# Consequences Following NSF - Imaging Options in CKD Patients

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## Consequences of NSF -

The main consequence of the recognition of an association between the administration of gadolinium based contrast agents (GBCAs) to patients in severe renal failure and the subsequent development of the rare condition Nephrogenic Systemic Fibrosis (NSF) has been that those involved in MRI must know even more about their patients than before. Specifically we must know the renal functional status of any patient referred for MRI that may require the use of GBCAs. This requires education of all those clinicians that refer for MRI such that they are able to communicate this information at the time of referral as well as training of MRI staff in order that this information can be obtained at the time of the 'pre-flight checklist' safety interview prior to any MRI study. Many departments such as our own have undertaken redesign of the referral form and MRI safety checklists so that we can now safely identify those patients 'at risk' i.e. those with severe renal impairment - chronic kidney disease (CKD) stages 4 & 5. The question then is what to offer a patient who would ordinarily be best served for diagnosis by a contrast enhanced MRI study but is 'at risk'. The first response is to determine if MRI without contrast will answer the clinical question, if it will not then the utility of alternative imaging options must be explored. The problem can be divided into those imaging studies of a general nature such as CNS, musculoskeletal and solid organ examinations and those related to vascular imaging which is the major area of concern.

## Alternative Imaging Modalities -

## CNS, Musculoskeletal and Solid Organ Imaging -

Often in patients with severe CKD the use of MRI for CNS studies is not first line but as a problem solving tool. CNS studies in CKD patients are most commonly used for evaluating the consequences of atherosclerotic disease (i.e. stroke) and administration of GBCAs will not be critical. Musculoskeletal imaging in this cohort also does not often mandate GBCA use, the commonest scenario that may is the patient with suspected spinal osteomyelitis but often much of the clinically critical information can be gained without GBCA use. Solid organ MRI assessment in severe CKD patients is not often required and in many instances careful attention to the unenhanced MRI acquisitions and correlation with prior non-MRI studies can allow diagnosis without resort to deployment of gadolinium contrast. Importantly these patients should have access to the highest quality MRI in order to maximise the information that can be gained without resort to GBCAs. When GBCA use is necessary then unfortunately for many solid organ MRI examinations the use of GBCAs for lesion detection or characterisation (e.g. in the liver) can be difficult to replace with other modalities though they should be explored and for example contrast-enhanced ultrasound with echo-enhancing contrast for liver imaging may provide an answer. Additionally the application of emerging techniques such as body diffusion imaging and ASL perfusion techniques may yield information diagnostically equivalent to contrast administration. Ultimately though in some cases when other modalities have been exhausted then contrast enhanced MRI may be the only modality that can answer a particular clinical problem and in these rare instances then an approach utilising the lowest dose of a cyclic GBCA and highest quality imaging may have to be employed with appropriate patient discussion and consent alongside risk reduction precautions such as attention to the dialysis regime around the time of GBCA administration.

## Vascular Disease -

The major disease burden of patients with severe stage CKD is cardiovascular and it is this area that most frequently requires imaging investigation. MRA, particularly contrast-enhanced (CE-MRA), has become a prime non-invasive imaging modality for the assessment of vascular disease and hitherto CE-MRA had been thought extremely safe even in patient with renal impairment. Indeed, contrast enhanced MRA has been particularly associated with NSF in part because of the high incidence of vascular disease but also because these have tended to be high contrast dose examinations. The main alternative non-invasive modalities for vascular imaging are non-contrast MRA (NC-MRA, of which there are various types), ultrasound with doppler imaging and CT angiography (CTA). How do these modalities compare to CE-MRA in diagnostic effectiveness ? Particularly, what are their advantages and disadvantages in the population of patients with renal impairment and how do their risk profiles and performance alter with differing degrees of renal dysfunction ? Importantly, it is not so much renovascular disease that may require to be imaged as in the population most at risk for potentially developing NSF the question of renovascular disease is usually irrelevant since it is predominantly patients with end stage renal failure already on dialysis with low urine output that are at risk. Reflecting this the majority of patients who have developed NSF associated with the use of GBCA enhanced MRA were not investigated for renovascular disease (since they were already on dialysis) but rather for other problems such as peripheral vascular disease, cerebrovascular disease or for central venous stenosis/thrombosis in relation to haemodialysis access difficulties. Hence the performance of alternative imaging modalities for patients with severe renal dysfunction is discussed in relation to both renovascular disease and more pertinently those other vascular beds that these patients are prone to disease in i.e. the lower limb arteries, the carotid arteries and the central veins.

