

# Shear-Wave Elastography for Assessing Renal Biomechanical Properties in People with HIV During Early Antiretroviral Therapy

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## Article

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# Abstract

This cross-sectional study evaluated shear-wave elastography (SWE) for detecting early renal elasticity changes in 120 treatment-naïve people with HIV one month after initiating antiretroviral therapy (ART), alongside 30 healthy controls. Based on renal function post-ART, participants were categorized into normal ( $n = 105$ ) and abnormal ( $n = 15$ ) groups. Baseline characteristics were comparable. Renal cortical mean Young's modulus, measured by SWE, was significantly lower in the renal dysfunction group after one month of ART. The area under the ROC curve for distinguishing groups was 0.663, with an optimal cut-off of 4.20 kPa yielding a sensitivity of 49.5% and specificity of 86.7%. Measurements demonstrated good reproducibility in controls. These findings indicate that SWE can detect early renal biomechanical alterations post-ART, though its limited sensitivity precludes standalone diagnostic use, suggesting a potential role as an adjunct to conventional renal assessments.

## Introduction

Kidney injury associated with human immunodeficiency virus (HIV) infection is a significant complication affecting long-term patient outcomes [1]. Studies indicate that up to 48.5% of people with HIV may develop chronic kidney disease, with progression occurring more rapidly compared to the general population [2]. In addition to classic HIV-associated nephropathy, the potential nephrotoxicity of antiretroviral therapy (ART)—such as proximal tubule injury induced by tenofovir disoproxil fumarate (TDF)—further elevates renal risk [3]. Conventional clinical indicators for renal function, including estimated glomerular filtration rate (eGFR) and urine protein tests, exhibit limited sensitivity in detecting early structural kidney changes such as interstitial inflammation and fibrosis [4, 5], which may lead to delays in intervention.

In recent years, shear-wave elastography (SWE) has emerged as a noninvasive, quantitative technique for assessing tissue stiffness, offering a new perspective for the early evaluation of kidney disease. The principle involves tracking the propagation speed of shear waves through tissue to directly calculate Young's modulus (kPa), thereby objectively reflecting tissue elasticity [6]. In chronic kidney diseases such as diabetic nephropathy and IgA nephropathy, SWE has demonstrated a significant correlation with the degree of renal fibrosis and shows higher reproducibility compared to traditional ultrasound elastography techniques like acoustic radiation force impulse imaging [7, 8]. Currently, there is limited research on the application of SWE in people with HIV, particularly regarding the assessment of renal elasticity during the early stages of ART.

Changes in renal function and structure following ART are time-dependent. Research suggests that direct viral infection and replication represent the initial step in renal cell injury, followed by a gradual decline in eGFR [9]. Clinical observations indicate that ART can reduce renal inflammatory burden by suppressing viral replication [10]. This implies that during the early treatment phase (e.g., within one month), conventional renal function markers may fail to reflect microscopic structural alterations, whereas SWE may provide additional biological information. To date, no study has rigorously examined

the following hypothesis in a well-defined treatment-naïve HIV population: in the early period after ART initiation, do individuals who exhibit a decline in eGFR or an increase in serum creatinine already demonstrate altered renal elasticity? Addressing this question is essential for determining the clinical utility of SWE in monitoring this population.

In summary, this study hypothesizes that SWE can detect early changes in renal elasticity within one month after ART initiation and that these changes correlate with early renal dysfunction. We aim to provide imaging evidence to optimize early monitoring strategies for HIV-associated kidney disease and to establish a foundation for further research.

## Results

### 1. Comparison of Baseline Characteristics Among Groups

No significant differences were observed in gender, age, body mass index, baseline serum creatinine, baseline estimated glomerular filtration rate, or baseline renal elasticity values among the control group, the HIV-1 group, and the HIV-2 group. Similarly, no significant difference was found in CD4+ T-cell count between the HIV-1 and HIV-2 groups. Details are presented in Table 1.

### 2. Comparison of Renal Elasticity in People with HIV One Month After ART

One month after initiating ART, the renal elasticity values in the HIV-2 group were significantly lower than those in the HIV-1 group ( $P < 0.05$ ). Results are summarized in Table 2.

