

NSF Risk Factors

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Introduction: Emerging evidence linking gadolinium based contrast agents (GBCAs) to nephrogenic systemic fibrosis (NSF) has changed medical practice patterns towards forgoing GBCA enhanced MR imaging, or substituting potentially less accurate and often radiation based imaging methods. This study explores the factors which affect NSF risk and demonstrates how risk can be managed by careful selection of GBCA dose, type and timing of injection with respect to dialysis and other factors.

Methods: A literature search was performed in the PubMed database for papers having the keywords ‘*Nephrogenic Systemic Fibrosis*’ and ‘*Nephrogenic Fibrosing Dermopathy*’ to include case series and reports with detailed clinical descriptions for each biopsy confirmed patient. Patient age, gender, race, type of GBCA enhanced imaging, GBCA type and dose immediately preceding diagnosis, lifetime GBCA dose, interval between GBCA administration and NSF symptom onset, estimated glomerular filtration rate (eGFR), dialysis, interval between GBCA administration and dialysis, acuteness of renal failure, presence of kidney transplant/failing kidney transplant, antiphospholipid syndrome, sedimentation rate, autoimmune disease, serum phosphorus, acidosis, epoetin, pro-inflammatory events were recorded on an Excel spreadsheet. The relevant part of this Excel spreadsheet was then sent to each corresponding author with a request to corroborate data we extracted from their articles and to fill in as much missing data as possible.

Results: Seventy-eight papers provided detailed information on 292 NSF patients with additional or corrected data from 25 corresponding authors.

Demographics: The gender distribution was approximately equally weighted in 261 cases with gender available (M:F = 136:125). For 279 patients with age reported, the mean was 50 years (8 to 87 years). Figure 1 shows the age distribution of NSF (red) compared to routine age distribution (green) for patients with GFR < 30 mL/min undergoing Gd MR exams suggesting that older age is protective.

Clinical features: Contractions (n = 93) or limited range of motion (n = 15) were reported in 37% of cases.

GBCA exposure: In 64 papers, history of GBCA administration was investigated by the authors or from supplemental data involving 243 patients, of which 220 (90%) had GBCA injections prior to NSF symptom onset.

Renal function: In 208 of the 292 NSF patients there was sufficient detail reported to determine whether or not the patient was on dialysis including HD (n = 150), PD (n = 17), CVVH (n = 4) or unspecified (n = 37) for a total of 80% on dialysis. Three patients with GFR > 30 mL/min were all in acute renal failure so that calculated GFR was overestimating true renal function.

Acute vs. chronic renal failure: In 126 patients for whom data allowed discrimination between acute and chronic renal failure, 56 (44%) had either acute renal failure (n = 25), acute deterioration of chronic renal failure (n = 25) or unspecified acute renal dysfunction (n = 6).

MR exam type: When the type of MR examination was provided (n = 112), 51% (n = 57) underwent GBCA-enhanced MRA which is commonly performed prior to initiating dialysis to check for potentially reversible renal artery stenosis.

Timely dialysis after GBCA injection: For the 36 patients in whom the interval between GBCA administration and dialysis could be determined, dialysis was performed the same day in 4 patients, a day later in 3 patients, 2 days later in 4 patients and ≥ 3 days later in 25 patients suggesting that the overwhelming majority of NSF patients on dialysis may have had a substantial delay between dosing and receiving dialysis or may have had poor quality dialysis due to reduced fistula or central catheter function.

Gd dose and type: In the 187 cases for which data on GBCA dose were available or could be estimated from the exam type, 23 (12%) patients appeared to receive a standard dose of GBCA (0.1 mMol/kg) and 164 (88%) patients received greater than a standard dose. A total of 63 patients received multiple doses of which 55 (87%) had at least 1 high dose. Gadodiamide (n = 167), Magnevist (n = 11) or multiple agents including Multihance have been injected within a short period prior to the onset of NSF symptoms.

Conclusion: This analysis of 292 reported cases suggests that about one third of NSF patients may develop contractions or limited range of motion. Reductions in risk as high as an order of magnitude appear to be attained with each of the following: 1) avoiding high dose (>0.1 mmol/kg), 2) avoiding nonionic linear chelates for patients with GFR < 30 mL/min, 3) dialyzing quickly following GBCA administration for patients already on dialysis, 4) avoiding injecting acute renal failure patients especially while serum creatinine is rising. Understanding these risk factors can refine practice patterns to allow safe GBCA enhanced MR in most patients.

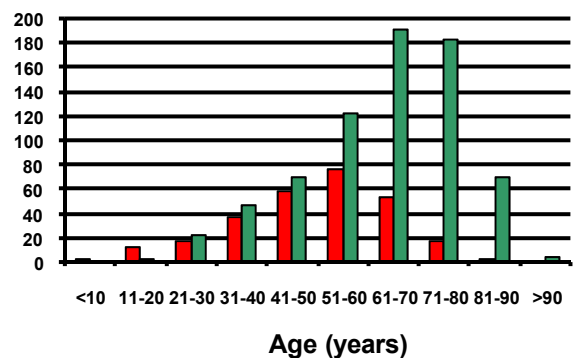


Fig. 1. Age distribution of NSF (red) and patients undergoing high dose Gd-MR with GFR < 30 mL/min. Note older age is protective.