

Kidney Ultrasound Elastography: Review

Böbrek Ultrason Elastografisi: Derleme

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ABSTRACT

Kidneys are the most important and the functional organs in the body. There are numerous of disorders affecting the kidneys. The most important disorder is chronic kidney disease because of being costly and going to failure. In recent years ultrasound elastography technics showed increasing development line, and more studies were performed about elastography on kidneys. The weighted amount of the elastography studies are about chronic kidney disease, kidney failure and allograft patients, while some of them are about kidney masses or diabetic nephropathy. Various studies presented various results. In this review we want to present the elastography studies about kidney.

Key words: kidney; elastography; chronic kidney disease

ÖZET

Böbrekler çok önemli ve fonksiyonel organlardır. Böbreği etkileyen çok sayıda hastalık vardır. Kronik böbrek hastalığı yüksek maliyeti ve yetmezliğe ilerlemesi nedeniyle en önemli hastalıktır. Son yıllarda sonoelastografi tekniği yükselen bir grafik çizmektedir ve böbrekler üzerinde sonoelastografi tekniği kullanılarak yapılmış değişik çalışmalar mevcuttur. Bu çalışmaların çoğunluğu kronik böbrek hastalığı, böbrek yetmezliği ve allograft hastalarını konu alırken, bazıları böbrek kitleleri ve diabetik nefropati hakkındadır. Farklı çalışmalarda farklı sonuçlar sunulmuştur. Bu derlemede böbrekler hakkında yapılan sonoelastografi çalışmalarını sunmayı planladık.

Anahtar kelimeler: böbrek; elastografi; kronik böbrek hastalığı

Abbreviations (Listed in Alphabetical Order)

Acoustic Radiation Force Impulse Elastography (ARFI)
Angiomyolipoma (AML)
Chronic Allograft Injury (CAI)
Chronic Allograft Nephropathy (CAN)
Chronic Kidney Disease (CKD)
Dimercaptosuccinic acid (DMSA)
estimated Glomerular Filtration Rate (eGFR)
Glomerular Filtration Rate (GFR)
Intravenous Pyelography (IVP)
kiloPascal (kPa)
Magnetic Resonance Imaging (MRI)

Pulsatility Index (PI)
Renal Cell Carcinoma (RCC)
Resistive Index (RI)
Real-time sonoelastography (RSE)
Region of Interest (ROI)
Real-time elastography (RTE)
Renal Transplant Recipients (RTRs)
Strain Elastography (SE)
Strain Index (SI)
Strain Ratio (SR)
Supersonic Shear Imaging (SSI)
Shear-wave Elastography (SWE)
Shear Wave Speed (SWS)
Shear Wave Velocity (SWV)
Transient Elastography (TE)
Tissue Mean Elasticity (TME)
Ultrasonography (USG, US)
Vesico Ureteral Reflux (VUR)
Zero-Crossing (ZC)

Kidneys

Kidneys are vital and important organs, anatomically and functionally depicted as parenchyma and sinus. Parenchyma consists of cortex and medulla, and sinus consists of fat, tubulatory collecting system, pelvis, blood vessels and nerves¹. There are numerous of disorders affecting the kidneys. Some of them are functional, systemic and diffuse, while some are local and massy, and also vascular, congenital, hereditary and acquired^{2,3}. Among all the disorders, chronic kidney disease (CKD) and transplanted kidneys are the subject of elastography in a majority of studies⁴⁻¹⁴. CKD is an important and costly health problem because of not only the increasing incidence and prevalence but also resulting in end-stage renal failure. The progression of CKD shows fibrosis involving first glomeruli or interstitial space¹⁵⁻¹⁹. Fibrosis can be detected only by the biopsy procedure, which is interventional and non comfortable for the patients. To detect the fibrosis, non-invasive and quickly obtained methods are essential for nephrologists not

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to waste time and to plan the treatment. The fibrosis changes the microstructure and elasticity of the tissue²⁰. Elastography presents the elasticity of the tissue but has not been placed in the routine diagnostic algorithm of the kidney disorders. In this review, we aim to discuss the USG elastography method in kidney disorders with the literature background.