### 3. Diagnostic Value of SWE for Early Renal Dysfunction

The ROC curve is shown in Figure 2. The area under the curve (AUC) for Emean in distinguishing between the HIV-1 and HIV-2 groups one month post-ART was 0.663 (95% CI: 0.528–0.799,  $P = 0.041$ ). The optimal cut-off value was 4.20 kPa, yielding a sensitivity of 49.5% and a specificity of 86.7%. These results indicate a limited diagnostic value for identifying ART-related renal injury at this early stage.

### 4. Intra- and Inter-observer Reproducibility and Agreement of SWE Measurements

Renal elasticity of the right kidney was measured and the RK-Emean was calculated for the 30 healthy volunteers by the same operator and by two different operators. The intraclass correlation coefficients for both intra- and inter-observer measurements exceeded 0.75, indicating good reproducibility (Table 4). Bland–Altman analysis (Figure 1) showed that the majority of data points fell within the 95% limits of agreement, demonstrating satisfactory consistency. For subsequent analyses in this study, measurements obtained by a single operator were used.

## Discussion

In this study, we applied shear-wave elastography to evaluate renal elasticity changes in treatment-naïve people with HIV one month after initiating antiretroviral therapy. The results demonstrated no significant differences in baseline renal function or elasticity values between the group with normal renal function (HIV-1) and the group with renal dysfunction (HIV-2) prior to treatment. However, one month after ART

initiation, a statistically significant difference in renal Young's modulus values emerged between the two groups. This suggests that SWE may reflect early renal stress or adaptive responses following ART initiation and could provide insight into the biomechanical characteristics associated with early changes in renal function. Wang et al. [11] used SWE to assess healthy individuals and patients with stage 1–3 chronic kidney disease, finding that age-adjusted Emean decreased during the early stages of renal impairment, supporting its potential role as an adjunct tool for evaluating early renal dysfunction. Similarly, Chen et al. [12] measured 162 patients at different CKD stages and observed significantly lower Emean values in moderate and severe groups compared to the mild group. These findings align with the results of the present study, collectively indicating reduced renal elasticity following renal impairment. This phenomenon may be associated with early microstructural alterations in renal parenchyma induced by HIV infection and ART medications. Potential mechanisms include local inflammatory responses triggered by direct viral infection of glomerular podocytes and tubular epithelial cells, as well as mitochondrial injury and intracellular edema in proximal tubules caused by certain ART drugs such as tenofovir [3]. These pathological processes can lead to interstitial edema, inflammatory cell infiltration, and cytoskeletal reorganization—particularly involving actin and vimentin in podocytes—thereby reducing overall tissue stiffness [13].

We assessed the reproducibility and agreement of SWE measurements of the right kidney in healthy volunteers. Bland–Altman plots showed that the majority of data points fell within the 95% limits of agreement. Intraclass correlation coefficient analysis indicated excellent intra-observer agreement (ICC = 0.908) and good inter-observer agreement (ICC = 0.780), both exceeding 0.75. Multiple studies [14–17] have similarly reported favorable reproducibility of SWE when evaluating visceral organs—including the liver, kidneys, spleen, and parotid glands—in people with HIV. Interestingly, in a study of a feline CKD model (n = 78) [18], SWE measurements yielded only moderate intraclass correlation (0.62). The authors speculated that, aside from greater difficulty in controlling respiratory motion in cats, a key reason may be inherent differences between human and animal subjects. Notably, the software used in clinical ultrasound systems is typically optimized based on human tissue properties rather than animal models. Overall, under the conditions of this study, SWE demonstrated good intra- and inter-observer reproducibility and agreement in measuring renal Young's modulus. This provides a reliable methodological foundation for the subsequent analysis of our results and supports the favorable reproducibility and consistency of SWE for assessing renal elasticity in people with HIV.

Although SWE parameters demonstrated statistically significant differences between the two groups, their diagnostic performance for early renal dysfunction was limited (AUC = 0.663), a finding consistent with other studies. Shi et al. [19] applied supersonic shear wave imaging in pediatric patients with glomerular disease and found that while the technique could effectively distinguish the disease group from healthy controls (AUC up to 0.936), it could not differentiate between different pathological types or disease grades. Similarly, Wu et al. [20] performed SWE measurements in 54 patients with chronic kidney disease who underwent renal biopsy and reported limited diagnostic efficacy for CKD staging (AUC < 0.7). Integrating these studies with our own results, we propose that several factors may collectively explain these findings. First, as a single-center exploratory study, our cohort of participants with renal

