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"IMPLEMENTING PROTOCOLS TO IMPROVE PATIENT SAFETY IN THE MEDICAL IMAGING DEPARTMENT WITH EMPHASIS ON USE OF GADOLINIUM FOR RENAL FAILURE"

Radiology

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ABSTRACT

Patient safety is a focal point in healthcare because of recent changes issued by CMS. Hospital reimbursement rates have fallen, and these reimbursement rates are governed by CMS mandates regarding patient safety procedures. Reimbursement changes are reflected in the National Patient Safety Goals (NPSGs) administered annually by The Joint Commission. Medical imaging departments have multiple areas of patient safety concerns including effective handoff communication, proper patient identification, and safe medication/contrast administration. This literature review examines those areas of patient safety within the medical imaging department and reveals the need for continued protocol and policy changes to keep patients safe. The purpose of this study was to determine the incidence of nephrogenic systemic fibrosis (NSF) in patients with chronic kidney disease (CKD) and moderate-to-severe impairment of kidney function who had not previously been exposed to gadolinium-based contrast agents (GBCAs) or referred to undergo contrast-enhanced MRI with gadobenate dimeglumine or gadoteridol.

KEYWORDS

Protocol, Medical Imaging, CMS, National Patient Safety Goals (NPSGs).

INTRODUCTION:

The Centers for Medicare and Medicaid Services (CMS) restructured reimbursement rates for healthcare facilities by adding patient safety as an additional measure to the payment formula.[1] All reimbursement changes are reflected in the National Patient Safety Goals (NPSGs) issued annually by The Joint Commission.[2] Specifically, NPSGs identify areas that need improvement and provide building blocks on how to make those improvements a priority within a healthcare organization. Improving handoff communication, patient identification, and medication administration procedures were some of the improvement goals highlighted in 2014.[2] Effective handoff communication, proper patient identification, and accurate contrast media administration are all major patient safety concerns in medical imaging departments. New technologies are available to improve staff communication such as electronic medical records (EMRs) and computer provider order entry systems (CPOEs). These technologies are important during patient transfer from one caregiver to another.[3] The use of radiofrequency identification (RFID) and bar code identification procedures assists in the decline in the number of wrong patient-wrong procedure occurences.[4–5] Technologists must be knowledgeable and well-informed of the precautions and protocols in place regarding contrast media administration.[6–7] This review examines the current literature regarding improvements in handoff communication, patient identification, and contrast media administration procedures in the medical imaging department.

METHODS:

Multiple journal archives and electronic databases were used to search the subject area of patient safety in the medical imaging department including European Journal of Radiology, Journal of Medical Imaging and Radiologic Sciences, and Journal of American College of Radiology. The searches were limited to academic, peer-reviewed journal articles published since 2008. The keywords used in the searches were handoff communication, medication safety, patient safety, contrast safety, radiofrequency identification (RFID), and patient identification.

Two multicenter prospective cohort studies evaluated the incidence of unconfounded NSF in patients with stage 3 CKD (estimated glomerular filtration rate [eGFR] in cohort 1, 30–59 mL/min/1.73 m^2) or stage 4 or 5 CKD (eGFR in cohort 2, < 30 mL/min/1.73 m^2) after injection of gadobenate dimeglumine (study A) or gadoteridol (study B). A third study (study C) determined the incidence of NSF in patients with stage 4 or 5 CKD who had not received a GBCA in the 10 years before enrollment. Monitoring for signs and symptoms suggestive of NSF was performed via telephone at 1, 3, 6, and 18 months, with clinic visits occurring at 1 and 2 years.

EFFECTIVE COMMUNICATION:

Patients move through multiple departments in a healthcare facility for a variety of clinical testing. During this process, patients are susceptible to errors and complications considering breakdowns in communication. The Joint Commission's 2014 survey on root causes for sentinel events listed communication as one of the top reasons for medical mishaps.[2]

HANDOFF COMMUNICATION:

