Southern California CSU DNP Consortium

California State University, Fullerton
California State University, Long Beach
California State University, Los Angeles

CONTRAST INDUCED NEPHROPATHY: PROTECTING KIDNEYS,
PROTECTING LIVES

A DOCTORAL PROJECT

Submitted in Partial Fulfillment of the Requirements

For the Degree of

DOCTOR OF NURSING PRACTICE

By

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ABSTRACT

Radiographic imaging procedures using iodinated contrast media are an essential part of the clinical management of many patient conditions, yet these procedures are not without complications. Iodinated contrast media can cause contrast-induced acute kidney injury (CI-AKI) or nephropathy (CIN). Contrast-induced nephropathy impacts healthcare costs and affects patient morbidities. It is a patient safety concern and a serious adverse event as it only happens after iodinated contrast exposure. For this quality improvement project, a radiology contrast media policy aimed at preventing kidney harm to patients at high risk for developing CIN was modified from the Veterans Integrated Systems Network (VISN) 22 Imaging Services, and implemented in a single outpatient vascular clinic of a large national healthcare system. Using The Johns Hopkins Quality and Safety Research Group Framework, the project lead worked to engage stakeholders and an interdisciplinary team to systematically implement a comprehensive organized change.

During the first six months of 2015, of 1289 vascular clinic outpatients, 62 were deemed high risk for CIN based upon policy criteria (4.8%). For most of these at risk patients (64.5%), the modified policy was appropriately implemented. Those who received the policy recommendations (including the intravenous (IV) hydration) experienced no unexpected or complications beyond those that accompany procedures using iodinated contrast media. No patient who received the recommended screening and follow up care was found to have CIN. By adhering to a policy of early screening,
stratifying, and IV hydration, quality could be improved for outpatients requiring iodinated contrast for radiographic imaging.
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Finally, a sincere thanks to my DNP Cohort 3 classmates Gina and Mira for sharing in this journey, and to my surgical attendings Samuel Eric Wilson, MD and Ian Gordon, MD for their assistance in helping me to improve the outcomes of our Veteran patients.
BACKGROUND

Radiographic imaging procedures using iodinated contrast media are an important part of the clinical management of many conditions, yet these procedures are not without complications (Hiremath, Akbari, Shabana, Fergusson, & Knoll, 2013). Despite the safe administration of approximately 80 million annual doses of iodinated contrast given worldwide, iodinated contrast can cause acute kidney injury (Hiremath et al., 2013). As the burden of illness and the aging population increase in the United States (U.S.), so does the challenge of radiographic clinical management due to risks of complications from such procedures. Contrast-induced kidney injury (CI-AKI) or nephropathy (CIN) impacts healthcare cost, and affects patient morbidity and quality of life (Brown et al., 2014). The Vascular Nurse Practitioner is in a pivotal role to lead a system change project aimed to address preventable CI-AKI.

One of the most commonly described adverse events of acute kidney injury is contrast-induced nephropathy (American College of Radiology, 2013). There is no consensus definition for this diagnosis; however, one commonly used is a rise in serum creatinine (sCr) of more than 25% or an absolute increase above baseline of 0.5 mg/dl within 48-72 hours after intravascular administration of iodinated contrast medium, and without any alternative etiology (Brown et al., 2014). In most cases, this is a transient decline in kidney function manifesting with no symptoms or oliguria, with the sCr normalizing within one to three weeks. However in other cases, CIN can progress to more serious acute kidney injury with oliguria (24 hour urine volume < 400 ml) occurring within 24-48 hours of iodinated contrast administration and persisting for two to five
days (Gleeson & Bulugahapitiya, 2004). Morbidity and mortality rates are significantly higher in this group when compared to those with no oliguria, as these patients suffer the consequences of associated permanent kidney injury, potential dialysis and unfortunately death (Gleeson & Bulugahapitiya, 2004).

