



## Radio-Diagnosis

## EFFICIENCY OF ACOUSTIC RADIATION FORCE IMPULSE IN CLINICAL SELECTION CRITERIA- PROSPECTIVE RENAL DONORS IN COMPARISON WITH ISOTOPE AND COMPUTED TOMOGRAPHY SCAN

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**ABSTRACT** **Background:** Chronic kidney disease is not a curable condition and it may progress into renal replacement therapy (RRT) or permanent transplantation if the suitable donor is available. Renal transplant is a definitive treatment option for end-stage renal disease (ESRD). If the live donor has an acceptable percentage GFR of kidneys, the lower normal GFR is preferred for donation. CT angiography (CTA) provides structural and vascular information. USG ARFI elastography is a quantitative measurement of the parenchymal stiffness. The encouraging findings observed in ARFI study by comparing ARFI tissue stiffness with the DTPA functionality percentage of kidneys. This data suggested us to investigate the ability of ARFI in predicting and comparing kidney DTPA split renal function. The main idea of the study is to assess whether ARFI utility in comparing DTPA renography split function percentage in selecting the donor kidney. It also confirms to find whether ARFI ultrasound, DTPA renography and CT angiography in selecting more suitable kidney for donation and clinical and surgical feasibility of transplantation.

**Result:** This retrospective data analysis was conducted at Apollo Main Hospital Chennai, most advanced tertiary care center in Asia during the period of June 2019 to December 2020 (19months) which includes 35 patients. There was 91.4% concordance between ARFI and DTPA renogram found 32 out of the 35 cases. Again when compared along with ARFI, DTPA and CTA correlation put together the clinical committee choice (Kappa value) is 0.825 which is increased than that of ARFI ultrasound prediction and DTPA together or separately.

**Conclusion:** The study showed that in the absence of DTPA facility, ARFI VALUE appears to be useful modality for donor selection. This opens up the possibility of utilizing ARFI measurements of the renal cortex in healthy prospective donors, who showed normal features on ultrasound kidneys and normal and compatible urine and blood parameters, to predict the kidney with differential percentage of renal DTPA function. Combining the above findings with better delineation of vascular anatomy using advanced 4D & 3D vascular Doppler and ARFI ultrasound system scan reduces the dependence of CT angiography. Since USG, ARFI and vascular Doppler would be adequate and alternative choice in any center, where there is case contraindication or non-availability of CTA and isotope scans.

**KEYWORDS :** Prospective renal donor, ARFI ultrasound, vascular doppler DTPA renography, CT angiography, clinical and surgical choice for transplant.

**BACKGROUND:**

Chronic kidney disease is irreversible condition and may progress into ESRD, leading gradually to transplantation. CKD in the world is exponentially increasing with comorbidities like diabetes, hypertension, obesity, high cholesterol and smoking and associated cardio vascular diseases. In the last decade it increased many folds. Live renal donor transplantation has a better outcome and longevity than cadaver renal transplant. The availability of cadaver kidney is very difficult and few for transplantation compared to the demand. Live donors taken after complete satisfactory matching with recipient parameter requirements. Thus the donor kidneys with normal functional morphology and less complicated vascular anatomy is preferred. The left kidney is a clinical surgical choice because of its longer vascular pedicle and the technical comfort in harvesting is often opted. In the, Presence of accessory arteries increases the risk and the operative time and complexity in surgery in both donor and recipient with resultant risks of donor arterial thrombosis. (1)

Imaging plays a very crucial role in evaluation of kidneys in prospective renal donors as well as in choice of the side for donation. Multiple modalities used so far like ultrasound, CT angiography and renal scintigraphy for this purpose. Ultrasound is a non-invasive, in expensive imaging modality commonly used for gaining structural and vascular Doppler mapping information. Over the years with the advances in technology, the ability of ultrasound imaging in providing structural and functional vascular information has showed remarkable increased in accuracy. Ultrasound recent advance of an ARFI is very useful diagnostic tool as it is quantitative measurement of tissue stiffness and measurement unit value is m/s. CTA provides structural and vascular information. CTA involves iodinated contrast allergic

reaction and radiation hazards. (2) Renal scintigraphy (Diethylene Triamine Pentacetic Acid or DTPA renography) assesses the split renal function in percentage also has radiation.