Handoff communication is defined as the process of passing complete and accurate patient-specific information from one caregiver to another.[3] During handoff communication, important information must be transferred to the receiving personnel to ensure patient safety and continuum of adequate care. Patient traffic through imaging services has expanded with the increase in numbers and complexity of diagnostic imaging procedures ordered. This increase in patient traffic exposes patients to an increase in medical errors.[8] Errors that occurred in imaging services were estimated to be approximately 13% and involved areas of examination requests, patient identification, image acquisition, radiological reports, and communication with the treating team.[8–10] There are different protocols for identifying and relaying important patient information. Some protocols examined were situation, background, assessment, and recommendations (SBAR) and introduction, patient, assessment, situation, safety concerns, background, actions, timing, ownership, and next (I PASS the BATON).10 Use of these standardized tools and other identification protocols and procedures help to inhibit handoff errors.[10] To have a unified system in place, effective communication and simplicity is key.[11] Integration of handoff communication protocols needs to be simple, effective, and tailored to different personnel. Effective handoff communication can lead to behavior change, but more importantly, it can convey critical information and ultimately save lives.[11] This action creates a stronger personal responsibility for healthcare workers at their facilities. However, the processes in place to safeguard patients against breakdown in communication are only effective if they are implemented and utilized at all times.

ELECTRONIC MEDICAL RECORD (EMR):

The EMR is a digital version of a patient's chart that contains the medical and treatment history and supports hospital wide patient care communication. The use of the EMR directly aids practitioners in making clinical decisions.[12] The information recorded in the EMR is available immediately and makes treatment plans easier to generate and track a patient's progress. In one study, during the implementation phase, it was discovered that having too many features in an EMR did not ease the use of the system, but rather increased its difficulty.[12] Collaboration among departments is needed to have a successful implementation of an EMR.[13] One study found a direct correlation with ease of the EMR use with computer efficiency.[14] Those participants that had lower computer efficiency were more reluctant to learn the system. Education and collaboration between departments, allied health professionals, and administrators were important components to the

success of an EMR implementation.[12–14]

COMPUTERIZED PHYSICIAN ORDER ENTRY (CPOE):

CPOE systems allow physicians to order exams and medications by computer without written documentation of the order. These systems have been implemented at hospitals nationwide, and CPOEs have improved healthcare communication.[12,15] CPOE systems were a benefit to hospitals by reducing medication errors because of increased legibility of orders and less reliability of second hand interpretation of a verbal order.[15] Although the use of a CPOE system decreased medical errors approximately 14.5%, only 40.4% of responding hospitals with CPOE systems reported using it for all orders.[15] As technology increases integration of the medical continuum of care, patient safety and medication safety improves.[12,15] The potential for HIPAA violations and external information leaks can increase when implementing a CPOE system if proper security measures are not in place. Web security and firewall installation are extremely important to protect online patient information. Internal breach of security is the most common information breach.[16] Explanations for employees violating web security were listed as accidental authorization and employees with limited authorization gaining additional access. Outside entities may also try to gain access to a hospital's IT infrastructure, but they have to go through the security firewall to access information. These entities include hackers, spies, terrorists, co-intruders, and professional criminals.[16] There are multiple areas of online patient access including PACS, nursing information system (NIS), laboratory information system (LIS), radiology information systems (RIS), and pharmacy information system (PIS). These are all information systems that need software to protect encrypted information from outside sources, and patient information needs to be protected from internal threats to privacy and confidentiality.[16]

PROPER PATIENT IDENTIFICATION:

NPSGs for 2014 listed patient identification as a goal for improvement.[2] These include name, date of birth, addresses, or any other information specific to the patient. The Joint Commission's 2014 survey on root causes for sentinel events listed communication as one of the top reasons for medical mishaps.

WRISTBANDS:

An important area of concern is proper patient identification. One study demonstrated lack of patient identification in multiple healthcare facilities.[17] This study was implemented to see if there was improved patient identification after the use of wristbands as a form of identification. Approximately 34% of patients were not arm banded and only one in six was asked to confirm their name. Wrong patient-wrong procedure had a high occurrence because of the lack of identification. During the study, it was difficult to change the culture where wristbands were not used and also difficult to implement policy changes. It was also demonstrated that 11% of diagnostic errors were in imaging areas, and these errors resulted from lack of identification and verification at first contact with the patient.[8]

RADIO-FREQUENCY IDENTIFICATION (RFID):

New technology aids in proper patient identification. RFID is a patient traceability system that minimizes the occurrence of adverse events by the unequivocal identification of the patient.[18] RFID has been used in different specialty areas since its development in the 1940s to track allied planes.[18] Currently, it is used in the medical setting to track personnel, supplies, and patients.4 The areas of improvement by using RFID include identification of medications, validation of medications, verification of right patient-right medication, and documentation of medication given.[19]

BAR CODE IDENTIFICATION:

