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Using Gadolinium-Based Contrast Agents: Six Key Steps for Success in Patient Management

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In comparison to iodinated contrast media, and with the smaller volumes needed for diagnostic imaging, Gd-based contrast agents (GBCA) have a more favourable renal profile and reduced nephrotoxicity. However, a relatively new condition has raised questions about the unrestricted administration of GBCA in patients with severe or end stage renal disease. New guidelines are needed to safely administer Gd-based contrast agents, in order to take advantage of the full benefits of using them, while avoiding further cases of nephrogenic systemic fibrosis (NSF). It is important to note that the number of new cases of this condition appears to have decreased significantly over the last year.

Whilst it is unclear whether the Gd detected in biopsies in patients with NSF was in its “free” ionic form or bound to its chelator molecule, these findings have contributed to the hypothesis that NSF might be a late adverse reaction to Gd contrast agents. The majority of cases of NSF have occurred after relatively high doses of Gd agents (i.e., > 0.3 mmol/kg bodyweight) for indications such as magnetic resonance angiography (MRA) or in patients who had repetitively undergone several contrast-enhanced MR examinations in a short period of time.

Exact Mechanism Not Fully Understood

The exact mechanism of NSF development is not clearly understood and the role of Gd has yet to be elucidated. However, it is undisputable that there is a clear association between Gd and NSF, whether in the administered chelate form, or, as is postulated by some authors, having been released from the chelate. There is no definite consensus in the MR community regarding the most important parameter that should be used to compare relative risk between agents, and it would be wrong to consider some Gd chelates as safer than others until more is know about the etiology of NSF. To this point, it is not yet understood why some patients developed symptoms of NSF within a few days after exposure to a Gd-based contrast agent, whereas in others the symptoms were reported months or even years after Gd administration. Another unclear finding relates to the incidence of NSF in patients with end stage renal disease. In this patient group, some institutions have estimated that approximately 3 - 5% seem to be at a risk of developing NSF after administration of high-dose Gd. However, the circumstances preventing the development of the condition in the remaining 95 - 97% of patients have not yet been determined.

In addition, other important factors have been described as potentially involved in the pathogenesis of NSF, e.g. acidosis, application of erythropoietin, and the existence of a proinflammatory state (such as caused by major surgery). However, it is uncertain which factor, or combination of factors, is most important.

Six Steps for Safe Routine Administration

Despite the fact that the exact mechanisms of the pathogenesis of NSF remain unclear, radiologists still need MR protocols that minimise the risk of the condition, such as minimising the volume of contrast for the specific clinical indication in daily clinical practice for patients with acute or severe renal failure. The following six recommendations are suggested as proposals for routine imaging of patients with impaired renal function in

view of NSF:

1. Consider the Risks and Benefits of Any Gd-Injection

In renally compromised patients, up-to-date serum creatinine levels must be available and point of care testing should be considered if lab values are older than a week. Based on these values, together with size, age, gender, and weight of a patient, eGFR parameters should be calculated in order to identify patients with values below 30 ml/min/1.73m2.

2. Reduce Contrast Dose

Generally, dosing of 0.1 mmol/kg bodyweight should not be exceeded, and repeated dosing within a week must not be performed. When data acquisition is carried out at 3.0T, even lower doses might be applicable due to inherent higher signal at higher magnetic field strength.

3. Consider Non-Contrast-Enhanced MRI/MRA

Some indications in clinical imaging do not necessarily require contrast media injection, especially in musculoskeletal and neuro-imaging. For angiographic studies, new and promising techniques have become available that no longer require contrast injection: steady state free precession (SSFP) MRA is void of contrast material and provides an excellent display of vascular morphology. Arterial spin labeling (ASL) or carbon- 13 injections also hold promise for arterial imaging without administration of Gd-based contrast agents.

4. Optimise the MR Examination Technically

Improved spatial and temporal resolution can nowadays be acquired with parallel acquisition imaging techniques. Additional modifications of standard procedures (e.g. venous compression or hybrid-MRA for peripheral vascular imaging) will further improve the image quality. The application of these new methods might permit a reduced dose, or even omission, of GBCA.

5. Consider Alternative Imaging Techniques

For in-patients at risk of developing NSF, alternative cross-sectional imaging techniques might be applicable to provide an appropriate diagnosis. Ultrasound with colour-coded haemodynamic information might be a good tool for assessing vascular disease in some patients. And those patients who are on long-term haemodialysis might be subjected to contrast-enhanced CT imaging.

6. Involve the Referring Colleague and Nephrologist

With a proactive communication regarding NSF towards the referring physician and involvement of a nephrologist the shadow of the disease might be lightened in the long run. Such an inter-professional alliance will increase awareness of the need for a dedicated risk assessment and alert stance with regards to NSF.

Conclusion

Although this condition is now a factor in our decision-making process, the beauty of contrast-enhanced MRI or MRA exams has not become the beast. Radiologists must involve themselves in the process of patient screening in order to identify those at risk of NSF. As clinicians, it is essential that we consider the needs of patients who are not at risk of this condition. As NSF has, to date, only been associated with severe or acute renal impairment, we should continue to have confidence in using the most appropriate GBCA in contrast enhanced MR techniques in that majority of patients not at risk, so they continue to receive the benefits of these techniques.

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