Elastography

Elastography was first described by Ophir et al.²¹. The working principle of elastography is based on the lesion or tissue stiffness. Standard USG device and elastography software are enough to establish the elastography. Basically two types of elastography can be counted as quasi static and dynamic differentiating each other from data collecting way and the software. Strain elastography (SE) is quasi static method. Shear-wave Elastography (SWE), Acoustic Radiation Force Impulse Elastography (ARFI) and Transient elastography (TE) are the dynamic types^{22,23}.

Dynamic Methods

(Acoustic Radiation Force Impulse Elastography, Shear-Wave Elastography, and Transient Elastography)

Shear-wave elastography uses shear-waves to collect the data. The propagation speed of the shear wave is measured in this method. The software processes the shear-wave propagation in very very short time and quickly (20.000 frame in second) and presents the quantifiable values. The unit of shear wave is m/sec and the tissue elasticity is kiloPascal (kPa) (Fig. 1 and Fig. 2). The elasticity formula is $E = \rho c^2$. The 'E' indicates the tissue elasticity, ' ρ ' (kg/cm³) indicates the tissue density, while 'c' (m/sec) indicates the shear-wave speed. But SWE has some limitations, such as lack of measurement in ascites medium. The operator independency is the superiority of SWE^{22,24}. The major handicap of SWE is the anisotropy, which is related with the tissue structure and the beam distribution. The renal cortical structure shows radial distribution from hilus to cortex. The USG beams come in different angles to the poles and equator of the kidney. If the beams come parallel to these structures, shear waves propagate perpendicularly, while beams come perpendicular shear waves propagate parallelly. This anisotropy causes discordance in the values of poles and equator^{23,25}.

ARFI is another method that uses shear-waves as SWE does. But the data acquisition of ARFI is different from the SWE. In ARFI the high energized short term

(0.03–0.04 msec) acoustic pulses, make the micrometric (1–20 μm) displacements in the examined tissue. Square shaped Region of Interest (ROI) is used to measure the micrometric displacements. The displacement generates the shear-waves. ARFI uses the displacement of the examined tissue using shear waves, but does not use the speed of shear-wave unlike SWE. The soft tissues are bright, while the hard tissues are dark in ARFI in gray scale screen. The unit of ARFI is m/sec. Operator independency and the quantitative data presentation are the advantages of ARFI, but does not have capability to present data in ascites mediums like in SWE^{22,26–28}.

TE is one of the methods that use shear-waves. The main usage area and the studies about TE is based on the liver. In this method, the USG probe applies external mechanical impulse to the related tissue, thus shear-wave generates in the related tissue. The speed and the displacement of the shear wave according to the deepness generate an image like in M-mode. So the major handicap of TE is lack of gray scale B-mode USG images. TE can only serve the M-mode USG images. The speed of the shear wave increases with the stiffness of the tissue. TE can not be used in the existence of perihepatic fluid. The evaluated area is 200 times bigger (3 cm³) than the biopsy. The unit of TE is kPa. In TE, the inter and the intra-observer variability is minimal. But there are also some limitations, such as obesity, does not have capability to present data in ascites mediums and in focal lesion. The main limitation about liver is the non capability of measurement in left lobe^{22,23,28–32}.

Quasi Static Method (SE)

Strain Elastography is different from shear-wave elastography methods in some ways. In SE the acoustic force is applied by the operator manually. The operator does not only produce the acoustic force, but also produces the dynamic force to the examined tissue, thus this method is semi-static. The operator or transducer applies compression and decompression pulses to the related lesion. The measurements should be collected in the decompression phase, to avoid the pressure effect. SE measures the displacement and the deformation of the lesion. The unit of SE is Strain Index (SI). SI, means the stiffness ratio of the adjacent tissue compared to the examined lesion. The stiffness of the hard lesions is higher, thus the displacement and deformation is lower. So, the strain of hard lesions is lower, but the SI of hard lesions is higher, because of the ratio. In this method, two ROIs