One study described bar code identification to track blood transfusions and its effect on safety.[5] During the implementation of this bar code identification system, it was found that near misses on blood transfusions increased while blood products administered to the wrong patient did not change. Another study also demonstrated increased reporting of near misses after the implementation of barcode usage, but they demonstrated a dramatic decrease in misidentification of lab specimens.[20] Portable label printers and mobile carts were used so identification of blood specimens could be done bedside and labeled immediately after the lab draw. In the former study, an increase of incidents from one near miss transfusion to 34 near miss transfusions was reported after the implementation of the bar coding system.[5] Of the 34 near misses, six would have caused an acute hemolytic transfusion reaction. The indication for increased identification of near misses was attributed to the bar coding system identifying mislabeled blood specimens automatically and did not rely on personnel reporting the incidents.[5, 20] There are many distractions that can occur to keep healthcare personnel from properly identifying a patient, and the use of a barcoding system helped to decrease these distractions and increase proper patient identification[5,20]

Adequate Medication/contrast Media Administration:

The two main types of contrast media used in imaging departments are iodinated and gadolinium-based contrast. Each type of contrast has its own safety hazards that imaging technologists must be aware. Iodinated media is commonly used in radiography, fluoroscopy, and CT. Gadolinium is used as an MRI contrast agent. Safety precautions prevent potential life threatening contrast reactions.

CONTRAST INDUCED NEPHROPATHY (CIN)

Contrast induced nephropathy (CIN) or contrast induced acute kidney injury (CI-AKI) are results of kidney damage by contrast administration. CIN is associated with cardiovascular complications, extended hospital stays, and stages 4–5 renal disease.[21] One study further characterized risk factors of CIN including diabetes mellitus, dehydration, age, contrast administration, choice of contrast, and number of studies conducted on patients in a designated amount of time.[22] CIN was diagnosed in patients who had a rise in creatinine level by more than 25% within three days after their procedure with no other known pathology or etiology for the creatinine spike.[22] The process to prevent CI-AKI varied from facility to facility, and the top facilities had a standardized treatment method before and after contrast agents were administered.[21] Estimated glomerular filtration rate (eGFR) was used to determine kidney function prior to exams. One researcher studied two separate facilities' pre- and post-procedure hydration. At one center, eGFR less than 60ml/min/m2 had a specific medication regime prior to the contrasted procedure. Normal saline was administered until sodium bicarbonate could be started one hour prior to exam. The sodium bicarbonate was continued after the exam for approximately six hours, and a 1200mg dose of N-acetylcysteine was administered before and after the procedure.[21] The patient was also kept NPO for only four hours prior to the exam to prevent dehydration. The second center had a few differences in protocol for pre-medicating patients prior to contrasted studies than the first center. The patient was NPO for approximately two hours prior to the study, and only normal saline was administered prior to and after the exam. All other factors remained the same at both facilities. Both of these centers ranked below the national average in CI-AKI incidences.[21] Administering sodium bicarbonate prior to contrasted studies diminished the occurrence of CI-AKI.[21–22]

NEPHROGENIC SYSTEMIC FIBROSIS (NSF):

Gadolinium-based contrast agents (gdbca) are used in MRI imaging. These contrast agents were initially deemed safe for patients in end stage 4-5 kidney failure. In 2006, the FDA issued warnings regarding gcba and the associated development of nephrogenic systemic fibrosis (NSF). The FDA mandated warnings be issued on all gdbcas. NSF affects the joints, skin, internal organs, but has not affected the face.[6] There is no treatment for NSF. However, research demonstrated NSF conditions improved with renal transplant.[23–24] Dialysis did not decrease the risk of developing NSF.[23] In one study, NSF had yet to be discovered in patients with stages 3and 4 kidney disease.[24] Several researchers agreed NSF was limited to patients in stage 5 kidney disease or patients with acute kidney injuries.[6,23–24] Consideration for administration of gdbca must be conducted on each patient. Radiologists and technologists must be aware of risk factors that are closely associated with development of NSF. Patients in stage 5 renal disease are most at risk.[6,23–24] Researchers also agreed patients with stage 3 kidney disease did not develop NSF after gadolinium administration.[6,23–24] Other factors for developing NSF include: patients 60 years and older, diabetes, lupus, history of renal disease, and multiple myeloma.[6] Patient screening must be implemented to ensure at risk patients are identified prior to gadolinium administration, and eGFR clearance is established prior to gdbca administration.[6,25]

