

NEPHROGENIC SYSTEMIC FIBROSIS (NSF)

GUIDELINES 2009

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What is Nephrogenic Systemic Fibrosis (NSF)?

- NSF is a rare and potentially fatal complication linked to the use of certain Gadolinium Based Contrast Agents (GBCAs) which affects patients with compromised renal function.
- It is characterized by collagen deposition and consequent multi-organ fibrosis primarily manifesting in the skin. Both the exact pathophysiology of, and importantly, a cure for NSF remain elusive.
- The primary group at risk are those patients with compromised renal function, either chronic kidney disease (CKD) or acute kidney injury (AKI).
- NSF is a reportable disease and all suspected cases should be reported to the Canadian Adverse Drug Reaction Monitoring Program (1-866-234-2345).

What GBCAs have been implicated in NSF?

- Gadodiamide (Omniscan; GE Healthcare, Milwaukee, WI) accounts for 80% to 90% of unconfounded published and reported cases.
- NSF has also been reported with gadopentetate dimeglumine (Magnevist; Bayer Schering Pharma AG, Berlin, DE) and gadoversetamide (OptiMARK; Mallinckrodt Inc, Hazelwood, MO).

How do I screen my patients and when should I obtain an eGFR?

- It is the opinion of the CAR that is not necessary to obtain an estimated glomerular filtration rate (eGFR) in all patients scheduled for GBCA administration.
- A pre-examination questionnaire should be accurately completed for every patient scheduled to undergo an MRI examination that could potentially require administration of a GBCA.

Appropriate questions could include:

Are you over the age of 60?

Do you have a history of:

- Heart attack?
- Peripheral Vascular disease?
- Organ transplant?
- Chemotherapy for malignancy?
- Kidney disease?
- High blood pressure?
- Diabetes?
- Stroke?

- If the screening questions reveal a risk factor for CKD or the patient is to receive more than the standard dose of a GBCA ('off-label' use), an eGFR should be obtained.
- If the patient is suspected of having AKI, then a nephrology consultation is suggested to more accurately assess the patient's renal function.
- Patients whose renal function is known are exempt from such screening. An eGFR obtained **within 3 months for out-patients**, as long as no interval hospitalization has occurred, or **within 48 hours for inpatients**, is acceptable.

What if my patient has Class 3, 4 or 5 CKD?

- As a rule, the lowest possible dose of GBCA's to achieve a diagnostic examination should always be used.
- Patients with Class 3 Chronic Kidney Disease (eGFR 30-60 mL/min/1.73m²) are at exceptionally low risk. Therefore, adjustment of dose and specific discussion of the risk of NSF is not required.
- Patients with Class 4 or 5 Chronic Kidney Disease (eGFR <30 mL/min/1.73m²) compose a higher risk group. The following steps should be undertaken:
 - While physicians should not deprive at-risk patients of clinically indicated contrast enhanced MR examinations, one should **confirm that a gadolinium enhanced MRI is necessary.**
 - If the exam is deemed critical, a nephrology consultation is recommended if it can be arranged in a timely fashion, however note that nephrology opinion regarding the need for such a consultation may vary regionally.
 - Gadodiamide (Omniscan), Gadopentetate Dimeglumine (Magnevist) and Gadoversetamide (OptiMARK) should be avoided in patients with an eGFR <30 mL/min/1.73m².
 - Informed consent should be taken for these patients well in advance of examination.
 - Repeated administration of GBCA's over short intervals should be undertaken with caution.
 - Hemodialysis has been shown to be effective in removing GBCAs but may not prevent NSF. However, it should be considered for high risk groups as soon as possible after MR examinations. Nephrologists may need to be consulted prior to exam.

How do I estimate risk?

The development of NSF after administration of GBCA's is confined to those with Stage 4/5 CKD (estimated at 2.4% per GBCA administration in a study of chronically dialyzed pts [1]) and those with acute renal failure (as high as 19% with high contrast dose studies [2]). It is important to emphasize that risk is influenced primarily by type of GBCA, level and acuity of renal dysfunction, and dose of GBCA's, and is likely to change the prevalence of NSF with heightened physician awareness and optimization of risk factor management.

1: Deo A, Foegel M, Cowper S. NSF: A population study examining the relationship of disease development to gadolinium exposure. *Clin J Am Soc Nephrol* 2: 264-267, 2007.

2: Prince MR, Zhang H, Morris M et al. Incidence of NSF at two large medical centers. *Radiology* 2008; 248 (3): 807-816.

The final word

It is crucial that these practice guidelines be tailored to the individual patient through consultation with the referring physician, radiologist, and when necessary, a nephrologist.

Reference: Padilla-Thornton AE, Rafat Zand K, Barrett B, Stein L, Andrew G, Forster BB. *Canadian Association of Radiologists National Advisory on Gadolinium Administration and Nephrogenic Systemic Fibrosis. CARJ. 2008;59(5):237.*