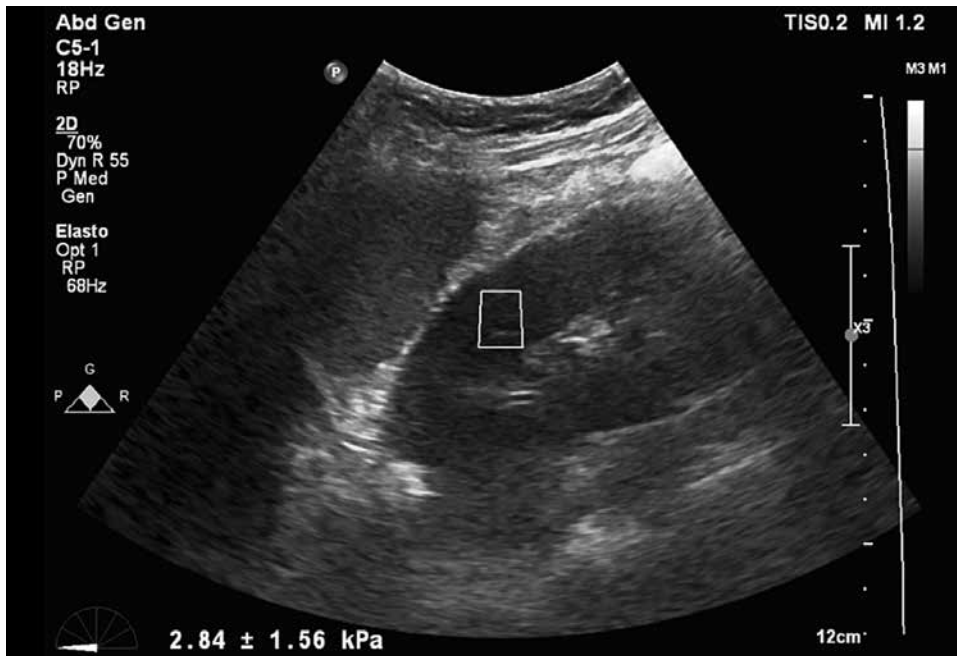


Figure 1. Shear wave elastography image of kidney parenchyma. The square indicates the measurement localization. The number below the figure indicates stiffness of the tissue in the unit of kPa.

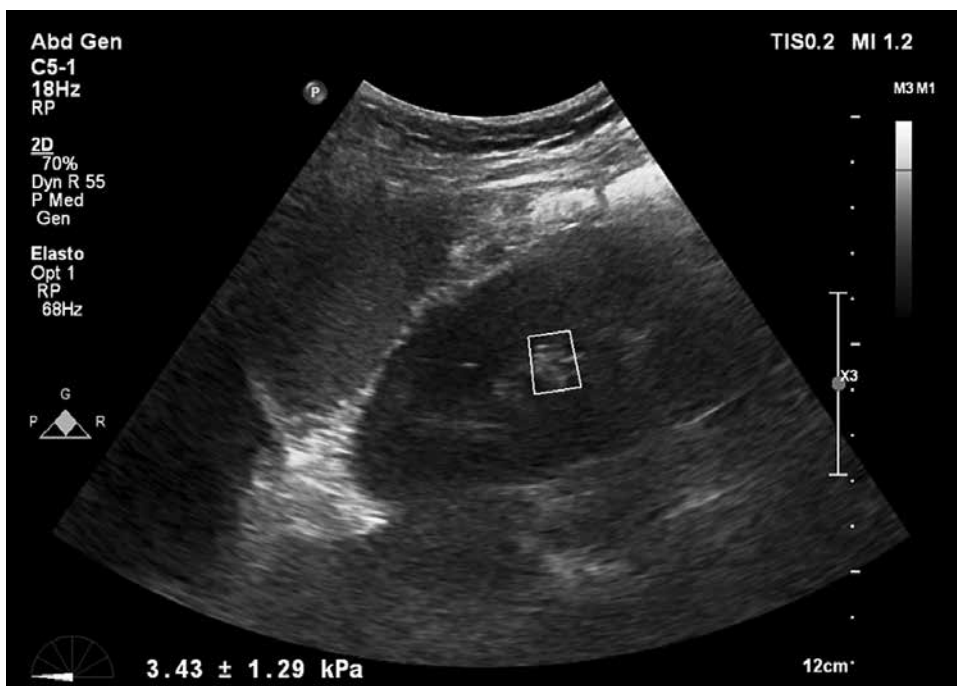


Figure 2. Shear wave elastography image of kidney sinus. The square indicates the measurement localization. The number below the figure indicates stiffness of the tissue in the unit of kPa.