Nephrogenic systemic fibrosis (NSF) is a new disorder exclusively observed in patients suffering from renal failure. Because it was initially assumed that the disorder was limited to the skin, the term "nephrogenic fibrosing dermatopathy" was chosen [(1)]. The recognition of the disorder's systemic nature with fibrotic changes in various organ systems led to the renaming of the disease as nephrogenic systemic

fibrosis [2]. Approximately 80 cases are cumulatively reported within European patients; the reports mainly originated from Austria and Denmark. A registry for Germany was opened in the summer of 2007 [4]. Gadolinium-containing magnetic resonance (MR) contrast agents seem to be associated with the disease development [5,6]. This overview summarizes the current knowledge about the pathogenesis, diagnosis, and therapy in order to increase awareness of this new syndrome.

EPIDEMIOLOGY:

Nephrogenic systemic fibrosis was only recognized after large numbers of patients were given gadolinium-based contrast agents. Before 1997 the disease was not reported. There was a change in clinical practice and use of high-dose gadolinium-enhanced magnetic resonance angiography (MRA) for improved imaging. Gadolinium-enforced MRA was used preferentially in patients with renal failure to avoid iodinated (X-ray) contrast agents. The increasing cumulative dosage of these gadolinium-containing contrast agents might have contributed to the development of NSF. Nevertheless, the combination of rapid, higher-than-approved doses of contrast agents and the clustering of cases were probably important factors that likely led to the recognition of this new syndrome.

Additional unknown risk factors might play a role in facilitating NSF. Nephrogenic systemic fibrosis is diagnosed with equal frequency in men and women and affects patients of all ages and ethnicities [7–9]. In a cohort of American dialysis patients, the frequency was 3 cases in 467 patients observed over 18 months, resulting in an estimation of 4.3 cases/1,000 patient-years [10]. The risk of triggering the disorder in these patients through a gadolinium application with different gadolinium-based agents was calculated to be 2.4% [10].

A recent European study found NSF in 17 (17%) of 103 patients with stage 5 chronic kidney disease (CKD) with and without dialysis after exposure to the gadolinium derivate gadodiamide (Omniscan, GE Healthcare Medical Diagnostics, Amersham, United Kingdom). Most of the patients in this study received high doses of gadodiamide (typically approximately 0.3 mmol/kg) for angiography [11]. Another study using Gadoteridol (ProHance, Bracco Diagnostics, Milan, Italy) in 141 patients receiving long-term hemodialysis found no NSF [12]. A further study found discrete clinical signs of NSF in 30% of hemodialysis patients after gadopentetate dimeglumine (Magnevist, Bayer Schering Pharma AG, Berlin, Germany) exposure. However, skin biopsies were not used to confirm the diagnosis of NSF in this patient cohort [13]. Prince et al. [14] assessed the incidence of NSF in 2 large medical centers in the U.S. Of 83,121 patients who received gadolinium-based contrast agents, 15 (0.02%) developed NSF. All of them got a high dose of the contrast agent that exceeded the standard dosage. Most of them suffered from acute renal failure at the time of administration; 8.9% of all patients with acute renal failure receiving gadolinium developed NSF. Wertman et al. [15] recently calculated the benchmark incidence of NSF with data from 4 large U.S. health care centers. The benchmark incidence of NSF ranged from 1 of 2,131 patients to 1 of 65,000 patients. This study confirmed previous findings showing that only patients with severe renal impairment and/or stage 4/5 CKD develop NSF.

RENAL FAILURE:

According to current knowledge, impaired renal function seems to be a conditio sine qua non for NSF. Nephrogenic systemic fibrosis was described in patients with stage 4 and 5 CKD without dialysis, patients requiring dialysis (hemodialysis and peritoneal dialysis), patients who had received renal transplants, as well as patients with acute kidney injury (AKI).

CKD is defined as either kidney damage or glomerular filtration rate (GFR) <60 ml/min/1.73 m^2 for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies [16]. Chronic kidney disease is classified into 5 stages according to the GFR. Stage 1 CKD is diagnosed as kidney damage with normal or increased GFR (>90 ml/min/1.83 m^2); stage 2 is diagnosed as kidney damage with a GFR of 65 to 79 ml/min/1.75 m^2. Stage 3 CKD is defined by a GFR of 35 to 62 ml/min/1.75 m^2, and stage 4 CKD is defined by a GFR of 19 to 32 ml/min/1.77 m^2. Stage 5 CKD is defined as established kidney failure with a GFR <17 ml/min/1.77 m^2 or permanent dialysis therapy [16].

