

A Review of Shear Wave Elastography (SWE) for Risk Stratification and Prognosis in Chronic Kidney Disease (CKD)

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Abstract: Chronic Kidney Disease (CKD) is a global health crisis with limited tools for early detection and risk stratification. Traditional methods struggle to identify early fibrosis, a key pathological feature of CKD progression. This review examines the potential of Shear Wave Elastography (SWE), a non-invasive imaging technique, for risk stratification and prognosis in CKD patients. We comprehensively evaluate the current literature on SWE's ability to detect and quantify renal fibrosis in CKD compared to conventional methods. The role of SWE in predicting CKD progression to End-Stage Renal Disease (ESRD) and its potential for treatment monitoring are critically appraised. Limitations of SWE and ongoing research efforts are also discussed. SWE shows promise for detecting early fibrosis and potentially stratifying CKD patients based on their risk of progression. However, standardisation issues and operator dependence require further investigation. Future research needs to validate SWE's clinical utility in large-scale, prospective studies.

Keywords: Chronic Kidney Disease (CKD), Shear Wave Elastography (SWE), Renal Fibrosis, Risk Stratification, Prognosis.

INTRODUCTION

CKD is a common condition in the general population with worldwide prevalence between 8% and 16% making it an underdiagnosed condition among patients and doctors [1]. Characterised by glomerular filtration rates of less than 60 ml of blood per minute per 1.73 m² of the surface of the glomerular filtration membrane. A GFR <60 ml/min/1.73 m², or an albuminuria of >30 mg/24 h or any other evidence of kidney damage (for example, hematuria or kidney abnormalities such as polycystic or dysplastic kidneys) that lasts for more than 3 months, [2] is known as CKD and is more common in low and middle-income countries than in high-income countries [3]. In general, the risk factors for CKD in most parts of the world continue to be diabetes/ hypertension, but aside from these risk factors, CKD is frequently attributed to glomerulonephritis/ infection/ environmental exposures (pollution of air, exposure to herbal remedies/ pesticides) in Asia/sub-Saharan Africa/ developing world [4].

Stage of CKD	GFR	Per cent of kidney function
Stage 1	Greater than 90ml/min	>90%
Stage 2	60-89 ml/min	60-89%
Stage 3a	45-59 ml/min	45-59%
Stage 3b	30-44 ml/min	30-44%
Stage 4	15-29 ml/min	15-29%
Stage 5	Less than 15 ml/min	<15%

Source: National institute of diabetes and digestive and kidney diseases (NIDDKD).

Early Stratification

The matter of early stratification has been discussed and put into prominence in relation to the overall program in the recent past [5]. Despite the numerous clinical risk-prediction models proposed, the majority of them have not been externally validated or have not demonstrated a level of accuracy that is useful for clinicians. Consequently, interest shifts to biomarkers to help in managing this aspect of stratification, which was established based on biomarkers that forecast the likelihood of an individual's prognosis, response to therapeutic products or propensity to develop side effects to those therapeutic products [6].

THE IMPORTANCE OF EARLY DIAGNOSIS

The early identification and diagnosis of a problem is crucial because it enables the people involved and their supporters to enhance its efficiency and effectiveness promptly, as well as reduce the chances of negative outcomes if it is a medical condition. As for the argument that wonders why asymptomatic patients should be tested for CKD, the following reasons have been provided: early detection of CKD may help to start and apply suitable treatments, and avoid exposure to nephrotoxic substances, both of which may help to delay the progression of CKD to ESKD [7]. The detection of CKD also defines a large risk concerning cardiovascular diseases, as it is indicated below. The Australian Health Review 'Coronary artery disease and myocardial infarction in young people,' which contains a section on 'Coronary risk factors,' as well as the 'Prevalence of and

risk factors for coronary heart disease in patients with diabetes mellitus.’ It may also contribute to appropriate dosage adjustment of medications and timely pre-CCRF [chronic kidney disease (CKD)] renal replacement therapy, which is vital to outcome [8].

Risk stratification.