Various studies were indirectly done to correlate the functionality of kidney with ultrasound features. Akoh et al showed that there is significant correlation between the divided kidney function and US kidney lengths. However, in the same study when the difference in length ranges from 0 to 2.3 cm, there was difficulty in deciding how much difference in kidney length represents a significant difference in function (3). An excellent correlation between USG—determined kidney volume and GFR was demonstrated by Sansui et al in his study (4).

3D and 4D power doppler Vascular imaging is less expensive has shorter examination time and produces good quality images of both larger and smaller vessels with or without the need of contrast. With a 10 cm field of view. With many departments ultrasound remains corner stone of vascular diagnosis acting as a well established first line imaging. CTA and MRI can be set aside for the patients after ultrasound assessment, if required. CEUS (Contrast enhanced ultrasound) and ARFI as a single examination expands the value of role of ultrasound. (5)(6) ARFI is a recent ultrasound advance in the field of elastography. Few studies in chronic kidney disease showed that there is a relationship between ARFI value and GFR. Bob et al found that ARFI values in patients with diabetic kidney disease and eGFRs <60 mL/min are significantly lower compared to those of patients with eGFRs >60 mL/min, and values decrease with the decrease in eGFR (7). Some studies were also done to elucidate the natural course of renal ARFI in the normal population. Ranjith et al

found that the ARFI value of renal cortex in healthy adults is in the range 2.82-2.90 m/s using the Acuson S3000 ultrasound machine (8). A well-established confounding factor for ARFI quantification is age related as evidenced by studies in chronic kidney disease patients. Gender, age, depth are related  $0.221+0.58$  m/sec to  $0.537$  m/sec +  $1.057$ m/sec + with 95% CI 0.635 – 0.832  $P<0.001$  in lower pole cortex (9)(10) in DM ARFI decreases with age (11) In their study in normal subjects, Harsh et al found that shear wave velocity decreased with age, however there is less statistical significance noted. The location of kidney, architecture and high tissue anisotropy is the limitations for application of ARFI box in kidneys (12). The ARFI measurements are to be taken with patient during breath holding and the average of 5 readings is used. (9)

The findings obtained in renal studies comparing tissue stiffness with the functionality of in kidney disease have shown a scope for us to investigate the possible ability in predicting the kidney with lower normal and upper normal value of DTPA split renal function percentage. The main purpose of the study is assessing whether ARFI of the kidney have sufficiently high or equal concordance with DTPA renography split function in percentage for predicting the donor kidney. The usual role and relevance of multi-modality imaging is also assessed by obtaining of advanced ARFI ultrasound, USG advanced vascular Doppler, DTPA renography and CT angiography. Later the final decision made by the in house clinical committee for transplant. Medical and non-medical factors that affects the voluntary live-related kidney donation. Commonest cause of rejection donor kidney is blood group incompatibility and to some extent diabetes, hypertension and surgical and medical complications. If nephrectomy is eminent it can be avoided by proper selection or withdrawal of the donor if required it should be strictly assessed Economic factors for both donors assessment and recipient management are also high in India. (13) (14) Therefore this evaluation is to find feasibility of the untapped potential of ultrasound ARFI modality in prospective renal donor evaluation which is simpler and no radiation like CTA and isotope to the donor.

#### METHODS:

This retrospective data analysis of the donor and recipients was conducted at Apollo Main Hospital Chennai, since it is most advanced tertiary care center in Asia during the period of June 2019 to December 2020 (19 months) includes 35 patients. A 3 years experienced academic resident and 25 years experienced radiologist with 10 years dedicated ARFI and vascular Doppler evaluator independently have assessed all cases of Prospective renal donors aged between 18 to 60years who underwent DTPA renography for split renal function, All the 35 patients had live transplantation during this period.

Renal cysts, stones, hydronephrosis, mass lesion or cortical thickness less than 0.8cm on ultrasound, obese subjects with a renal depth of >8cm from the skin surface were excluded in the study.