The extent of renal failure that triggers NSF is not known. There are only a few cases with a GFR >17 ml/min/1.77 m^2 reported. To the authors' best knowledge, there is no case with a reported GFR >35 ml/min/1.71 m^2. Although severe renal impairment seems to be a major condition, caution should be advised in recommending a safe range for gadolinium exposure above a specific GFR until further details of the disease are elucidated.

GADOLINIUM EXPOSURE:

The association between the occurrence of NSF and preceding gadolinium exposure within the context of an MR study was first demonstrated in 2006 by Grobner [5] and his team in Austria in 5 patients and by Marckman et al. [6] in 19 patients from Denmark. An evaluation of an American patient cohort indicated gadolinium exposure for patients before the manifestation of NSF. Gadolinium was found in the skin of the patients [17,18]. This association led to warnings by the Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medicinal Products regarding the use of gadolinium-containing contrast agents in patients suffering from renal failure [19,20].

In normal renal function, free gadolinium is removed by the kidney with a half-life of approximately 1.5 hours. In impaired renal function, this half-life is significantly longer. Two consecutive hemodialysis sessions remove approximately 91% of the gadolinium, whereas the peritoneal dialysis is significantly less effectively and only removes approximately 72% of the gadolinium after 5 days [21–23].

A recent meta-analysis by Agarwal et al. [24] demonstrated a significant association between gadolinium-based contrast agent exposure and NSF. Nevertheless, at the time of this writing it cannot be decided whether or not the risk of occurrence of NSF differs for the various gadolinium-containing contrast agents (table 1).The majority of patients with NSF cases had a prior administration of gadodiamide (Omniscan, GE Healthcare Medical Diagnostics), although the product is used in only approximately 15% of magnetic resonance imaging (MRI) studies worldwide [25]. It has been hypothesized that the occurrence of NSF after the application of gadodiamide is related to the lower stability and increased occurrence of toxic free gadolinium in the gadodiamide complex [26,27]. Nevertheless, in some of the studies the gadodiamide dose was very high; thus it has to be considered that the high dosage rather than gadodiamide itself facilitated the development of NSF in these cases [5,6,28–31]. According to the FDA, no MR contrast agent can principally be regarded as safe, because NSF has also been observed after exposure to other gadolinium-containing contrast agents in the U.S. [19]: Gadopentetane dimeglumin (Magnevist, Bayer Schering Pharma AG), gadobenate dimeglumin (MultiHance, Bracco Diagnostics), gadodiamide (Omniscan, GE Healthcare Medical Diagnostics), gadoversatemide (Optimark, Mallinckrodt, St. Louis, Missouri), and gadoteridol (ProHance, Bracco Diagnostics). However, in some patients, coadministration of gadobenate dimeglumin (MultiHance, Bracco Diagnostics) and gadodiamide had been described [27]. Nephrogenic systemic fibroses have been reported after administration of Gadoterate meglumin (Dotarem, Guerbet SA, Aulnay-sur-Bois, France), gadobutrol (Gadovist, Bayer Schering Pharma AG), gadoxet acid dinatrium (Primovist, Bayer Schering Pharma AG), or gadofosveset trinatrium (Vasovist, Bayer Schering Pharma AG) (Table1). But, the repeated gadolinium exposures seems to increase the risk of NSF by 5- to 10-fold as compared with single gadolinium exposure [32-34].

Table 1. Gadolinium Chelates for Use in Magnetic Resonance Imaging

Generic Name	Brand Name	Chemical Structure	Charge	Elimination	Protein Binding	Approving Body
Gadodiamide	Omniscan	Linear	Nonionic	Renal	None	FDA EMEA
Gadoversetamide	OptiMARK	Linear	Nonionic	Renal	None	FDA
Gadopentetic acid	Magnevist	Linear	Ionic	Renal	None	FDA EMEA
Gadobenic acid	MultiHance	Linear	Ionic	97% renal, 3% bile	<5%	FDA EMEA
Gadoxetic acid	Primovist	Linear	Ionic	50% renal, 50% bile	<15%	EMEA
Gadofosveset	Vasovist	Linear	Ionic	91% renal, 9% bile	>85%	EMEA
Gadoteridol	ProHance	Cyclic	Nonionic	Renal	None	FDA EMEA
Gadobutrol	Gadovist	Cyclic	Nonionic	Renal	None	EMEA
Gadoterat	Dotarem	Cyclic	Ionic	Renal	None	EMEA

OptiMARK is not yet licensed in Europe, whereas several other compounds are not approved by the Food and Drug Administration (FDA) but are available in Europe.