are required to measure and compare the stiffness (Fig. 3 and Fig. 4). The major limitation of the SE is operator dependency. The window width and the transducer pressure affects the image quality. The window should be arranged as optimal as the lesion size. The compression and the decompressions should be done slightly and not very slow or not very fast (0.5–2 compressions in a

second). The distance between the lesion and the transducer should be less than 3–4 cm to acquire more reliable data. This method has an advantage about providing data in ascites medium, unlike others^{20,22,23,33,34}.

The major limitation of all elastography methods are small sample size. For example strain ratio needs to rate

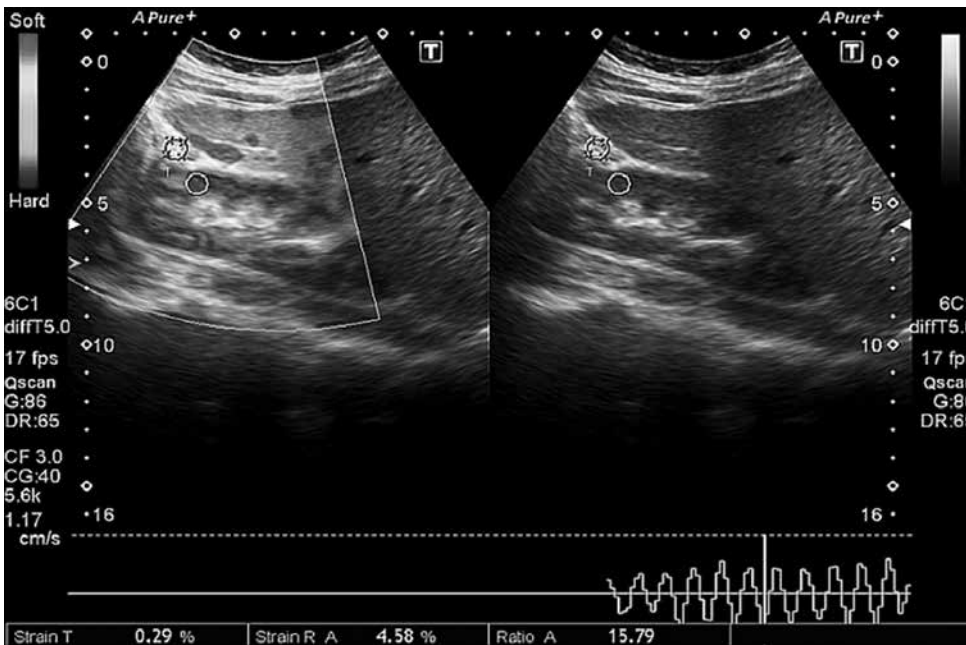


Figure 3. Strain elastography image of the kidney parenchyma. The image shows active elastography mode of ultrasonography (USG). The screen was divided into three parts as right, left and bottom. The color coded left side indicates elastography mode, while the right side is gray scale B-mode USG image. The bottom indicates the sinusoidal wave, which allows the operator to follow the compression and decompressions. The circles indicates the region of interests (ROI). One ROI was adjusted to the parenchyma while the other was in the perirenal fat tissue. The strain ratio was given below the screen.