dysfunction was relatively small ( $n = 15$ ), which may have limited statistical power and increased result variability. Second, early renal injury can be pathologically heterogeneous, manifesting primarily as interstitial edema or focal tubular damage. SWE reflects the average tissue stiffness within the region of interest and may therefore be less sensitive to early, focal lesions [21]. Third, our definition of renal dysfunction was based on changes in eGFR and serum creatinine—indicators that themselves exhibit a lag in early injury and are not fully synchronous with structural changes in the renal parenchyma. Additionally, SWE measurements can be influenced by operator experience, patient respiratory cooperation, and surrounding perirenal tissues, potentially introducing measurement error. Consequently, SWE is currently not suitable as a standalone tool for early screening, though it may hold unique value in longitudinal monitoring.

This study has several limitations. The absence of renal biopsy confirmation represents a major methodological constraint. Although changes in SWE-derived elasticity values suggest alterations in tissue mechanical properties, they cannot directly distinguish specific pathological types (e.g., interstitial inflammation, fibrosis, or edema) or establish a direct causal link with ART drug nephrotoxicity. Second, the sample size was modest, particularly the small number of participants in the renal dysfunction group, which may affect the statistical robustness of the conclusions. Third, the study employed a single-center, cross-sectional design and did not include long-term follow-up, precluding an assessment of the correlation between dynamic changes in SWE values and renal function progression. Finally, all participants received an ART regimen containing tenofovir (TDF/TAF), and no comparative subgroups based on drugs with differing nephrotoxicity risks were established.

Despite these limitations, our study preliminarily supports the feasibility of using SWE for early monitoring after ART initiation. Future research should aim to develop a multimodal framework for early renal injury assessment. First, conducting multicenter, large-sample longitudinal cohort studies is essential to clarify the trajectory of SWE parameters over time and their value in predicting CKD progression. Second, integrating SWE with emerging biomarkers of tubular injury (e.g., NGAL, KIM-1, IL-18) to explore the efficacy of a combined "imaging-biomarker" model for the early diagnosis and phenotyping of HIV-associated kidney disease. Furthermore, stratified comparisons of the long-term effects of different ART regimens (e.g., tenofovir-containing vs. tenofovir-sparing regimens) on renal elasticity could provide evidence for individualized therapeutic strategies. Through these approaches, SWE has the potential to evolve from a research tool into a clinically useful adjunct for monitoring.

In this cohort of treatment-naïve people with HIV, those who developed renal dysfunction one month after initiating ART exhibited lower renal Young's modulus values compared to those with preserved renal function, suggesting that SWE may provide insight into early functional changes in the kidney. However, the sensitivity and specificity of SWE alone for diagnosing early renal impairment remain limited, and it cannot currently replace conventional renal function measures.

As a noninvasive elastographic technique, SWE holds potential as an adjunctive tool in the early monitoring of HIV-associated kidney disease, complementing traditional assessments by enabling

dynamic observation of renal parenchymal elasticity. Further studies with larger sample sizes and longitudinal designs are warranted to clarify the optimal timing and clinical significance of SWE in the management of kidney disease in people with HIV.

## Materials and Methods

### 1. Study Participants

This was a single-center, cross-sectional study involving treatment-naïve individuals with HIV who visited the AIDS outpatient clinic of our hospital between January 2024 and January 2025. The study protocol was approved by the Ethics Committee of Jinjiang Municipal Hospital (Shanghai sixth People's Hospital Fujian) (Approval No.: jjsyyl-2024-083). All methods were performed in accordance with the relevant guidelines and regulations. Written informed consent was obtained from all participants.

#### 1.1 HIV Group

A total of 120 eligible individuals with HIV were enrolled. Inclusion criteria were: (1) age 18–65 years; (2) meeting WHO diagnostic criteria for HIV infection and being treatment-naïve (no prior ART); (3) completion of one month of standard ART (a regimen based on tenofovir [TDF or TAF]/lamivudine plus dolutegravir or efavirenz); and (4) normal baseline renal function (eGFR  $\geq 90$  mL/min/1.73 m<sup>2</sup> and urine protein-to-creatinine ratio  $< 30$  mg/g). Exclusion criteria included: (1) comorbid diabetes, hypertension, or other chronic kidney diseases; (2) active opportunistic infections or malignancy; (3) pregnancy or lactation; and (4) structural kidney abnormalities on ultrasound (e.g., cysts, stones).