Complete and comprehensive sonography done in required position using SIEMENS ACUSON 3000 color vascular Doppler and ARFI in built high end latest advanced equipment. The kidneys size, parenchymal echogenicity and pelvic calyceal system are assessed for donor suitability, and in the same position the shear wave ARFI elastography done with curvilinear transducer of 4C1. In each individual 5 measurements (8) were obtained from renal cortex and average values is taken. The ARFI measuring box size was 0.8 square cm. These result value being displayed in meters/second (m/s). If the ARFI measurement showed, XXX on the screen, this value considered as invalid, the reason being, movement, depth and box position. The maximum depth at which ARFI elastography box is 8cm. in the present equipment.

Tc-99m DTPA diuretic renal study with posterior view done using SIEMENS SYMBIAT6DUAL HEAD GAMMA CAMERA. Tc-99m DTPA 5 mCi is given IV bolus followed by Furosemide 1mg/kg (max: 40mg) IV bolus (F-0protocol). DTPA undergoes GFR but it neither reabsorbs from distal nor secrete from proximal tubules. It is a useful tool for obtaining renal function. The dynamic scintigraphy shows extra renal lesions in the retro peritoneum (15)

#### Acquisition parameters were:

- 64\*64matrix
- Zoom1.0
- “vascular” phase - 1-2 second images for 1-2 minutes, followed by
- “functional uptake cortical transit” phase - 10-15 second images for about 5 minutes and then

- “excretion phase” - 20-30 second images for about 20minutes
- All these phases constitute a total scan time of 20-30 min. All of the functions actually occur concurrently but phases are named according to times when one or the other dominates.
- “post-micturition erect image” (for the same duration as the last frame of the renogram). (16)

Renal cortical tracer uptake, intra-renal transit time and drainage of tracer is noted. Post-void films are taken. Total GFR and SPLIT RENAL FUNCTION are calculated in the normal kidneys of prospective donor. About 90% excretes in 24 hours'. Absorption of kidney is 0.42 rad/mCi and by bladder is 0.55 rad/mCi. DTPA was chosen because of high binding and stability (17)

In the present innovative comparative study, ARFI and split function of either kidney was measured in each donor by the above described method.

#### DATA INTERPRETATION:

Among the right and left kidney in a donor, the kidney with the lower ARFI value has showed was labeled as 'ARFI selected kidney'.

The kidney with lower normal kidney split function percentage in renal scintigraphy was labeled as 'DTPA renogram selected kidney'.

CT angiography without any complexity in anatomy was considered as suitable for donation after CT angiography. If both kidneys did not have any complexity in anatomy, the one matching with renal scintigraphy was taken as suitable till recently. Whichever kidney was selected till recently by these criteria was labeled as CTA selected kidney.

So far Ultrasound scan, DTPA scan and CTA along other parameters matching and surgical feasibility of donor kidney is selected labeled as donor of 'clinical committee choice'.

#### Sample of data collected

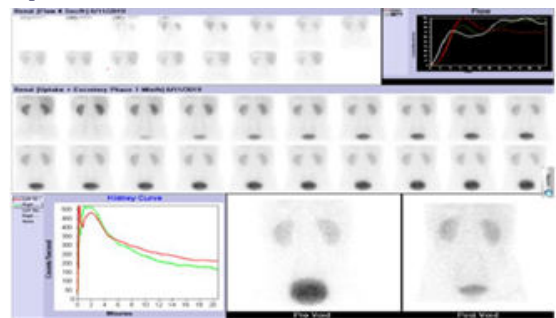


Fig.A

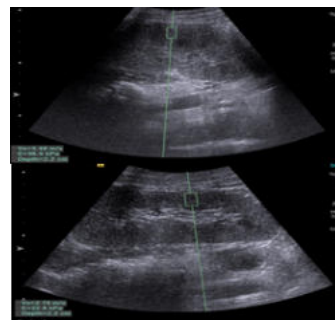


Fig. B

The image (A) represent DTPA renogram of a donor showing split function of right kidney as 52% and left kidney as 48%. The image (B) represent ARFI of right kidney as 3.2m/s and that of left kidney as 2.7m/s for the same donor. So the left kidney is ideal choice.

#### STATISTICAL ANALYSIS:

All continuous variables were represented by mean  $\pm$  SD. Categorical variables were represented by %. Comparison of categorical variables was done either by Chi-square test or Fisher's exact test. Kappa values were computed to know the agreement between different in diagnostic modalities. Data analysis was carried out by IBM SPSS statistics for

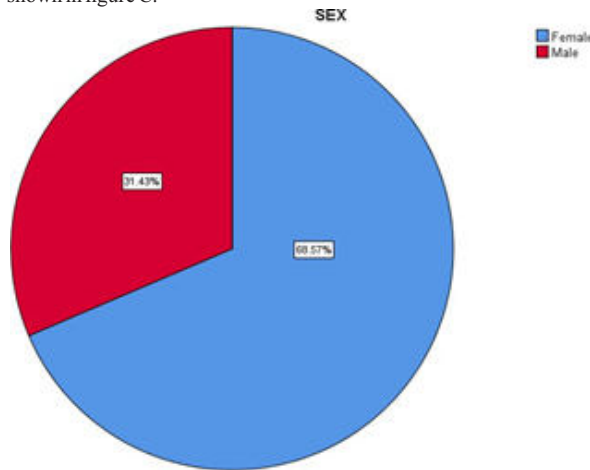
windows; Armonk;NY version 25.0.All p values < 0.05 was considered as statistically significant.

**RESULTS**

There was 91.4% matching observed between ARFI value and DTPA renogram 32 out of the 35 cases. When the selection of left kidney was made by ARFI, there was 100% concordance noted. There was only 72.7% (8 out of 11 cases) agreement noted when the selection of right kidney was made by ARFI.

Kappa value, which is a measurement of agreement between ARFI ultrasound prediction and DTPA renography prediction, is 0.785. This is strongly suggestive of substantial agreement.

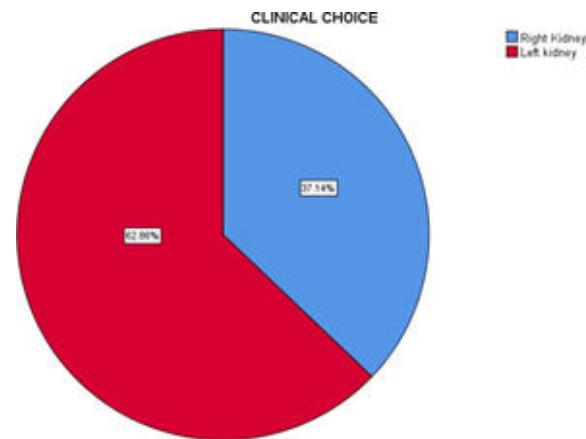
In our study 68.57% cases were female and 31.43 % cases were male as shown in figure C.



**FIGURE C:**

During comparison 24 times ARFI selected the left kidney for donation, there was a concordance of 62.5% with the clinical committee selection choice. Whereas among the 11 times ARFI selected the right kidney for `donation, there was a concordance of 36.4% with the clinical committee choice. There is a low measurement of agreement found between ARFI prediction and clinical committee choice especially when a right-side selection was made by ARFI. when during comparison 27times of DTPA renogram selected the left kidney for donation, there was concordance of 62.9% with the clinical committee selection choice as shown in Figure D. Where as among the 8 times, DTPA selected the right kidney for donation, there was concordance of 37.5% with the clinical committee choice and this proved there is direct agreement with ARFI is very close choice without DTPA.

**CLINICAL COMMITTEE CHOICE**



**FIGURE D:**

This indicates when the difference in DTPA split function is less than 10% in all our cases. The clinical committee choice of the side selections determined by the technical feasibility of the surgical

procedure which in turn is influenced by the complexity of vascular anatomy suggested by CTA and a preference for left side due to the longer vascular pedicle.

There was 100% accordance with all imaging and clinical committee choice when the left side kidney was selected by DTPA for donation. When the right side kidney was selected by DTPA for donation, there was 82.2% concordance with the clinical committee choice. Kappa value measurement of agreement between CT angiogram prediction and clinical committee choice is 0.825 which is suggestive of good agreement. The slightly lower similarity when the right side selection was made by CTA is because of the preference for left side due to its longer vascular pedicle. CTA helps in renal artery stenosis and intra renal branches in renal donor and anatomy before surgery. CTA-volume rendering imaging replaced older and digital conventional angiography in many centers and CTA helpful in post-transplant angioplasty stent patently (18).

**Table.1**

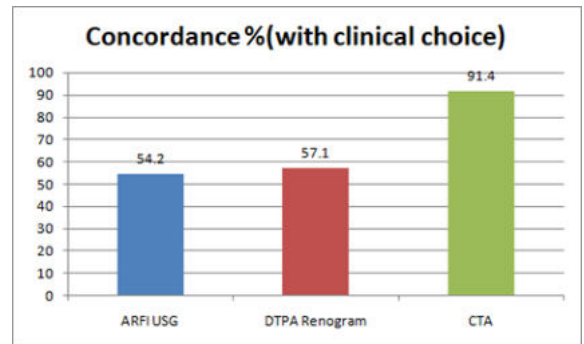
	TOTAL CASES	RIGHT SIDE SELECTED	LEFT SIDE SELECTED
ARFI USG & VASCULAR DOPPLER	35	24	11
DTPA RENOGRAM	35	27	8
CTA	35	16	19
CLINICAL COMMITTEE CHOICE	35	13	22

**Table.2**

SELECTION MADE IN AGREEMENT WITH CLINICAL COMMITTEE CHOICE			
	OVERALL	RIGHT SIDE SELECTED	LEFT SIDE SELECTED
ARFI USG & VASCULAR DOPPLER	54.2%	36.4%	62.5%
DTPA RENOGRAM	57.1%	37.5%	62.9%
CTA	91.4%	82.5%	100%

**Reason for 82-100% on CTA is due to combination of ARFI + DTPA + Clinical committee agreement**

**CONCORDANCE PERCENTAGE CLINICAL COMMITTEE CHOICE**



**FIGURE E:**

**Concordance percent with clinical committee choice with all the parameters taking into consideration ARFI 54.2 % DTPA 57.1 % CTA 91.4%.**

**DISCUSSION**

Taking into light the huge numbers of chronic kidney disease ESRD patients in requirement of renal transplantation, there is an urgent need to increase the number of transplant surgeries to be carried out in the world. There is a long waiting list and period of waiting for years the cadaver kidney is due to high prevalence of ESRD. This imply more number of live donor transplants will have to be done. To achieve this, more number of surgeries has to be carried out even in smaller centers. Pre- transplant evaluation of live donor is a crucial check point in this process. Apart from matching of the required blood and urine parameters, imaging studies done to evaluate the anatomic and functional feasibility forming a major part of pre-transplant workup.

Ultrasonography, renal scintigraphy and CT angiography are commonly used imaging modalities for this purpose till date. The renal scintigraphy is used to assess the functional capability, in particular split or differential functionality of the normal kidneys. The CT angiography provides information of the vascular anatomy of the kidneys.

In order to reduce the complexity and avoid isotope and CT scan radiation dose, ultrasound modality with advanced and latest ARFI, Vascular Doppler, a non-invasive, innocuous and relatively inexpensive imaging modality with widespread availability, provides reliable information on kidney size, presence of focal cystic or solid lesions, collecting system abnormalities and presence of nephrolithiasis. Doppler ultrasound can assess the condition of donor renal vascular structures and their anatomy mapping in 3D and 4D (presence of accessory arteries or early bifurcations). ARFI elastography is a very recent and breakthrough advance in ultrasonography that has proved its usefulness in donor kidney selection. Renal ARFI studies have shown encouraging results in chronic kidney disease patients. In the present scenario there is an evident relationship noted between the ARFI value of the kidney and the glomerular filtration rate. So it seemed logical to assess whether ARFI of the kidneys in a prospective donor can be used to compare the differential renal percentage function of the kidneys and thus predict the suitable kidney for donation.

Since ARFI kidney is a relatively new breakthrough in the all solid organs research field, in spite of extensive reviewing literature we are unable to find an exact comparative study. Hence we sincerely ventured an attempt to do the retrospective data analysis the utility of ARFI for renal donor selection. ARFI of donors  $0.247 \pm 0.58$  (19) However, individual studies like ARFI kidneys for CRF, tumors etc. were available. Bob et al (7) found that ARFI value was decreasing with progression in the stage of the kidney disease.