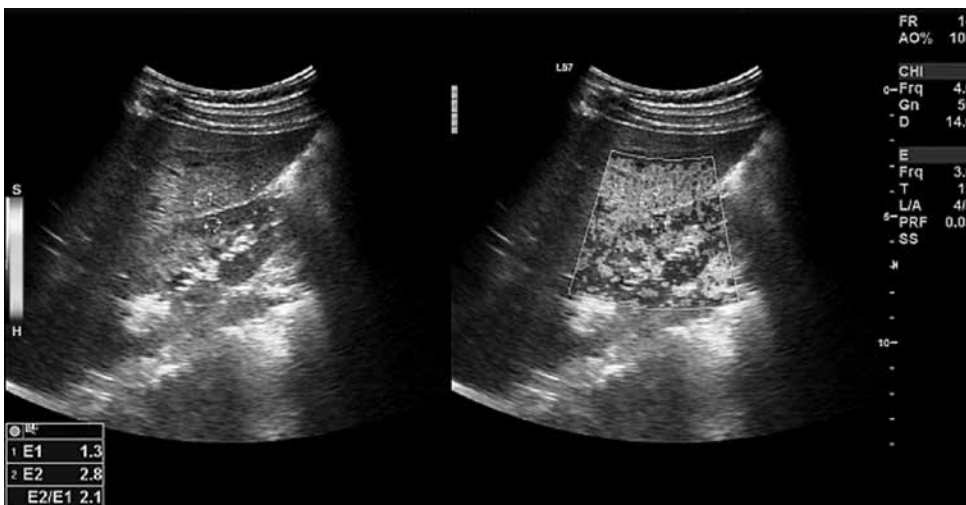


Figure 4. Strain elastography image of the kidney parenchyma. The right side of the image indicates the elastography mode. Two ROIs seen in the left side image. One of them was adjusted to the liver parenchyma while the other was on the kidney parenchyma. The numbers below the screen indicates the strain ratio of the parenchyma and the adjacent tissue.

the two adjacent tissue. The operator can only adjust the ROI size according to the parenchyma/sinus and the perisplenic soft tissue. To avoid the tissue wrong sampling, operator should use maximum sampling ROIs. Maximum ROI should present the the more reliable value. But using maximum ROI will take a lot of time. In addition to ROI size, the organs have three dimensions but the US systems allows the operator to measure in two dimension. If operator can measure whole the kidney this measurement will present only two dimensional one slice value³⁵. This means that, operator should take more measurements from different aspects of the kidney. This procedure also takes more time.

Literature Review

In the advanced search mode of Pubmed using the words 'kidney elastography', picking the MeSH terms and Title/Abstract, 49 results were listed. Some of them were about animals³⁶⁻⁴², some of them were about MRI or MR elastography⁴³⁻⁵², some of them were about other organ systems⁵³⁻⁶⁵, some of them were about elastography technic^{28,66-69} and some of them were about non elastography related kidney studies⁷⁰. We excluded these articles. The rest amount of related articles were 13^{4,5,8-11,13,14,25,71-74}. But, pubmed search missed some articles^{6,7,12,35,75}, that was mentioned in this paper (Table 1).