Grouping of people based on their health requirements helps the health centres to serve as a means of targeting in a cheaper way, since they get to put more effort per individual than if targeting the whole population. Highly complex is a small group of patients that will require the most extensive and specialised care. This group, which is estimated to constitute less than 5% of the population, has at least one chronic condition, and most have other comorbid psychosocial conditions or issues complicating their care [9].

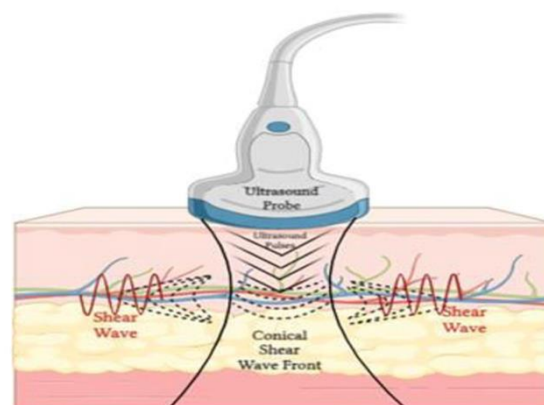
Risk stratification of CKD

Risk assessment in chronic kidney disease (CKD) plays a significant role in the patients’ care. It entails staging the patients according to the likelihood with which they will progress to ESRD and complications related to the same, which would then assist in proper management and overall patient results. Risk stratification is critical in the management of CKD in the following ways: First, early Identification enables the identification of patients with a high risk of rapid disease progression who require interventions. In the case of Guiding Treatment, patients are classified based on certain risks that support the perception that treatment options can be personalised. Resource Allocation shows that identifying and studying high-risk patients helps avoid wasting resources and improve Outcomes. The development of strategies aimed at preventing escalation and worsening of the condition in high-risk patients [10]. The KDIGO 2012 CKD guidelines issued a new risk stratification using eGFR and ACR, which was presented using the heat map of risk. This predicts the risk associated with the patient’s progress on the basis of his/her eGFR and ACR and directs the remedy approach [11]. Risk assessment is paramount for the CKD care process, as it maps out the approach to early intervention and patient classification. Other approaches using eGFR and albuminuria are considered very effective, whereas new approaches with biomarkers, genes, and modern technologies have the potential to improve the effectiveness of the risk assessment. Managing current issues and exploiting advanced technologies will be necessary in the optimisation of the results being obtained by patients with CKD [12].

SWE TECHNOLOGY

Shear Wave Elastography (SWE) qualifies as a valuable addition to other diagnostic imaging techniques as it can quantify and visualise the elasticity of a tissue. It’s able to be used in relation to almost all specialisations in medicine, such as liver, breast, and thyroid imaging. More recently, SWE has been explored as a diagnostic method in the identification of kidney disease, be it

Chronic Kidney Disease (CKD), Acute Kidney Injury (AKI) or complications related to kidney transplantation. Fig 1



Grounding in Shear Wave Elastography (SWE)

SWE is based on some fundamental principles of physics, such as the properties of the shear waves in tissues. To effectively assess the diagnostic potential of SWE, these principles should be known.

Particle displacement in the form of Shear Waves and Tissue Stiffness, to be precise.

Shear waves are transverse waves whose energy transfer is in a direction perpendicular to the direction of wave propagation. While compression waves that are being used in conventional ultrasound procedures propagate through the tissues at high velocities, shear waves are slower to travel through the tissues, and their velocities depend more on the mechanical characteristics of the tissues, specifically their hardness. In SWE, these waves are created by ultrasound pulses, and their travel is applied to determine the hardness of the tissues [13].

The generation and propagation of shear waves are also known as SH-waves.

The procedure is initiated with the generation of intense and well-directed ultrasonic beams through the tissue. They exert small vibrations in small as well as limited areas and thus generate shear waves which move radially away from the point of impulse. The speed of these shear waves or wave frequency is also influenced somewhat by the stiffness of the tissue under examination; stiffer tissues yield faster shear wave propagation [14].