EMEA = European Agency for the Evaluation of Medicinal Products.

TABLE 1: Data on Patients Enrolled and Evaluated in the Study

Patient Population Characteristics	Study A			Study B			
	Total (N = 366)	Cohort 1[a] (n = 321)	Cohort 2[b] (n = 45)	Total (N = 176)	Cohort 1[a] (n = 163)	Cohort 2[b] (n = 13)	Study C (N = 405)
Initial safety population[c] (no.)	363	318	45	171	159	12	405
Patients who discontinued the study during the first year[d]	68 (18.7)	63 (19.8)	5 (11.1)	35 (20.5)	33 (20.8)	2 (16.7)	31 (7.7)
Patients who died during the first year	41 (11.3)	26 (8.2)	15 (33.3)	13 (7.6)	11 (6.9)	2 (16.7)	46 (11.4)
Population at 1-year follow-up for NSF analysis[e]	295 (81.3)	255 (80.2)	40 (88.9)	136 (79.5)	126 (79.2)	10 (83.3)	374 (92.3)
Patients not in 1-year follow-up who returned for 2-year follow-up	14 (3.9)	13 (4.1)	1 (2.2)	5 (2.9)	5 (3.1)	0	7 (1.7)
Patients who discontinued the study during the second year[d]	29 (8.0)	28 (8.8)	1 (2.2)	20 (11.7)	20 (12.6)	0	7 (1.7)
Patients who died during the second year	13 (3.6)	10 (3.1)	3 (6.7)	6 (3.5)	5 (3.1)	1 (8.3)	45 (11.1)
Population at 2-year follow-up for NSF analysis[e]	269 (77.1)	240 (75.5)	40 (88.9)	121 (70.8)	111 (69.8)	10 (83.3)	374 (92.3)

Note—Data are no. (%) of patients in the safety population. Patients who died within follow-up period are included. NSF = nephrogenic systemic fibrosis.
[a]Patients with an estimated glomerular filtration rate (eGFR) of 30–59 mL/min/1.73 m².
[b]Patients with an eGFR < 30 mL/min/1.73 m².
[c]All patients enrolled in study C and patients enrolled in studies A and B who received contrast agent.
[d]Includes patients lost to follow-up, patients who withdrew consent, patients who were excluded for protocol violations (e.g., received a second gadolinium-based contrast agent), and patients who discontinued the study for other reasons.
[e]All patients who had an eGFR < 60 mL/min/1.73 m² at baseline who received the prescribed study agent (gadobenate dimeglumine or gadoteridol) in each study, who had data at follow-up evaluations, and who received no other GBCA during the entire follow-up period.