Table 1. The articles that we discussed

Reference	Elastography type	Patient population	Study design	Conclusion
Ardnt 2010 et al. Noninvasive evaluation of renal allograft fibrosis by transient elastography--a pilot study	TE (Fibroscan)	Renal transplanted 55 patients, Biopsies were performed in 20 patients.	Evaluates the feasibility of TE for the assessment of renal allograft fibrosis. Stiffness was significantly correlated to the extent of interstitial fibrosis (Pearson r: 0.67, P: 0.002, R(2): 0.45) and inversely related to eGFR (Pearson r: -0.47, P: 0.0003, R(2): 0.22). The stiffness values of chronic allograft injury Banff grades 0-1 differed significantly from grade 2 (P: 0.008) and grade 3 (P: 0.046).	Parenchymal stiffness measured by TE reflects interstitial fibrosis in kidney allografts.
Asano et al. Acoustic radiation force impulse elastography of the kidneys: is shear wave velocity affected by tissue fibrosis or renal blood flow?	ARFI (Siemens Acuson S2000)	319 CKD, 14 healthy volunteers	Identify the main influencing factor of the SWV. The SWV decreased concurrently with a decline in the eGFR. A low SWV was obtained in patients with a high brachial-ankle pulse wave velocity. Despite progression of renal fibrosis in the advanced stages of CKD, these results were in contrast to findings for chronic liver disease, in which progression of hepatic fibrosis results in an increase in the SWV. Considering that a high brachial-ankle pulse wave velocity represents the progression of arteriosclerosis in the large vessels, the reduction of elasticity succeeding diminution of blood flow was suspected to be the main influencing factor of the SWV in the kidneys.	Diminution of blood flow may affect SWV values in the kidneys more than the progression of tissue fibrosis.
Dillman et al. Can Shear-Wave Elastography be Used to Discriminate Obstructive Hydronephrosis from Nonobstructive Hydronephrosis in Children?	SWE (Siemens)	37 children	Children underwent elastography of the kidneys immediately before and immediately after diuretic renal scintigraphy (reference standard for presence of urinary tract obstruction). Median SWS measurements, as well as change in median SWS (median SWS after diuretic administration minus median SWS before diuretic administration) were correlated with the amount of time required for kidney radiotracer activity to fall by 50% after intravenous administration of the diuretic ($T_{1/2}$). Median SWS measurements were compared with degree of obstruction and degree of hydronephrosis with analysis of variance.	US SWS measurements did not enable discrimination of obstructive hydronephrosis from unobstructive hydronephrosis in children.
Gao 2013 et al. Renal transplant elasticity ultrasound imaging: correlation between normalized strain and renal cortical fibrosis	SE (Echolnsight, Epsilon Imaging)	20 renal transplant	The hardness of the renal cortex in renal transplant allograft patients using a normalized ultrasound strain procedure measuring quasi-static deformation. Normalized strain is defined as the mean developed strain in the renal cortex divided by the overall mean strain measured in the soft tissues from the abdominal wall to pelvic muscles. Banff scoring.	Renal cortex strain is strongly correlated with grade of renal cortical fibrosis. Normalized strain is superior to developed strain in distinguishing moderate from mild renal cortical fibrosis.
Gao 2013 et al. Corticomedullary strain ratio: a quantitative marker for assessment of renal allograft cortical fibrosis	SE (Siemens Acuson Sequoia 512)	Renal allograft 33 patients	Correlation between the corticomedullary SR and cortical fibrosis in renal transplants. on Banff scoring. We calculated the corticomedullary SR (cortical normalized strain/medullary normalized strain; normalized strain = developed strain/applied strain [deformation from the abdominal wall to the pelvic muscles]).	Strain values vary in different compartments of the kidney. The corticomedullary SR on USG elasticity imaging decreases with increasing renal cortical fibrosis, which makes it potentially useful as a noninvasive quantitative marker for monitoring the progression of fibrosis in renal transplants.
Gao 2014 et al. Ultrasound strain zero-crossing elasticity measurement in assessment of renal allograft cortical hardness: a preliminary observation	SE (quasi-static ultrasound elastography)	38 renal transplant patients	USG strain ZC elasticity measurement can be used to discriminate moderate cortical fibrosis or inflammation in renal allografts, we assessed cortical hardness with quasi-static USG elastography in renal transplant patients who underwent kidney biopsy. Banff scoring.	ZC is a new strain marker that could be straightforward to interpret and perform, making it a potentially practical approach for monitoring progression of cortical fibrosis or inflammation in renal allografts.
Goya 2015 et al. The role of quantitative measurement by acoustic radiation force impulse imaging in differentiating benign renal lesions from malignant renal tumours	ARFI (Siemens Acuson S2000)	60 patients with renal lesions; benign, malign and infectious	Evaluate the diagnostic performance of ARFI for differentiating benign lesions from malignant renal tumours. The final diagnoses were determined via pathologic (n = 33), clinical (n = 13) and imaging findings (n = 14). The SWV values of the renal tumours were analysed according to the final diagnoses.	ARFI imaging may be useful for differentiating between benign renal lesions and malignant renal tumours.