Tissue Stiffness: Its Quantification and Localisation

SWE technology is also incorporated on the ultrasound transducers, where shear waves are transmitted and their propagation is recorded. This speed is obtained by tracking the displacement of the tissue particles over the period of time that the shear waves last. This data is then mathematically analysed to generate a quantitative map of the stiffness of the tissue referred to as an elastogram. Elastograms depict the differences in the elasticity and

rigidity of tissues, where colours are used to show different levels of elasticity.

The ultrasound transducers now available for use in SWE are capable of focusing the ultrasound pulses and, at the same time, measuring the shear wave movements. High-frequency transducers are favourable for SWE applications owing to their high resolution, but have less penetration depth ^[15].

Cos Signal Processing Algorithms and Elastography

SWE systems make use of signal processing, which is enhanced to help in the determination of the shear waves' speeds. These techniques use Doppler-based methods or the time-of-flight analysis to quantify the tissue displacement resulting from the shear wave. The said elastography algorithms derive from these measurements quantitative stiffness values and fabricate a composite elastogram ^[16].

Real-Time Imaging and Quantification

In fact, one of the main strengths of SWE can be considered its ability to work in real-time imaging. This feature is rather important for dynamic examinations, where the biopsies have to be directed or the changes in the stiffness of the tissues have to be evaluated. Real-time SWE can be of great benefit to the clinician as it enables him/her to make reliable decisions on the patient's condition during the examination process ^[17].

Calibration and Standardisation

Thus, for obtaining reproducible and precise data, SWE systems should be calibrated sufficiently and the experiments carried out according to the guidelines. Calibration can be defined as a process of ensuring that the system being used has standard measurements for Shear wave velocity, which in this case can be obtained from the different devices used, and in different environments. The generalisation of SWE protocols is deemed relevant for proper cross-study comparisons in clinical work ^[17].

Use of SWE in the assessment of kidney-related diseases

Thus, SWE is not invasive and can be used in the assessment of different renal diseases, making this field novel in the application of SWE. Due to the structural and biochemical complexity of the kidneys, they represent not only a difficult but also an attractive organ for SWE technology ^[18].

SWE and CKD Diagnosis

This review aims to discuss the possibilities of Shear Wave Elastography (SWE), which is a non-invasive imaging technique, in the diagnosis and staging of renal fibrosis compared to conventional techniques.

Conventional Methods for CKD Diagnosis:

- **Blood Tests:** Blood urea nitrogen and serum creatinine are used to monitor the kidney, but these lack specificity in identifying fibrosis.

- **Urine Tests:** UACR shows proteinuria but does not give a measure of fibrosis of the glomerular wall or the capsule.
- **Renal Biopsy:** Considered the gold standard for diagnosis, it is invasive and entails certain risks to the patient's health.

SWE: A Promising Alternative:

SWE counts on the measurement of tissue elasticity, where elasticity is higher in fibrotic tissue. Here's how it compares to conventional methods: Here's how it compares to conventional methods:

- **Non-invasive:** Thus, there is no danger encountered by SWE because it does not have the risks that a biopsy poses.
- **Objective and Reproducible:** SWE measurements are objective and dependent to a lesser extent on the observer, as with visual assessment in biopsies.
- **Serial Monitoring:** SWE can be made on different occasions to capture disease progression in different time periods.

Several studies have evaluated SWE for CKD diagnosis:

- **Diagnostic Accuracy:** SWE was 93% sensitive and 89% specific in diagnosing moderate to severe fibrosis ^[19].
- **Correlation with Biopsy:** For instance, there are research articles that reveal that the SWE measurements, specifically Young's modulus, are directly proportional to the level of fibrosis based on the biopsies done on kidney patients; for instance, Research Gate, Evaluation of Potential Influences on SWE in CKD and Control Groups, 2017.

SWE for Risk Stratification: Evaluate: Existing Evidence Suggests Potential:

Non-invasive assessment of fibrosis: SWE quantifies the hardness of the tissue, the degree of which is proportional to renal fibrosis, a critical factor in the progression of CKD. As reported from the literature, there exists a strong and positive correlation between SWE measurements (Young's modulus) and the extent of fibrosis determined on renal biopsies.