Participants were classified based on renal function one month after ART initiation: those with normal renal function were assigned to the HIV-1 group (n=105; 77 male, 28 female; median age 38 years [IQR 28.0, 53.0]), and those with abnormal renal function to the HIV-2 group (n=15; 8 male, 7 female; median age 49 years [IQR 31.0, 56.0]). Renal dysfunction was defined as: 1) a decline in eGFR  $\geq 25\%$  from baseline; or 2) an increase in serum creatinine  $\geq 26.5$   $\mu\text{mol/L}$  or  $\geq 1.5$  times the baseline value.

#### 1.2 Healthy Control Group

Thirty healthy volunteers (control group) were enrolled (20 male, 10 female; median age 40 years [IQR 34.5, 49.0]). Inclusion criteria were: (1) age, sex, and BMI matched to the HIV group; (2) no history of HIV infection or other chronic diseases; and (3) normal renal function (eGFR  $\geq 90$  mL/min/1.73 m<sup>2</sup> and negative urinalysis).

### 2. Shear-Wave Elastography Examination

Renal SWE was performed using a Philips EPIQ 7 ultrasound system equipped with a convex array probe (C5-1). The elastography mode was set to "Renal," with a frequency range of 2–6 MHz, depth of 8–12 cm, and a sample box covering the mid-cortical region of the kidney (avoiding the medulla and collecting system).

Participants were placed in the prone position with the bilateral renal areas fully exposed. After confirming the absence of structural abnormalities via conventional grayscale ultrasound, the operator located the longitudinal section of the kidney and switched to SWE mode. During measurement, the probe was applied without external pressure, and participants were instructed to hold their breath briefly. The sample box was placed within the mid-cortical area, and the image was frozen once the elastogram stabilized. A circular region of interest (ROI) with a diameter of 5 mm was manually outlined, and the mean Young's modulus value (E<sub>mean</sub>, kPa) was recorded. For each kidney, three measurements were taken at the upper, middle, and lower poles. The parameter RK-E<sub>mean</sub> was calculated as the average of all measurements from the right kidney, LK-E<sub>mean</sub> as the average from the left kidney, and E<sub>mean</sub> as the overall average across both kidneys (Figure 1).

For the healthy control group, two senior sonographers with more than five years of SWE experience independently measured the right renal elasticity and calculated the RK-E<sub>mean</sub>. Intra- and inter-observer reproducibility and agreement were assessed using the intraclass correlation coefficient and Bland–Altman analysis.

### **3. Data Collection**

The following data were collected for all groups: age, sex, body mass index, estimated glomerular filtration rate (calculated using the CKD-EPI formula), serum creatinine, CD4+ T-cell count, and the mean Young's modulus values of both kidneys.

### **4. Statistical Analysis**

Data were analyzed using SPSS software version 26.0. Normality of continuous variables was assessed with the Shapiro–Wilk test. Normally distributed data are presented as mean  $\pm$  standard deviation (SD); non-normally distributed data are described as median and interquartile range [M (IQR)]. Categorical variables are expressed as number and percentage [n (%)].

For comparisons among the three groups (control, HIV-1, HIV-2): continuous variables meeting normality and homogeneity of variance were analyzed using one-way ANOVA, with pairwise comparisons conducted using the LSD t-test. Otherwise, the Kruskal–Wallis H test was used for overall comparison, followed by the Mann–Whitney U test with Bonferroni correction for pairwise comparisons. Categorical variables (e.g., sex) were compared using the chi-square test or Fisher's exact test, as appropriate.

For comparisons between the two HIV groups (HIV-1 vs. HIV-2): independent t-tests or Mann–Whitney U tests were used according to data distribution. Receiver operating characteristic (ROC) curve analysis was performed using E<sub>mean</sub> at one month post-ART as the test variable and group assignment as the state variable to evaluate the diagnostic value of SWE for early renal dysfunction.

Intra- and inter-observer reproducibility and agreement were evaluated using the intraclass correlation coefficient and Bland–Altman analysis. An ICC > 0.75 was considered indicative of good agreement. All statistical tests were two-sided, and a P-value < 0.05 was considered statistically significant.

# Declarations

## Data availability

The data sets generated and/or analyzed during this study are available from the corresponding author on reasonable request.