In the general population of patients without a history of kidney disease and receiving an intravenous iodinated contrast-enhanced computerized tomography (IV-CECT) scan, the risk of developing CIN is low at less than 1% (Andreucci et al., 2014). In a recent meta-analysis, the pooled mean incidence of CIN (November 1, 2002 to November 10, 2012) was cited to be 4.96% and associated with pre-existing kidney disease, diabetes, presence of malignancy, advanced age, and chronic use of non-steroidal anti-inflammatory drugs (Moos, van Vemde, Stoker, & Bipat, 2013). Still, CIN remains one of the leading causes of hospital-acquired acute kidney failure and is linked to a higher risk of in-hospital and one year mortality, even in patients who do not require dialysis (Bansai et al., 2014). Disturbingly, once CIN develops, management is primarily supportive as there is no current treatment which can reverse CIN; prophylactic strategies need to be considered as a reasonable best practice approach to reduce its development (Mohammed, Mahfouz, Achkar, Rafie, & Hajar, 2013).

Much work has been done on this topic in terms of systematic reviews, consensus statements and prevention guidelines. CIN has a predictable time course and is amenable to prevention, yet implementation of clinical recommendations has not been widespread. Among the reasons for this is the lack of a single widely accepted consensus guideline, treatment algorithm, or protocol for prevention. Multiple disciplines (radiology,
cardiology, nephrology, and urology) as well as the Agency for Healthcare Research and Quality (AHRQ) recognize the importance of addressing this clinical issue and have addressed preventive measures with published guidelines; however specific recommendations vary (American College of Radiology, 2013; Caixeta & Mehran, 2010; Detrenis, Meschi, del Mar Jordana Sanchez, & Savazzi, 2007; KDIGO, 2012; McCullough et al., 2006; National Quality Measures, 2009, 2014; Owen, Hiremath, Myers, Fraser-Hill, & Barrett, 2014). Also, treatment of CIN suffers from a lack of randomized control trials; studies up to now have been inadequately controlled observational studies (Brett, 2015).

Moreover, Weisbord et al. (2008) state the routine assessment of risk status and implementation of preventive interventions, such as intravenous (IV) fluids, are considerably more difficult in patients who undergo non-emergent IV-CECT image studies versus other procedures like coronary angiography. As healthcare reform continues to extend from the structured inpatient areas to the more unstructured outpatient settings, practical and fiscal challenges have become substantial. Many radiology suites are not adequately equipped or staffed to administer IV fluids, and most insurers do not authorize routine hospital admission for this purpose (Weisbord et al., 2008).

Lastly, there is a need to heighten recognition of the overall small, but inherent risks in the use of iodinated contrast mediums. One particular concern is that physicians and practitioners who refer patients for iodinated contrast procedures may not always be fully informed about the risks of CIN. Among those who ordered IV-CECT scans, Weisbord et al. (2009) found that over half were not fully informed regarding risk factors.
associated with CIN and reported having little to no training or experience with this condition. They recommended educational efforts focusing on risks and preventive strategies for CIN as an important measure to ensure patient safety and prevent iatrogenic outcomes.

**Statement of the Problem**

CIN is a serious complication following administration of iodinated contrast media. This is particularly true for patients at higher risk for acute kidney injury, notably those with peripheral vascular disease (PAD). Peripheral arterial disease is very common in those with chronic kidney disease (CKD); with a coexisting prevalence among those ages ≥ 70 years, at 25% to 37% (Liew, Bartholomew, Demirjian, Michaels, & Schreiber, 2008). Chronic kidney disease and PAD share the same cardiovascular risk factors, as both are clinical manifestations of diffuse atherosclerosis. Patients with PAD require intra-arterial iodinated contrast medium to diagnose and treat (Kroneberger et al., 2015). Further, they require repeat IV-CECT specifically, computed tomography angiography (CTA) for surveillance purposes (Kirkpatrick, Trinh, Williams, Gordon & Wilson, 2014; Kougiás et al., 2014). CTA is the most effective imaging modality for visualizing arterial flow; however patients with PAD and pre-existing kidney disease are at added risks for CIN due to repeat exposure to contrast materials (Kougiás et al.).