TABLE 3: Underlying Medical History of Study Patients

Underlying Medical History	Study A			Study B			
	Total (N = 363)	Cohort 1 (n = 318)	Cohort 2 (n = 45)	Total (N = 171)	Cohort 1 (n = 159)	Cohort 2 (n = 12)	Study C (N = 405)
Nephrotoxic drug therapy	6 (1.7)	4 (1.3)	2 (4.4)	4 (2.3)	4 (2.5)	0	7 (1.7)
Diabetic nephropathy	86 (23.7)	66 (20.8)	20 (44.4)	49 (28.7)	46 (28.9)	3 (25.0)	180 (44.4)
Renal artery stenosis	6 (1.7)	6 (1.9)	0	3 (1.8)	3 (1.9)	0	8 (2.0)
Polycystic kidney disease	4 (1.1)	4 (1.3)	0	8 (4.7)	7 (4.4)	1 (8.3)	13 (3.2)
Systemic lupus erythematosus	1 (0.3)	1 (0.3)	0	0	0	0	7 (1.7)
Multiple myeloma	1 (0.3)	1 (0.3)	0	0	0	0	1 (0.2)
Hypertensive nephropathy	193 (53.2)	176 (55.3)	17 (37.8)	121 (70.8)	111 (69.8)	10 (83.3)	161 (39.8)
Renal cell carcinoma	24 (6.6)	22 (6.9)	2 (4.4)	11 (6.4)	9 (5.7)	2 (16.7)	2 (0.5)
Glomerulonephritis	7 (1.9)	5 (1.6)	2 (4.4)	3 (1.7)	3 (1.9)	0	20 (4.9)
Acute kidney injury	10 (2.8)	9 (2.8)	1 (2.2)	2 (1.2)	2 (1.3)	0	2 (0.5)
Renal atrophy	4 (1.1)	2 (0.6)	2 (4.4)	1 (0.6)	1 (0.6)	0	0
Hepatorenal syndrome	3 (0.8)	3 (0.9)	0	0	0	0	1 (0.2)
IgA nephropathy	3 (0.8)	1 (0.3)	2 (4.4)	0	0	0	4 (1.0)
Nephroangiosclerosis	1 (0.3)	1 (0.3)	0	2 (1.2)	1 (0.6)	1 (8.3)	10 (2.5)
Pyelonephritis	3 (0.8)	2 (0.6)	1 (2.2)	1 (0.6)	1 (0.6)	0	0
Urinary tract cancer (bladder)	6 (1.7)	6 (1.9)	0	3 (1.7)	3 (1.9)	0	0
Calcineurin inhibitor–induced nephropathy	1 (0.3)	1 (0.3)	0	0	0	0	1 (0.2)
Buerger disease	0	0	0	2 (1.2)	2 (1.3)	0	1 (0.2)
Focal hyalinosis	1 (0.3)	1 (0.3)	0	1 (0.6)	1 (0.6)	0	0
Oncocytoma	1 (0.3)	1 (0.3)	0	1 (0.6)	1 (0.6)	0	0
Schönlein-Henoch purpura	1 (0.3)	0	1 (2.2)	0	0	0	0
Chronic allograft nephropathy	1 (0.3)	0	1 (2.2)	0	0	0	0
Contrast agent–induced nephropathy	1 (0.3)	1 (0.3)	0	0	0	0	1 (0.2)
Oxalate nephropathy	1 (0.3)	0	1 (2.2)	0	0	0	0
Medullary sponge kidney	0	0	0	1 (0.6)	0	1 (8.3)	0
Sarcoidosis	3 (0.8)	3 (0.9)	0	0	0	0	0

TABLE 4: Exposure to Investigational Product During Baseline MRI Examination

Examination, Exposure	Study A			Study B		
	Total (N = 363)	Cohort 1 (n = 318)	Cohort 2 (n = 45)	Total (N = 171)	Cohort 1 (n = 159)	Cohort 2 (n = 12)
All						
Patients with product exposure (no.)	361[a,b]	317[a]	44[b]	171	159	12
Contrast agent received (mmol/kg), mean ± SD	0.11 ± 0.04	0.1 ± 0.04	0.11 ± 0.05	0.1 ± 0.05	0.1 ± 0.05	0.12 ± 0.04
CNS (brain, spine)						
Patients with product exposure (no.)	106	97	9	39	39	0
Contrast agent received (mmol/kg), mean ± SD	0.09 ± 0.02	0.09 ± 0.02	0.08 ± 0.04	0.07 ± 0.03	0.07 ± 0.03	
Chest (heart, lung)						
Patients with product exposure (no.)	11	11	0	4	4	0
Contrast agent received (mmol/kg), mean ± SD	0.11 ± 0.05	0.11 ± 0.05		0.15 ± 0.06	0.15 ± 0.06	
Upper abdomen (liver, kidney, pancreas)						
Patients with product exposure (no.)	106	96	10	62	55	7
Contrast agent received (mmol/kg), mean ± SD	0.09 ± 0.03	0.09 ± 0.03	0.08 ± 0.03	0.1 ± 0.05	0.1 ± 0.05	0.1 ± 0.01
Lower abdomen (uterus, ovaries, prostate)						
Patients with product exposure (no.)	16	11	5	20	20	0
Contrast agent received (mmol/kg), mean ± SD	0.09 ± 0.03	0.1 ± 0.03	0.07 ± 0.03	0.1 ± 0.01	0.1 ± 0.01	
MR angiography						
Patients with product exposure (no.)	95 [96][b]	77	18 [19][b]	13	10	3
Contrast agent received (mmol/kg), mean ± SD	0.14 ± 0.05	0.14 ± 0.05	0.16 ± 0.03	0.2 ± 0.06	0.2 ± 0.07	0.17 ± 0.02
Other						
Patients with product exposure (no.)	27 [28][a]	25 [26][a]	2	33	31	2
Contrast agent received (mmol/kg), mean ± SD	0.1 ± 0.04	0.1 ± 0.04	0.08 ± 0.05	0.1 ± 0.04	0.1 ± 0.04	0.1 ± 0.01