Table 1 (continued). The articles that we discussed

Reference	Elastography type	Patient population	Study design	Conclusion
Goya 2015 et al. Acoustic radiation force impulse (ARFI) elastography for detection of renal damage in children	ARFI (Siemens Aconon S2000)	88 children, 20 healthy controls	To investigate the contribution of ARFI quantitative USG elastography for the detection of renal damage in kidneys with and without VUR. Patients were assessed according to severity of renal damage on DMSA scintigraphy.	Decreasing SWV of renal units with increasing grades of VUR.
Goya 2015 et al. Acoustic radiation force impulse imaging for evaluation of renal parenchyma elasticity in diabetic nephropathy	ARFI (Siemens Aconon S2000)	114 diabetic nephropathy, 281 healthy	Evaluate the changes in the elasticity of the renal parenchyma in diabetic nephropathy using ARFI acoustic radiation force impulse imaging. The changes in the renal elasticity were compared between the different stages of diabetic nephropathy and the healthy control group.	ARFI imaging could be used for the evaluation of the renal elasticity changes that are due to secondary structural and functional changes in diabetic nephropathy.
Grenier 2011 et al. [Imaging and renal failure: from inflammation to fibrosis]				Article in French
Grenier 2013 et al. Renal ultrasound elastography				Review
Grenier et al., 2012 Quantitative elastography of renal transplants using supersonic shear imaging: a pilot study	SWE	43 kidney transplant recipient, followed by biopsy	The reliability of quantitative ultrasonic measurement of renal allograft elasticity using SSI. Banff score.	Quantitative measurement of renal cortical stiffness using SSI is a promising non-invasive tool to evaluate global histological deterioration.
He WY 2014 Tissue elasticity quantification by acoustic radiation force impulse for the assessment of renal allograft function	ARFI	52 stable renal function, 50 biopsy-proven allograft dysfunction	Renal allograft stiffness using ARFI quantification in patients with stable renal function and those with biopsy-proven allograft dysfunction. ARFI quantification, given as SWV. The RI was calculated by pulsed-wave Doppler ultrasound, and clinical and laboratory data were collected.	Tissue elasticity quantification by ARFI is more accurate than the RI in diagnosing renal allograft function.
Lukenda V 2014 Transient elastography: a new noninvasive diagnostic tool for assessment of chronic allograft nephropathy	TE (Fibroscan Echosense)	52 Renal transplant recipients	CAN is the most common cause of kidney allograft failure. Protocol biopsies remain the "gold standard" in CAN recognition. Usefulness of TE for the assessment of kidney allograft fibrosis in RTRs.	Parenchymal stiffness obtained by TE reflects interstitial fibrosis. Therefore, TE provides the opportunity for noninvasive screening of CAN.
Menzilcioglu 2015 et al. Strain wave elastography for evaluation of renal parenchyma in chronic kidney disease	SE (Toshiba Aplio 500)	58 patients with CKD, 40 healthy individuals	Determine the difference of SI value of renal parenchyma between patients with CKD and healthy individuals.	SI value can be used to differentiate patients with CKD and healthy individuals. We have not shown that it can reliably differentiate different stages.
Orlachio 2014 et al. Kidney transplant: usefulness of real-time elastography (RTE) in the diagnosis of graft interstitial fibrosis	SE (real-time elastography-RTE)	50 patients with graft fibrosis	Evaluate the usefulness of RTE in the diagnosis of graft interstitial fibrosis. TME was calculated by two blinded operators. All patients underwent biopsy after RTE. Banff score.	RTE was able to evaluate kidney fibrosis and could be used as complementary imaging during follow-up of renal transplant patients.
Özkan 2013 et al. Interobserver variability of ultrasound elastography in transplant kidneys: correlations with clinical-Doppler parameters	SE (real-time elastography-RTE)	42 adult renal transplant recipients	Evaluate the ability of investigators to use sonoelastography to detect differences in renal cortical stiffness and assess the relationship between stiffness and clinical-Doppler parameters.	SR showed significant positive correlation with RI and PI but sonoelastography has also wide range intra- and low interobserver agreement in renal transplants.
Tan 2013 et al. Real-time elastography for distinguishing angiomyolipoma from renal cell carcinoma: preliminary observations	SE (real-time elastography-RTE) (GE Logiq E9)	47 lesion detected patients 19 RCC, 28 AML	Diagnostic performance of sonoelastography for differentiating AML from RCC. The elasticity patterns and the strain ratio were evaluated independently by two observers. Blue areas in < 50% of lesion, considered type 1 or type 2) by both radiologists, whereas 18 of 19 renal cell carcinomas were classified as having a low-strain elastographic pattern (blue areas in \geq 50% of lesion, considered type 3 or 4) by both radiologists.	Real-time elastography may be useful in differentiating AML from RCC, by use of both elasticity patterns and strain ratios.