**Renovascular Disease -**

The 'at risk' patients with this clinical question will be in CKD 4 (or possibly pre-dialysis CKD 5) as the question is irrelevant in those established on dialysis. Imaging tests for evaluation of the renal vasculature must be robust, reproducible and sensitive not only for renal artery disease itself but also for other disorders that may be the cause of the clinical scenario and tests that assess the potential response to revascularisation are desirable. The available alternatives to CE-MRA are NC-MRA, ultrasound, CTA and conventional invasive angiography. For ascertainment of the cause of renal failure (e.g. in acute kidney injury) then ultrasound is the first choice to determine renal size and exclude obstructive uropathy. Doppler examination can help to evaluate renal vasculature. If duplex is abnormal or inconclusive then for non-invasive arteriographic imaging the choice is between CTA with its drawbacks of defined risk of CIN and radiation exposure, non-contrast MRA which is not yet validated and the as yet not fully determined risks of CE-MRA with the use of low dose cyclic GBCA. It is likely that NC-MRA would be the appropriate next step with a normal study being reassuring. After that the risk of low dose cyclic CE-MRA must be weighed against radiation risk and high potential for CIN with CTA while invasive angiography probably has little diagnostic role.

**Peripheral Arterial Occlusive Disease -**

The investigation of peripheral arterial occlusive disease is important in patients with renal impairment as they are prone to multilevel and particularly below knee tibial arterial disease , hence they have a high incidence of critical lower limb ischaemia (CLLI - Fontaine stage 3 & 4) with limb threat. In the imaging of CLLI the diagnostic performance of imaging tests for the small below knee vasculature is crucial as it is the quality of this distal run-off that determines the durability of any therapeutic strategy even for aortoiliac level interventions.

For initial evaluation of PAOD then ultrasound is unfortunately probably of little use and hence the use of NC-MRA can be considered as this may provide enough information to plan intervention. CTA can be used in patients already established on dialysis but the risk of CIN is high for those with less severe renal impairment. In reserve low dose cyclic CE-MRA can be employed with its (probably low) risk weighed against CIN risk and radiation dose from CTA. For the follow-up of known disease patterns and peripheral grafts then ultrasound duplex studies are useful just as they are in patients with normal renal function. For follow-up of stents and stent grafts then CTA is the most appropriate modality when patients are in chronic end stage renal failure with no residual renal function to preserve, however, where there is residual renal function then the decision becomes more difficult and the information obtained from the other modalities should be carefully assessed to check that enough diagnostic information can be obtained.

**Carotid Artery Disease -**

For suspected carotid disease then ultrasound is the clear first port of call, if this is abnormal some vascular surgeons may proceed on the basis of the duplex findings given the scenario of an at risk patient but if angiographic imaging is imperative then NC-MRA is a useful second line test just as it was before the adoption of CE-MRA with CTA held in reserve for those patients with pacemakers or other MRI contra-indications.

**Central Venous Occlusive Disease -**

Suspected central venous occlusive disease is perhaps the most problematic area as the none of the other modalities perform well and this was a burgeoning area of contrast enhanced MRV practice prior to the discovery of the NSF link. NC-MRA is the most attractive modality to try in the first instance with resort to conventional venography where that fails.

**Cardiac MRI -**

With the high cardiovascular disease burden in this patient group cardiac MRI techniques have potentially great utility, the one area requiring GBCAs that cannot be satisfactorily replaced by other modalities currently is assessment of myocardial viability/scar with delayed enhancement MRI (though there is some initial work with delayed enhancement CT).

**Conclusion -**

The strategy for deciding as to whether an alternative non-invasive modality to CE-MRI for a patient at high risk of NSF if administered GBCAs is appropriate is dependent upon the particular patient clinical scenario requiring investigation. These choices are not simple but require the careful consideration of accuracy versus benefit and potential risks in each situation.