[a]Data were available for 25 of 26 patients undergoing MRI for another application (CNS + MR angiography). Dose was impossible to calculate for one patient in cohort 1 who was administered 65 mL of gadobenate dimeglumine, because the weight of the patient was not recorded.
[b]Data were available for 18 of 19 patients undergoing MR angiography; dose was impossible to calculate for one patient in cohort 2 who was undergoing abdominal MR angiography, because the volume of gadobenate dimeglumine administered was not recorded.

TABLE 5: Exposure to Investigational Product During Routine Follow-Up Examinations

No. of Follow-Up Examinations, Cohort	Study A[a]		Study B[b]	
	No. of Patients	Volume Administered Per Procedure[c] (mL)	No. of Patients	Volume Administered Per Procedure[c] (mL)
One examination				
Cohort 1[d]	41	6–45	15	7–20
Cohort 2[e]	5	11–40	3	15
Two examinations				
Cohort 1	12	7–50	4	6–34
Cohort 2	—	—	—	—
Three examinations				
Cohort 1	2	3 × 8 mL; 8 mL + 2 × 15 mL	1	3 × 18
Cohort 2	—	—	1	8, 11, and 12
Four examinations				
Cohort 1	1	3 × 17 mL + 8 mL	1	4 × 18
Cohort 2	—	—	—	—
Five examinations				
Cohort 1	1	5 × 6	—	—
Cohort 2	—	—	—	—

Note—Dash (—) indicates no follow-up MRI examinations performed.
[a]Patients received gadobenate dimeglumine.
[b]Patients received gadoteridol.
[c]Presented as range (min, max) for multiple patients undergoing one or two follow-up examinations and as specific volumes for individual patients undergoing three, four or five follow-up examinations.
[d]Patients with an eGFR of 30–59 mL/min/1.73 m².
[e]Patients with an eGFR less than 30 mL/min/1.73 m².

CONCLUSION:

Advances in healthcare have vastly improved patient life expectancy, but also put patients at risk during treatment. Updating policies and procedures throughout the entire hospital and healthcare setting is important to keeping patients safe. Imaging services have multiple areas with potential lethality if protocols and procedures are not followed. Effective handoff communication, proper patient identification, and safe contrast media administration are areas that should be addressed by radiology managers to ensure patient safety in the medical imaging department. Considering the recent NPSGs, these areas of concern should be constantly updated to ensure adequate patient care and safety in the medical imaging department.

The patients enrolled in each study and the numbers of patients available for evaluation at each follow-up point are presented in Table 1. Of the 366 patients enrolled in study A, one received a GBCA other than gadobenate dimeglumine, one was too large for the scanner, and one had an eGFR of 63.6 mL/min/1.73 m2 at the time of the examination. These three patients were therefore excluded from study A. Similarly, of the 176 patients enrolled in study B, two underwent an unenhanced MRI examination, two were claustrophobic, and one had an eGFR of 64.2 mL/min/1.73 m2 at the time of the examination. These five patients were similarly excluded from study B. The NSF analysis populations available for studies A and B therefore comprised 363 and 171 patients, respectively (318 and 159 in cohort 1 of each study, respectively, and 45 and 12 patients in cohort 2 of each study, respectively). Although the studies were designed to permit the enrollment of all subjects regardless of age, only adult subjects were enrolled at each center. The demographic characteristics of the patients enrolled in each of the three studies are provided in Table 2, whereas a summary of the underlying renal history of each patient population is given in Table 3.

For studies A and B, the populations evaluated for NSF comprised 363 and 171 patients, respectively, with 318 and 159 patients in cohort 1 of each study, respectively, and with 45 and 12 patients in cohort 2, respectively. No signs or symptoms of NSF were reported or detected during the 2 years of patient monitoring. Likewise, no cases of NSF were reported for any of the 405 subjects enrolled in study C.

To our knowledge, and consistent with reports in the literature, no association of gadobenate dimeglumine or gadoteridol with unconfounded cases of NSF has yet been established. Study data confirm that both gadoteridol and gadobenate dimeglumine properly belong to the class of GBCAs considered to be associated with the lowest risk of NSF.

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