In addition, AKI on top of pre-existing CKD is a common yet underappreciated risk factor for adverse outcomes following any vascular procedure (Huber, et al., 2015). In a longitudinal study, Kougiás et al. (2014) looked at the impact of repeat subsequent IV-CECT on kidney function in patients who underwent surgical interventions for occlusive and aneurysmal procedures. Of the patients who underwent endovascular aortic
aneurysm (EVAR) repair, 32%-52% progressed to CKD at 18 months and CIN was an important risk factor for worsening kidneys. Even more, they identified a cumulative iodinated contrast load effect on kidney function over time with standard surveillance imaging, which uniquely contributed to kidney decline and permanent kidney injury. Supporting the idea of additive risk, Liew et al. (2008) found patients with combined CKD and PAD had an approximate four-fold increased risk for death compared with a no disease group, and nearly a two-fold increased risk for death compared with single disease groups. Similarly, Huber et al. found the prevalence of kidney disease among patients requiring vascular surgery to be high with 49% of patients developing AKI during hospitalization, resulting in a significant increase in mortality and costs at 90 days. Alarmingly, Boggs (2016) states the estimated cost of a CIN related hospital stay averages more than $10,000 per episode. Based on the evidence, there is a gap and clinical need to identify patients with vascular disease who are at risk for CIN, implement quality improvement measures to reduce patient harm and prevent kidney injury.

**Supporting Framework**

Evidence-based therapies aimed at improving patient health, even when backed by good evidence, are often not translated into practice because of barriers and organizational complexities. This could lead to variations in care, errors of omission with substantial cause for preventable harm (Pronovost, Berenholtz, & Needham, 2008). Further, translating evidence into clinical practice at the point of care is an overwhelming challenge for health systems as well as for individual practitioners (Kitson & Phil, 2009). Because this project involved translating evidence into consistent practice at the point of care along with a healthcare systems change, a collaborative integrative strategy was
used. The strategy was the Johns Hopkins Quality and Safety Research Group translating evidence into practice approach (Pronovost et al., 2008). This strategy seemingly fit well as it offered an integrative collaborative approach, emphasizing explicit methods for translating evidence into practice, so that ultimately the right care for the right patient occurred at the right time, every time (Figure 1).

The overall precepts of this strategy included envisioning the problem within the larger healthcare system and engaging collaborative interdisciplinary teams centrally (stages 1-3) and locally (stage 4). Thus, the strategy focused on systems rather than individuals, engaged interdisciplinary teams to assume ownership of the improvement project, created centralized support for the technical work, encouraged local adaption of the intervention, and created a collaborative culture within the local and larger units (Pronovost et al., 2008).

To meet this overall goal, there were four key components. The first was to summarize the meaning of the evidence. In April 2014, the VHA-Veteran Integrated Service Network (VISN) 22 Imaging Services outlined a policy on contrast media which included a comprehensive protocol titled “Iodinated Contrast Media Screening Procedures.” This protocol (algorithm format) discriminates an arm for IV contrast media and CIN preventive interventions (Appendix A). This protocol was endorsed by several local radiologists, however it was not standardized into local practice or systematically implemented. A challenging issue was the radiologist and the administrative department expected the ordering provider to carry out this protocol without any training. The protocol is complex requiring providers to conduct screenings, stratify patients as being low to high risk for CIN, and then based on protocol criteria arrange for the patient to
have the recommended preventive IV hydration. Many providers including the vascular team remained unaware of this protocol as practices across the medical center were inconsistent, and a location to do the preventive IV hydration for outpatients was not identified. Patients were affected, as they were denied scheduled imaging studies by the department and asked to return to their providers for additional orders.

Because vascular outpatients require frequent IV-CECT images, the Vascular Nurse Practitioner decided to take a systematic departmental approach. In order to ensure success with standardizing any new practice change, one of the first steps was to identify local leaders and change agents who would be responsible for implementing the change, facilitating, and keeping the process moving forward (Newhouse, Dearholt, Poe, Pugh, & White 2007). The Chief of Vascular Surgery, the Vascular Nurse Practitioner, key stakeholders and interdisciplinary team members were identified and convened in June 2014 to summarize the meaning of the evidence and begin the next step of identifying interventions.