## Ethics Statement

The study protocol was approved by the Ethics Committee of Jinjiang Municipal Hospital(Shanghai sixth People's Hospital Fujian) (Approval No.: jjsyyl-2024-083). Informed consent was obtained from all participants in the study.

## Author contributions

Y.S. and F.Y. contributed to study design, clinical data collection, and manuscript drafting. G.L. contributed to study design and manuscript review. N.G. contributed to manuscript review and data analysis. J.G., M.C., S.H. and J.L. contributed to ultrasound data quality control. C.L. contributed to clinical data quality control. K.W. contributed to laboratory data quality control. All authors have read and approved the final manuscript.

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## Competing interests

The authors declare no competing interests.

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Tables

Table 1. Comparison of Baseline Characteristics Among Groups

| Variable                                    | HIV-1 Group<br>(n=105)  | HIV-2 Group<br>(n=15)   | Normal Group<br>(n=30)  | Statistic<br>( $\chi^2$ /F/H) | P value |
|---------------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------------|---------|
| Male/Female, n                              | 77 / 28                 | 8 / 7                   | 20 / 10                 | $\chi^2 = 2.69$               | 0.259   |
| Age, years                                  | 38.00 (28.00, 53.00)    | 49.00 (31.00, 56.00)    | 40.00 (34.50, 49.00)    | H = 1.61                      | 0.447   |
| BMI, kg/m <sup>2</sup>                      | 21.72 (19.70, 23.50)    | 20.96 (20.30, 23.90)    | 21.75 (20.60, 22.60)    | H = 0.02                      | 0.994   |
| CD4+ count, cells/ $\mu$ L                  | 263.00 (150.00, 417.80) | 205.00 (120.00, 350.00) | 775.50 (661.25, 855.50) | H = 69.74                     | <0.001  |
| Serum creatinine (baseline), $\mu$ mol/L    | 68.64 $\pm$ 12.10       | 76.32 $\pm$ 11.19       | 69.26 $\pm$ 11.88       | F = 2.71                      | 0.070   |
| eGFR (baseline), mL/min/1.73 m <sup>2</sup> | 107.10 (92.50, 128.50)  | 108.00 (95.00, 127.00)  | 109.50 (102.00, 121.75) | H = 0.43                      | 0.809   |
| RK-Emean (baseline), kPa                    | 4.01 (3.30, 5.20)       | 4.27 (2.80, 4.70)       | 3.94 (3.50, 4.30)       | H = 0.61                      | 0.737   |
| LK-Emean (baseline), kPa                    | 4.14 (3.60, 4.80)       | 3.90 (3.60, 4.30)       | 3.92 (3.50, 4.30)       | H = 3.33                      | 0.190   |
| Overall Emean (baseline), kPa               | 3.96 (3.50, 4.90)       | 3.93 (3.40, 4.40)       | 3.93 (3.50, 4.30)       | H = 1.26                      | 0.533   |

Data are presented as median (interquartile range) or mean  $\pm$  standard deviation, as appropriate. Categorical data are shown as counts. EGFR, estimated glomerular filtration rate; RK-Emean, mean Young's modulus of the right kidney; LK-Emean, mean Young's modulus of the left kidney.

Table 2. Comparison of Renal Elasticity Values Between Groups One Month After HAART

| Variable                  | HIV-1 Group<br>(Normal Renal Function,<br>n=105) | HIV-2 Group<br>(Abnormal Renal Function,<br>n=15) | Statistic            | P value      |
|---------------------------|--------------------------------------------------|---------------------------------------------------|----------------------|--------------|
| <b>RK-Emean, kPa</b>      | 4.02 (3.60, 5.20)                                | 3.57 (3.10, 4.40)                                 | <i>U</i> =<br>533.50 | <b>0.040</b> |
| <b>LK-Emean, kPa</b>      | 4.38 ± 0.87                                      | 3.90 ± 0.57                                       | <i>F</i> =4.41       | <b>0.030</b> |
| <b>Overall Emean, kPa</b> | 4.20 (3.60, 5.20)                                | 3.68 (3.40, 4.20)                                 | <i>U</i> =<br>533.50 | <b>0.040</b> |

Data are presented as median (interquartile range) for non-normally distributed variables (RK-Emean, Overall Emean) or mean ± standard deviation for normally distributed variables (LK-Emean).

