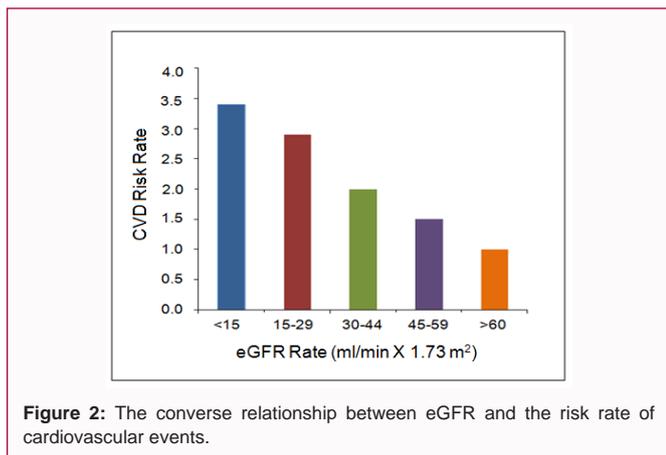


Figure 2: The converse relationship between eGFR and the risk rate of cardiovascular events.

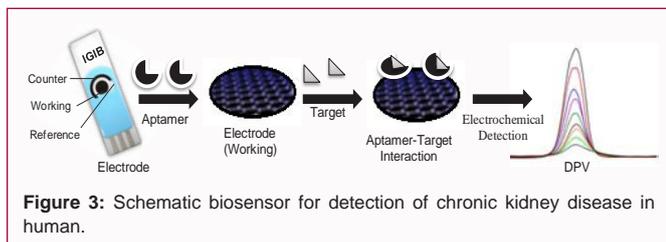


Figure 3: Schematic biosensor for detection of chronic kidney disease in human.

and the National Kidney Disease Education Program [10]. CKD is divided into 5 stages based on the severity of the disease which is determined by glomerular filtration rate (GFR). The occurrence of CKD and end-stage kidney disease (ESKD) is rising worldwide. This growing population of patients with CKD suggests a dramatic growth in the ESKD population. The majority of these die from CVD prior to progressing to ESKD or requiring renal replacement therapy. CKD has emerged as an important risk factor for CVD, with 10- to 30-fold higher risk relative to those with normal renal function. CKD can be recognized and treated aggressively at the early stage to improve morbidity and mortality as well as to delay or avoid progression of ESKD and CVD. Early referral to a nephrologist has been verified to advance outcomes in those with CKD [11]. The majority of the patients with CKD will die from a CVD event prior to progressing to ESKD [12]. The deteriorating renal function and increasing albuminuria independently predict the amount of calcified atherosclerotic plaque in the coronary arteries [13] and an increasing frequency of clinical CVD events [14]. Annual mortality rates approximating 24% have been observed in patients with stage 2 and stage 3 CKD, with 45% mortality rates in stage 4 CKD [15]. The atherosclerotic risk in communities study prospectively followed a cohort of individuals between 45 and 64 years of age and demonstrated that a decrease in GFR was an independent risk factor for recurrent and de novo CVD

Table 1: CKD stages with respect to GFR.

S. No.	CKD Stages	GFR (ml/min/1.73m ²)
1	Stage 1	Normal or high level >90 ml/min.
2	Stage 2	60-89 ml/min.
3	Stage 3a	45-59 ml/min
4	Stage 3b	30-44 ml/min.
5	Stage 4	15-29 ml/min.
6	Stage 5	<15 ml/min.

[16]. Thus, a pragmatic approach to reduce the global burden of renal and cardiovascular diseases has to be adopted. The present methods for detection of CKD are GFR, ultrasound, CT scan, kidney biopsy, creatinine assay, albumin, and blood urea nitrogen estimation. All these methods are either time consuming or expensive and based one or more tests for confirmation of the disease. The greatest challenge in managing kidney disease is that many of individuals are unaware of the condition until significant damage has occurred. Lack of symptoms in the early stages of the disease indicates that, CKD can easily go undetected, leading to progressive damage and loss of kidney function. Ultimately, dialysis or kidney transplantation is required, which increases the risk of CVD to patients and puts a substantial burden on healthcare. There are many biomarkers which can evaluate more accurate GFR, but still not widely available [17-25]. It evident that majority of patients with CKD dies from cardiovascular diseases (CVD) prior to progression of ESKD [12,18,19]. Chronic kidney diseases are significant risk factors for CVD [12,14,18-21]. The risk of CVD is 10- to 30-fold higher among individuals with CKD [21] and severity of kidney disease is associated with increased rates of CVD causing death [16]. Patients with kidney disease are up to 20 times more likely to die from a heart attack or stroke than dialysis. CVD remains the leading cause of death for people on dialysis and for people who have a transplanted kidney [22]. Thus, beneficial approaches targeting those CKD biomarkers to develop point of care diagnostics for CKD progression using biosensors. At present, no such type of biosensor is available to detect CKD in the patients at early stages [23-25]. Electrochemical biosensor has become an attractive option for high throughput analysis combined with advantages of easy handling and rapidity detection of CKD. Hence, an initiative is being taken to design an easy to use electrochemical aptamer based biosensor in which protein (aptamer) binds with specific marker and resulting signals are electrochemically detected as changes in current with respect to control for detection of CKD in early stages which can prevent the occurrence of CVD disease in human (Figure 3). Ultimately, it prevents the kidney failure as well as heart failure in human.

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