This team met and conducted a review of the literature. The team members agreed that the contrast media policy and protocol were best practices per the American College of Radiology (2013, 2015). However, due to limited outpatient resources, the IV hydration protocol component of the policy needed to be modified. In late July, the protocol was adopted with specific modifications for the vascular outpatient clinics. The original IV hydration protocol called for one liter of normal saline to infuse at 250 mL over 4 hours pre, and one liter of normal saline to infuse at 250 mL over an additional 4 hours post IV-CECT procedure. As seen in Figure 2, the modifications shortened the pre and post-procedure hydration delivery times to one liter of normal saline to infuse over 2
to 3 hours pre, 250 mL normal saline to infuse over 30 minutes post IV-CECT procedure, and added patient instructions to orally hydrate with at least one quart of fluids the day before and the day after contrast exposure (unless contra-indicated by their primary care provider).

**Figure 2.** VHA-Veteran Integrated Service Network (VISN) 22 Imaging Services (December 2013) Policy and Procedures: Contrast Media, modified for Vascular Outpatient Clinics.
The second key component addressed barriers to implementation. During this phase the stakeholders shared concerns and identified potential gains and losses associated with the implementation of the recommendations. In addition, stakeholders and key members of the interdisciplinary team were asked to physically and conceptually walk through the steps and observe what was required to complete the interventions. This required communicating with involved staff, looking at structures, and resources. The team took the physical walk, viewing the process from the perspective of those having to undergo the procedure and requiring the IV hydration protocol. Through this, they identified several issues: (a) RN staff and procedures were lacking to provide the IV hydration, (b) nursing leadership was unaware of the protocol, (c) there were no processes for providers outlining how to accomplish or arrange the IV hydration for outpatients, (d) few providers were aware of CIN or prevention strategies, and (e) there were no administrative or standard operative procedures regulating this process.

The Vascular Nurse Practitioner, engaged the interdisciplinary team to meet with the nursing administration, discussed the issues and negotiated consideration of use of the hospital’s infusion center for the pre and post procedure hydration. This interaction was well received, and the infusion center and nursing staff were secured as the location for the hydration.

The third key component was to measure how often patients received the recommended therapy (process measures) and to evaluate whether patient outcomes improved (outcome measures). The plan was to measure these outcomes continuously by comparing baseline data against the identified outcomes. To measure the current situation, the Chief of Vascular Surgery, Vascular Nurse Practitioner, Safety Risk
Manager (QM) and the Surgical Quality Improvement nurse (QI) met to decide baseline metrics. After a follow up meeting with the information technology specialist (DSS), a computerized real time database scorecard was set up to capture aggregate data on vascular outpatients requiring IV-CECT and associated risk factors. Associated risk factors in this data set included age, diabetes, serum creatinine and estimated glomerular filtration rates (eGFR) laboratory values both pre and post IV-CECT (if obtained). Data collection was set up to begin capturing retrospectively for fiscal year 2013. A data trail was set up in fiscal year quarters beginning with the first quarter of 2013; which covered the months October 1 to December 31, 2012, second quarter January 1, to March 31, 2013, third quarter April 1 to June 30, 2013, and July 1 to October 31, 2013. It was established that process measures of patients who met criteria for the protocol would be tracked and compared to those who actually received the hydration protocol. These data would be expressed in frequencies and percents, and used to determine the level of adherence to this policy.

The fourth and final key component of the strategy occurred at the unit level and ensured all patients reliably received the intervention. This strategy includes the “four Es” approach to improve reliability: Engage, educate, execute, and evaluate. This approach recognizes the importance of cultural change, contextual factors, and staff engagement.

As seen in Figure 1, the first E is to engage all vascular clinic staff by explaining the rationale for the policy implementation and to gain support for the need to consistently screen and hydrate high risk outpatients requiring IV-CECT image studies for CIN prevention. At this phase, stories were shared about the ownership of the
problem along with the frustrations and chaos experienced by patients and staff when standardized processes were not clear. As Kitson and Phil (2009) state, the learning organization model is one where the organization embraces continuous learning and change, so whenever knowledge, new knowledge, or interventions emerge, these are interrogated, tested, adapted, adopted, and evaluated by all involved.