RK-Emean, mean Young's modulus of the right kidney; LK-Emean, mean Young's modulus of the left kidney.

**Table 3. Diagnostic Performance of SWE Parameters for Early Renal Dysfunction One Month Post-ART**

| Parameter            | AUC (95% CI)        | Optimal Cut-off (kPa) | Sensitivity | Specificity |
|----------------------|---------------------|-----------------------|-------------|-------------|
| <b>RK-Emean</b>      | 0.661 (0.523–0.799) | 3.65                  | 69.5%       | 60.0%       |
| <b>LK-Emean</b>      | 0.677 (0.542–0.812) | 4.24                  | 56.2%       | 80.0%       |
| <b>Overall Emean</b> | 0.663 (0.528–0.799) | 4.20                  | 49.5%       | 86.7%       |

SWE, shear-wave elastography; ART, antiretroviral therapy; AUC, area under the receiver operating characteristic curve; CI, confidence interval; RK-Emean, mean Young's modulus of the right kidney; LK-Emean, mean Young's modulus of the left kidney.

**Table 4. Intra- and Inter-observer Reproducibility of Renal SWE Measurements**

| Measurement Type | Intraclass Correlation Coefficient (ICC) | 95% Confidence Interval |
|------------------|------------------------------------------|-------------------------|
| Intra-observer   | 0.908                                    | 0.808 – 0.956           |
| Inter-observer   | 0.780                                    | 0.538 – 0.895           |

SWE, shear-wave elastography. ICC > 0.75 is generally considered to indicate good reproducibility. Measurements were performed on the right kidneys of 30 healthy volunteers.