TE, transient elastography; eGFR, estimated glomerular filtration rate; ARFI, acoustic radiation force impulse elastography; CKD, chronic kidney disease; SWV, shear-wave velocity; SWE, shear-wave elastography; SWS, shear-wave speed; US, ultrasonography; SR, strain ratio; USG, ultrasonography; ZC, zero-crossing; VUR, vesico ureteral reflux; DMSA, dimercaptosuccinic acid; SSI, supersonic shear imaging; RI, resistive index; CAN, chronic allograft nephropathy; RTRs, renal transplant recipients; RTE, real-time sonoelastography; TME, tissue mean elasticity; AML, angiomyolipoma; RCC, renal cell carcinoma.

Table 2. Summary of the studies according to patient population, elastography type and study design

Children	Dillman et al., Goya et al. 2015
Transplanted kidney	Arndt et al., Gao 2013 et al., Gao 2013 et al., Gao 2014 et al., Grenier et al., He WY et al., Lukenda et al., Orlicchio et al., Ozkan et al.
CKD	Asano et al., Menzilioğlu et al.
SWE (ARFI, SWE and TE)	Arndt et al., Asano et al., Dillman et al., Goya 2014 et al., Goya 2015 et al., Goya 2015 et al., Grenier et al., He WY et al., Lukenda et al.
SE	Gao 2013 et al., Gao 2013 et al., Gao 2014 et al., Menzilioğlu et al., Orlicchio et al., Özkan et al., Tan et al.
Inter-intraobserver variability	Asano et al., Goya 2015 et al., Grenier et al., Orlicchio et al., Özkan et al.
Mass	Goya 2015 et al., Tan et al.
Diabetic nephropathy	Goya 2015 et al.

CKD, chronic kidney disease; ARFI, acoustic radiation force impulse elastography; SWE, shear-wave elastography; TE, transient elastography; SE, strain elastography.

In the studies about CKD, renal transplant recipient (end-stage CKD) or transplanted patients most of the studies revealed that elastography allows the operator to differentiate the fibrotic cortex from non-fibrotic freely from the elastography method (Table 2). Anyway, there is no adequate and reliable data about differentiating the grades of fibrosis⁴⁻¹⁴. Perhaps in near future these results should assist the clinicians to use elastography instead of biopsy. It is obviously clear that more studies are needed about elastography and kidneys. Although there is a consensus about differentiating the fibrosis, inter and intra-observer compatibility is low yet^{5,14}. This may be related with the different measurement points (adjusting the ROI different regions) and the lack of number of samples. The more sampling should increase the inter and intra-observer compatibility.

Cortical elasticity has not only the field about CKD but also can be used in the diabetic nephropathy. Goya et al reported a treshold to distinguish the diabetic kidney and apparently normal kidney with the sensitivity of 84.1% and the specificity of 67.3%⁷².

There are few studies about children. Goya was reported decrement in SWV with increasing grades of VUR, while Dilman reported as elastography did not allow to disctriminate the obstructive hydronephrosis from non-obstructive hydronephrosis^{35,75}.

Goya et al and Tan et al used elastography for characterization of the masses. Goya et al reported that benign and malignant lesions' SWV were higher than those of intact renal parenchyma, while haematomas' SWV values were lower⁷¹. Tan et al focused on the angiomyolipomas (AML) and renal cell carcinomas (RCC), using two different observers and real time elastography. In

conclusion they finished suggesting real-time elastography to differentiate RCC and AML⁷⁴.

Conclusion

Sonographic elastography is a new developing technic, and various studies have been made using elastography in kidneys. Most of the studies are made on the transplanted or CKD kidneys to evaluate the effectiveness of elastography in the evaluation of corticomedullary fibrosis to preserve the patient from the invasive method, biopsy. And also most of the studies were performed using SWE elastography. The results showed that, SWV values increase with the degree of fibrosis and perhaps in near future especially SWE would take the place of biopsy.

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