The second E is education and sharing of the evidence that support this intervention. For this project, a simple needs assessment was conducted on current vascular providers which included residents, attending physicians, radiologist, and nurse practitioners who order IV-CECT studies. The needs assessment was a brief 8 item survey (Appendix C) with a follow up discussion by the Vascular Nurse Practitioner. The survey was designed in collaboration with the Chief of Vascular Surgery to assess the vascular clinic provider’s general knowledge of CIN, experience, awareness, attitude (willing to comply) and perceived barriers to implementing the protocol. The survey was deployed at the Surgical Healthcare Monday morning meeting in November 2014. This survey was used as an “ice breaker” to formally introduce the project and discuss the implementation plan. This generated so much interest that grand round discussions on CIN prevention were later conducted by the Vascular Chief Resident in the months of December 2014 and January 2015, as part of resident staff education.

Other educational opportunities during this phase included two interdepartmental mini “lunch and learn” updates on CIN prevention conducted by the Vascular Nurse Practitioner and the Chief of Vascular Surgery. All involved clinic staffs from vascular, radiology, and the infusion center were invited to attend. In addition, the Vascular Nurse Practitioner did a special education class for the infusion center nurses focusing on the IV
hydration protocol and the importance of monitoring patients for fluid overload. She also did several “just in time” snippets on CIN prevention to monthly rotating vascular residents during clinic group huddles. Flyers of the protocol were made and handed out as process reminders. A poster of the protocol was made and remains displayed in the clinic huddle room as a visual cue reminding providers to “screen, stratify, hydrate and follow up.” Flyers were also made to educate patients on the process to receive the protocol which included instructions on oral hydration. Ongoing education continues to occur as the vascular resident providers rotate every 4 weeks. According to Kitson and Phil (2009), multifaceted interventions are more effective than single strategies, especially if barriers to change are identified.

The third E is to execute. For ordering IV-CECT, the team developed an instant automatic pop up “view alert” to be triggered when a patient has an eGFR < 60ml/min, and an IV hydration protocol quick link order set. The pop up view alert was created as a trigger to instantly alert the ordering provider that the patient has low or impaired kidneys. The order set was created as a quick link to standardize practice so that the patient receives the correct IV solution, volume, and time delivery rate of the protocol. Both these links were embedded into the electronic medical record with opportunities to add or alter as needed. In addition to the links, the team worked on a standardized operating procedure (SOP) for the vascular clinic. In October 2015, the team presented the SOP to the Clinical Practice Council. This SOP outlines the current process, clarifies multi-departmental responsibilities and serves as a communication tool as this process involves many patient handoffs. Both the presentation and the SOP were well received by the Clinical Practice Council and the SOP was accepted and circulated as a Memorandum
of Understanding between departments. The council further recommended this project be submitted to the systems redesign work team for hospital wide implementation.

The last E is to evaluate the intervention success. The policy was formally introduced to the vascular providers in December 2014. The evaluation plan consists of collecting data to determine the population characteristics of patients at high risk for CIN, measures of outcome processes including protocol adherence, and measures of unintended consequences or any new harm as a result of the kidney protective hydration protocol intervention (e.g., volume overload, patient arrhythmias, need for emergency room visit, need for hospital admission, need for alternative measures, etc.).

**Project Aims**

This quality improvement project is to improve clinical practice by implementing a radiology policy on contrast media aimed at preventing kidney harm to patients at high risk for developing CIN. To accomplish this, a local vascular clinic standard operating procedure (SOP) outlining departmental responsibilities and processes for screening, stratifying and IV hydrating patients at high risk for CIN, was developed. Once approved by the appropriate bodies, this SOP would be implemented for the institution. In order to accomplish the project aims, following approval of the modified contrast media policy (December 2014), the primary strategies would be directed towards engaging an interdisciplinary and stakeholder group, to implement this policy in an outpatient vascular clinic of a large national healthcare system. In order to complete this project, the following strategies were delineated per the project timeline (Appendix D):

- Collaborate to design an ongoing tracking system (scorecard) that captures the number of IV-CECT studies ordered by the outpatient vascular clinics (new,
follow-up, post-op, vascular wound) at baseline starting with FY 2013 and continuing thru post implementation.