Association with CKD progression: Several research works show that some scores obtained through SWE are associated with the future progression of CKD. As observed in the study ^[19], more patients with increased SWE had a much higher probability of experiencing rapid decline in eGFR. Currently, there is ample evidence that SWE works in identifying the risks of CKD progression and ESRD; however, these findings need further research. Longitudinal studies: Establishing long-term cohort programs and comparing the acquired SWE values with the patients' real CKD status and ESRD evolution will help to enhance the findings. Combined with other data, the use of SWE data in addition to

conventional prognosticators (eGFR, UACR), and for that matter, genetics could enhance the accuracy of risk prediction. Development of risk models: Using SWE to construct clinical risk factors that may include other factors that may be associated with CKD progression and ESRD may be more beneficial in a more direct approach toward risk stratification models.

SWE for Treatment Monitoring:

SWE's ability to measure tissue stiffness makes it ideal for monitoring changes in renal fibrosis over time. By tracking changes in SWE measurements (e.g., Young's modulus), clinicians can assess treatment effectiveness and potentially:

- **Identify early signs of treatment failure:** Early detection allows for timely adjustments to treatment regimens before significant fibrosis progression occurs.
- **Differentiate between responders and non-responders:** SWE can potentially help tailor treatment strategies for individual patients based on their response to specific therapies.
- **Reduce reliance on invasive biopsies:** Serial SWE measurements offer a non-invasive alternative for monitoring fibrosis changes, minimising the need for repeated biopsies.

Supporting Evidence:

While research on SWE for treatment monitoring is ongoing, initial findings are promising. Studies suggest a correlation between changes in SWE measurements and response to anti-fibrotic therapies [Kidney International, Shear wave elastography for monitoring treatment response in patients with chronic kidney disease, 2021].

Limitations and Future Directions:

Early Stage Detection: The above rationale implies that SWE may not have the same ability to detect the mild stage of fibrosis as much as the severe stage. **Standardisation:** There is obviously a requirement for protocol and interpretation standardisation to increase the clinical use of SWE [Quantitative Imaging in Medicine and Surgery, Integrating shear wave elastography and estimated glomerular filtration rate to enhance diagnostic strategy for renal fibrosis assessment in chronic kidney disease, 2020]. In current literature, SWE was found to have potential in CKD diagnosis, but there are existing restrictions. Issues such as standardisation of protocols and their interpretations across the healthcare centres have remained a challenge [Quantitative Imaging in Medicine and Surgery 2020]. Furthermore, the evaluations could be affected by the operator technique, which exists for SWE. These problems are still being investigated, and attempts to define the values for fibrosis stages are being made. Moreover, there is ongoing interest in SWE for CKD in the context of the development of personalised medicine that may rely on assessing fibrosis progression to select the individual's appropriate treatment option.

CONCLUSION:

Blood and urine tests are the most commonly used methods that provide little information regarding the fibrosis of the kidney, which is an important feature in the progression of CKD. Serum creatinine offers good accuracy, but renal biopsy, which is the most accurate, is invasive with risks. Thus, there is SWE, which has been identified as offering a better solution. It is free of radiation and pain, has no interferences from patients and provides the possibility to observe variations in disease status. [19] showed the test's good accuracy in diagnosing moderate to severe fibrosis using SWE. Also, previous studies have shown the correlation between quantitative data obtained with SWE measurements and the amount of fibrosis present in biopsy samples. The issues may be lower sensitivity at early fibrosis staging and the necessity of the protocols' standardisation for broader application. However, SWE has the possibility to be the Association of its kind, or at least the best known one and people all around the world would know something about it. Hence, SWE has the potential to transform the management of CKD with more research to determine the cut-off values that correspond to various fibrosis stages, examine its use in monitoring treatment and incorporate it with other imaging techniques. Thus, SWE can become an essential tool in CKD diagnosis due to the ability to perform repeated scans without causing harm to the patient, providing objective quantitative data that can help start interventions earlier and improve the patients' outcomes.

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