## Figures

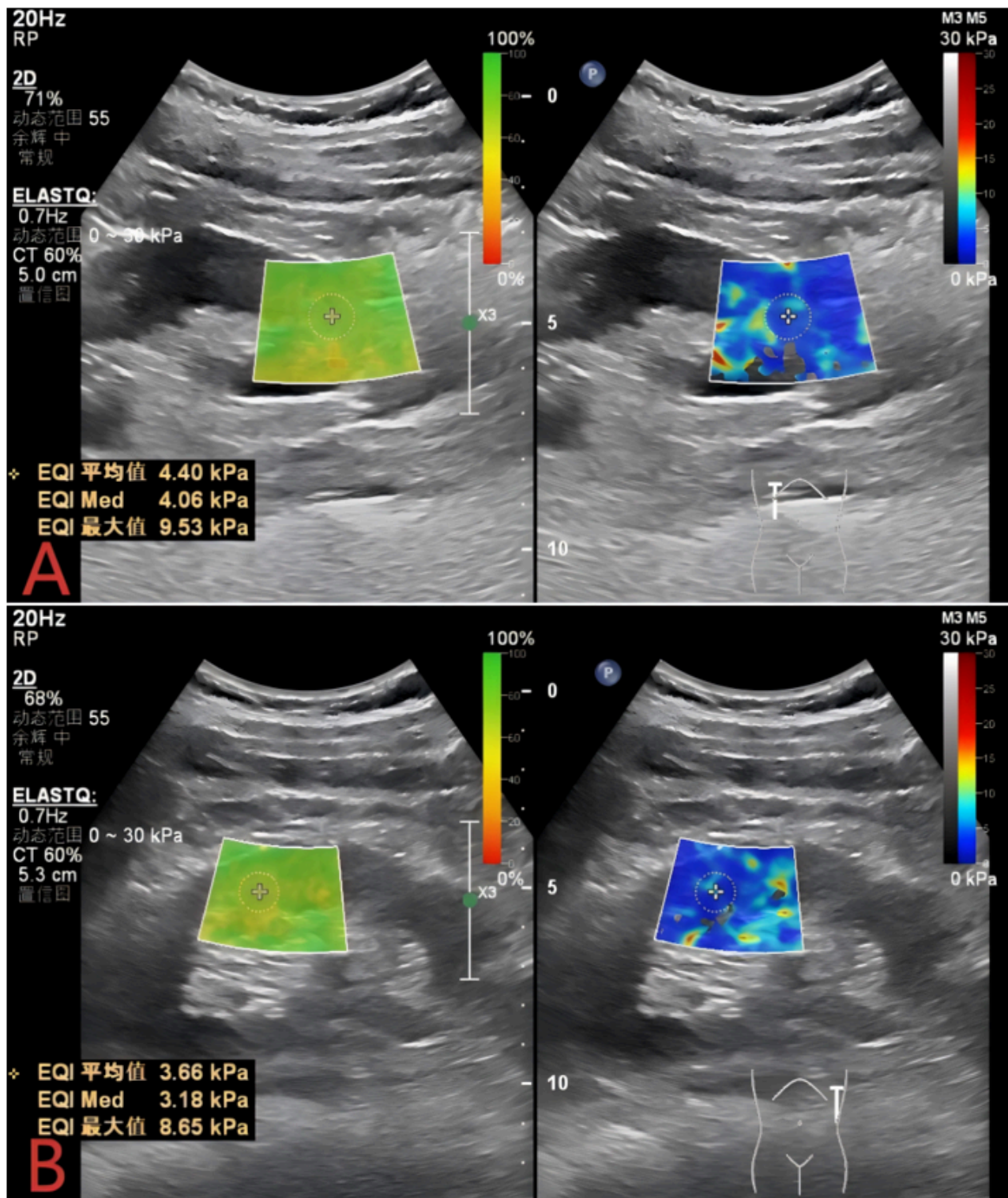


Figure 1

Representative SWE measurements in an HIV-infected individual

(A) SWE measurement of the kidney in a treatment-naïve HIV-infected patient before initiating antiretroviral therapy (ART), showing a mean Young's modulus value (E<sub>mean</sub>) of 4.40 kPa. (B) SWE measurement of the same patient one month post-ART, demonstrating an E<sub>mean</sub> of 3.66 kPa.

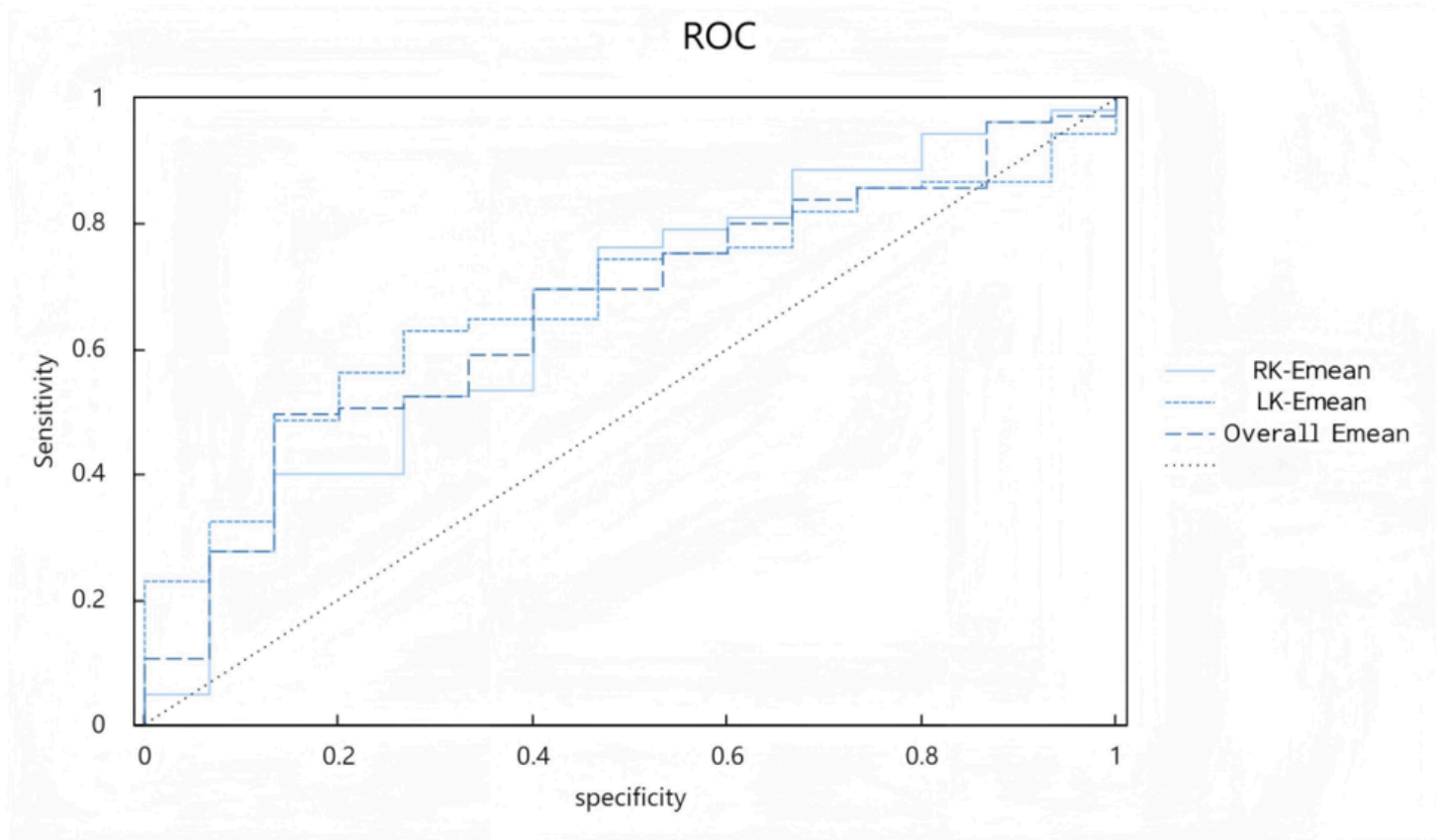


**Figure 2**

ROC curve of SWE for detecting early renal impairment in HIV-infected patients following ART.

The ROC curves compare three diagnostic parameters: RK-E<sub>mean</sub>, LK-E<sub>mean</sub>, and Overall E<sub>mean</sub>. Sensitivity is plotted on the y-axis, while specificity is shown on the x-axis. The diagonal reference line represents random probability. The curves indicate that RK-E<sub>mean</sub> (AUC=0.661), LK-E<sub>mean</sub> (AUC=0.677), and Overall E<sub>mean</sub> (AUC=0.663) exhibit limited diagnostic value for detecting early renal impairment in HIV-infected patients following ART.

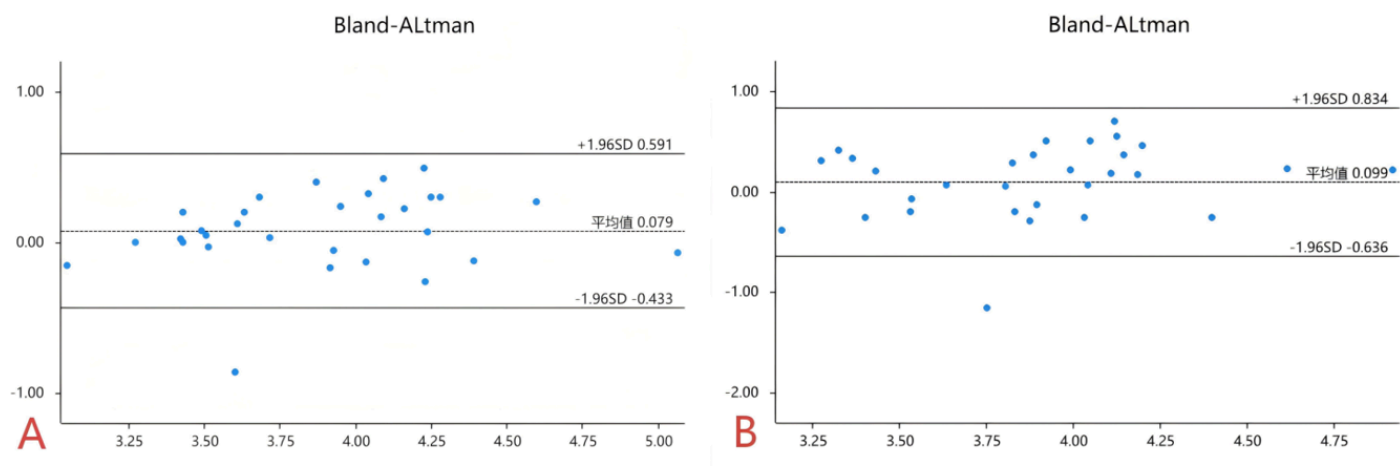


**Figure 3**

Bland-Altman plot of SWE measurements of right renal elasticity in the control group, assessed by the same operator and by different operators.

For the same sonographer (A) and between different sonographers (B), the SWE measurements of right renal elasticity in the healthy control group mostly fell within the 95% limits of agreement, demonstrating good agreement.