- Based on this system, identify the overall baseline number of vascular outpatients who met the criteria for the hydration protocol prior to implementation.
- Using this baseline data, collaborate with the interdisciplinary work team to plan for a quality improvement approach which includes a process for screening, stratifying and IV hydrating vascular outpatients at risk for CIN.
- Present this plan to the surgical healthcare group for review and feedback.
- Conduct a needs assessment of current vascular provider’s knowledge, experience, attitudes (willing to comply) and perceived barriers on both CIN prevention and best practice guideline implementation.
- Build on a quick link order set for standardizing the IV hydration protocol.
- Educate vascular providers on CIN through a variety of methods.
- Educate the infusion center nursing staff, radiology and all clerical staffs in “lunch and learn” format about CIN and the IV hydration protocol.
- Begin tracking metrics (Quarter 2, FY 2015 to present) of vascular outpatients referred for IV-CECT by vascular providers, who met criteria and whether or not they received the pre and post IV hydration as outlined in the protocol.
- Evaluate quarterly retrospective chart reviews six months after implementation to determine process and outcome measures (Quarter 2, Quarter 3 FY 2015).
• Collaborate with the interdisciplinary work team to propose and publish a vascular clinic SOP outlining the current process and interdepartmental responsibilities for screening, risk stratifying and IV hydrating patients at high risk for CIN in order to standardize practice.

• Once practice standardized, present this project to Clinical Practice Council and recommend this project be considered a model for best practice hospital wide implementation.
REVIEW OF LITERATURE

Search and Appraisal Methods

A comprehensive review of the literature was conducted for this quality improvement project. The following databases were searched for publications, PubMed, CINAHL, Cochrane Library, Sage Journals Online, and google.com/scholar. Evidence relevant to three topics was sought: contrast induced nephropathy or contrast induced acute kidney injury, guidelines or consensus statements, and vascular disease risks. MeSH and key terms were used; these included the following: prevention of, intravenous contrast media, intravenous contrast, iodinated contrast media, peripheral vascular disease, vascular disease, acute kidney injury, guideline adherence, provider adherence, and changing provider behavior. Search limits were English, humans, published within the past 5 years, NOT arterial or intra-arterial. Sources of evidence found are seen in Tables 1–3. Critically appraised evidence summaries are found in (Appendix K).
Table 1

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*Note.* Articles excluded based on title, duplications and relevance to project topic.

Table 2

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*Note.* Articles excluded based on title, duplications and relevance to project topic.
Overview of Contrast Induced Nephropathy

Intravenous iodinated contrast mediums are often used to improve the diagnostic accuracy of radiographic image modalities, as they enhance the vascular system, organs, and soft tissue. A commonly described adverse event is the acute deterioration of kidney function or CIN, also known as CI-AKI (Stevens, Levin, & Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group, 2013); CIN is a leading cause of iatrogenic acute kidney injury and remains one of the most serious adverse effects associated with iodinated contrast mediums (Heyman, Rosenberger, Rosen, & Mogher, 2013). Patients who require dialysis as treatment for CIN suffer dramatic increased mortality rates at one year and have a projected median two-year survival rate of only 19% (Owen et al., 2014).

Typically, CIN involves an increase in sCr, peaking over two to five days, which in most cases, normalize within one to three weeks after the exposure to intravascular iodinated contrast medium (Stacul et al., 2011). Although rare, some patients may progress to a more serious renal impairment with oliguria (24 hour urine volume less than 400 ml), requiring hospitalization; even more rarely (less than 1%) some may require dialysis (Owen et al., 2014). Recent epidemiological evidence supports the notion that...
even mild, reversible acute kidney injury can lead to persistent damage, and severe acute kidney injury can be accompanied by an irreversible decline of kidney function with progression to end-stage kidney failure (Fliser et al. 2012). CIN is associated with increased morbidity, mortality, and medical resource consumption (Moos et al., 2013); it is the third most common cause of hospital-acquired acute kidney failure behind impaired kidney perfusion and nephrotoxic medications (Jorgensen, 2013).

Uncommon in patients with normal pre-existing kidney function, CIN is more likely in patients with pre-existing kidney disease and risk factors (Owen et al., 2014). The incidence of CIN varies from less than 1% to as high as 25% or higher in the diabetic population (Katzberg & Lamba, 2009; J. McDonald et al., 2013; R. McDonald et al., 2013; Moos et al., 2013; Pattharanitima & Tasanarong, 2014). