Acute dysfunction of renal transplants: Contrast ultrasound assessment

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Learning objectives

To illustrate Doppler and Contrast Ultrasound findings in acute rejection of renal transplants. To evaluate the advantages and limitations of contrast ultrasound as a potential routine assessment for all cases of graft dysfunction.

Background

There are many potential causes of acute dysfunction in the immediate and early post-transplant period. Vascular causes include Renal Artery Stenosis, Graft thrombosis - either arterial or venous and pseudoaneurysms, which may form post operatively or after renal biopsy. Urological causes include hydronephrosis of the graft, urinary leak, and fluid collections.

A third category consists of causes which are the most difficult to distinguish from one another sonographically. These are Acute Tubular Necrosis, Acute Rejection and Toxicity of immunosuppressive drugs such as Cyclosporin (1).

Acute rejection can affect up to 40% of transplants (2). Although this may be entirely asymptomatic, clinical features can include fever, graft tenderness, oliguria and proteinuria. Biopsy is the only convincing method to distinguish this from ATN, with histology showing interstitial inflammation, with or without haemorrhage, tubulitis and arterial or venous endothelitis.

The vast majority of renal transplants are assessed using B mode and colour Doppler Ultrasound.

Contrast Ultrasound (CEUS) is already used in the evaluation of liver lesions, and more recently there have been several studies on the potential use of CEUS in optimising assessment of the post operative renal transplant.

Imaging findings OR Procedure details
Sonovue (Bracco, Italy) is the most widely used contrast agent with Ultrasound and consists of a central sulphur hexafluoride core with a surrounding phospholipid monolayer.

The contrast allows evaluation of the microcirculation as harmonic signals generated during resonance and therefore tissue contrast are generated from the microbubble spheres (3).

When a bolus of the contrast is given, evaluation of the graft can be performed by analysing the time-intensity curve (choosing a region of interest and plotting the uptake and washout characteristics over time), or by destruction of the microbubbles in a scanning plane and then observing refill.

A continuous infusion is the only way of creating the ideal steady state plasma microbubble concentration, followed by destruction of the microbubbles with a high MI beam, but this is impractical in the bedside setting, whereas the bolus technique is far more suitable.

Recording microbubble passage at low MI and periodically destroying them at high MI to evaluate tissue bed reperfusion is known as 'Functional' microbubble ultrasound. This can produce a destruction reperfusion curve (as shown in Figure 1) and with this, quantify tissue perfusion (4,5).

The arteriovenous transit time is another important parameter to measure when using CEUS. This is the time taken for injected contrast bolus to cross the renal circulation, which can be measured by straddling the spectral Doppler gate over both the transplanted renal artery and vein.

Loss of forward diastolic flow and elevated resistive indices are non-specific features of graft rejection/dysfunction on conventional US (6, 7).

At our institution, the largest living donor transplant centre in the UK, and the largest facility in Europe for nephrology, dialysis and transplantation, we have been using contrast ultrasound increasingly to enhance the assessment of acute renal transplant dysfunction.

Some pathologies can be detected with no additional benefit from contrast enhancement - such as hydronephrosis. See Figure 2.
Rejection

Recognised signs of acute graft rejection on B mode US include increased size, overall increased echogenicity (see Figure 3), decreased echogenicity of the renal pyramid, focal zones of lucency in the cortex and patchy lucent areas involving both cortex and medulla with coalescence. (8,9). See Figure 3.

However, in practice these signs are rare, and even if present, are not enough to confidently diagnose rejection.

Normal renal transplant.

In a contrast ultrasound study of a health renal transplant, the intrarenal arteries should begin to enhance by 20 seconds, with complete enhancement soon after - See figures 4 and 5.

Perinephric haematomas.

A small haematoma is a common finding post operatively. Small haematomas which cause no significant mass effect usually resorb over time and require no additional intervention. See Figure 6.

Renal vein thrombosis

Although arterial or venous thrombosis is relatively rare, with a prevalence of 0.5-6.2%, it is a major cause of graft loss in the early post transplant period (2).

Infarct

Colour and Power Doppler do show areas of absent perfusion following infarction, but CEUS delineates the infarcted area more clearly, which can be smaller than expected from the Doppler images. See Figures 9, 10 and 11.

AV Fistula.

These can occur during surgery, or after renal biopsy performed for the investigation of rejection. Contrast Ultrasound is not necessary in this case as Colour Doppler with spectral tracings shows the site of abnormal communication where there is significantly high velocity turbulent arterialised flow. See Figure 12.
Considering the recently published studies on contrast ultrasound in evaluating renal transplants, there has been a trend to look at parameters derived from the time intensity curves, transit times and destruction-reperfusion kinetics.

Kay et al studied 20 consecutive renal transplant patients and confirmed reproducibility of the Sonovue TIC data in transplant patients and quantified regional variation in perfusion. Renal microbubble perfusion measured as the area under the time intensity curve (AUC) correlated with the transplant eGFR at 3 months post transplantation (3).

In another study, Arteriovenous transit times were shown to be increased in renal transplants with acute rejection to a greater degree than in grafts with ATN, and considerably more than in controls grafts (10).

Benozi et al studied 39 transplant patients. The authors found that Resistive indices were elevated in both ATN and Acute rejection. Mean computed peak enhancement (PEAK) and Regional blood flow (RBF) were lower in both pathologies. However, the ratio of Regional blood volume (RBV) and the ratio of Mean Transit time (MTT) were lower in ATN. Also, Time to Peak (TTP) was significantly higher in acute rejection cases (11).

Lebkowska et al studies 18 patients and found positive correlations between eGFR and the following parameters

- Blood flow in the renal arteries,
- Flow time of contrast from the artery within renal hilum to the renal cortex.

Negative correlations were found between eGFR and

- Renal artery resistive indices
- Time from renal artery contrast to maximal enhancement of the pyramids
- Time difference of contrast enhancement of the cortex and the pyramids (12).
**Fig. 1:** Figure 1. A destruction reperfusion curve, where the x axis is time, and the y axis is signal intensity. Using the formula $y = A(1 - e^{-\beta t})$, where $A =$ signal amplitude plateau which reflects blood volume/microvascular cross sectional area. $\beta =$ rate of rise of signal intensity which reflects microbubble speed and is the gradient of the curve. The Product of $A\beta$ is a surrogate of perfusion.
Fig. 2: Figure 2. Hydronephrosis of the transplanted kidney. Severe pelvicalyceal dilatation. It should be noted however, that very mild PC dilatation is a feature of healthy new renal transplants.
Fig. 3: Figure 3. Rejection in a transplanted kidney showing increased echogenicity throughout the graft.
Fig. 4: Figure 4. Each of the following two sets of images are taken from a contrast study of a normal renal transplant (CPS mode, Siemens). The images on the left are the CEUS, and the images on the right are the B mode equivalent. After around 20 seconds post injection of 2.4mL Sonovue, the intrarenal arteries begin enhancing.
Fig. 5: Figure 5. 35 seconds post contrast - Complete enhancement throughout the graft reflecting the high flow. There is delayed and relatively less filling of the medullary pyramids.
**Fig. 6:** Figure 6. A small subcapsular haematoma found post-operatively. The image on the left is a CEUS image at 2 minutes 14 seconds post Sonovue injection. There is a hypoechoic area which is outlined by the callipers, measuring 6.3 x 1.9cm at the upper pole of the graft. This demonstrates no enhancement and has well defined margins due to adjacent renal cortex. The hypoechoic area is much more difficult to define on the B mode image (right).
**Fig. 7:** Figure 7. Renal Vein Thrombosis. Colour Doppler shows some reduced arterial flow within the graft. Studying the spectral trace reveals reversal of normal forward diastolic flow (See white arrows), which should normally be above the baseline. No venous Doppler trace was detected.
Fig. 8: Figure 8. Renal Vein thrombosis. Contrast Ultrasound demonstrates markedly reduced arterial flow, with no significant change in the minimal enhancement between the early or delayed phases. The image below demonstrates markedly reduced arterial flow at 1 minute 50 seconds post Sonovue injection. A normal graft would be completely enhanced at this stage.
Fig. 9: Figure 9. Lower pole infarct. Colour Doppler shows an area of absent perfusion in the lower pole of the graft (White arrow).
Fig. 10: Figure 10. Lower pole infarct. In the same patient, Power Doppler confirms the findings of absent perfusion in the lower pole (White arrow).
Fig. 11: Figure 11. Lower pole infarct. CEUS in the same patient as Figures 9 and 10. 32 Seconds post injection of 2.4mL Sonovue the image shows a small area of non-enhancement at the lower pole in keeping with an infarct (White arrow). The size of the infarct is notably smaller than that suggested by the Colour and power Doppler.
Fig. 12: Figure 12. AV Fistula. Colour Doppler with spectral tracings shows the site of abnormal communication where there is significantly high velocity turbulent arterialised flow.
Conclusion

The additional information on the microvasculature provided by assessment with CEUS is likely to prompt the increase in its use in the evaluation of acute dysfunction of renal transplants. Whereas many abnormalities are detected on conventional B mode and colour Doppler, the confirmation of ATN from rejection still requires biopsy. It is anticipated that ongoing studies will build on the several small scale recently published works and will confirm which of the additional parameters derived from CEUS assessment may be reliable enough to reduce the need for biopsy confirmation of acute rejection.

Personal Information

References


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