Each ultrasound, machine having ARFI and vascular doppler loaded system technology is not uniform and an independent standardization needed. Guo *et al.* (8) demonstrated a mean shear-wave velocity value of 2.15 m/s in 327 healthy participants in Acuson S2000 ultrasound system. Using Philips iU22 Ultrasound machine, Harsh et al demonstrated a mean renal cortical shear wave velocity of around 1.5 in healthy adults (20). Ranjith et al found that the ARFI value of renal cortex in healthy adults is in the range 2.82-2.90m/s using the Acuson S3000 ultrasound machine. This proves the system uniqueness (8).

With these available data, a ARFI pilot control study in our radiology and imaging sciences department was done on 30 prospective renal donors. We obtained  $2.8 \pm 0.86$  m/s. Acuson S3000 ultrasound system, mean value obtained by Ranjith et al which is 2.86 was similar to our control mean value. So  $2.86 \pm 0.86$  (2.0-3.7) was considered as the range in normal range of ARFI (8).

The results of the control pilot study showed a 90% concordance between ARFI based prediction of suitable kidney for donation and the DTPA based prediction. On the basis of this, small sample size was calculated and full-fledged workup was carried out.

There was substantial agreement between ARFI prediction and DTPA renogram prediction of donor kidney for transplant ( $\kappa$  value=0.785). Out of 35 cases, ARFI selected the left kidney for donation in 24 prospective donors. All these selections in agreement with the DTPA renogram selection. However, out of the 11 cases in which ARFI selected the right kidney, 3 were not matched with the DTPA renogram selection. ( In all these cases, the difference in split function by DTPA renogram was just 2% and the difference in ARFI values was 0.2m/s). This discrepancy could be attributed to the ARFI related depth or technical reason for right kidney compared to left resulting in a reduced measurement of ARFI value or due to DTPA scan Limiting of right kidney compared to left.

There was less agreement when both the together concordant ARFI value and DTPA renogram selection with the actual kidney transplanted possibly due to clinical committee reasons like vascular pedicles appearance or clinico-surgical reasons. On the other hand, there was an almost good agreement between CT angiogram prediction and actual kidney transplanted ( $\kappa$  value=0.825). Out of 35 cases, CT angiography selected the left kidney for donation in 19 prospective donors. All these selections concurred with actual kidney transplanted possibility to surgical feasibility and longer pedicle and useful harvesting.

## CONCLUSION

The study showed that ARFI value and DTPA study closely similar for donor selection in view of functionality of donor kidney. Even though DTPA shows excretory function and ARFI shows tissue elasticity, there seems to be correlation of DTPA function with morphological shear wave ARFI elastography value. This opens up the possibility of using ARFI measurements of the kidney parenchyma in healthy prospective donors, who showed normal features on routine ultrasound kidneys and normal urine and required blood parameters and to predict the kidney the lower and upper normal split percentage function that is displayed in DTPA scan.

This DTPA scan was considered so far as good and only available modality standard. After the advent of advanced ARFI elastography for donor selection showed an alternative to DTPA scan with comparative measurements obtained in this study.

For better delineation of vascular anatomy advanced Doppler ultrasound systems even in 3D and 4D images can reduce the dependence on CT angiography. For this however some more research and skilled training needed and higher skilled operator gives more accuracy in the fields of ARFI and Doppler vascular ultrasound technology and to develop customized techniques for renal donor evaluation is necessary.

If implemented, these measures will reduce the dependence on renal scintigraphy and CT angiography in pre-transplant donor evaluation. As on today vascular Doppler and ARFI ultrasound will offer multiple advantages to the prospective donor selection. For example: renal scintigraphy and CT angiography are imaging modalities that require specific infrastructure and expertise. Radiation hazard they cause can be avoided. Thus using multi-modality imaging can be avoided in future and a single modality mode imaging vascular Doppler imaging, ARFI usage will bring down the medical expense as well as expand the live-donor renal transplantation programme.

Our limitations include inability to find a similar study in the searched literature during the time of our study. ARFI values have to be taken in the same machine and ARFI technique machines are slightly expensive. The study is operator skill oriented.

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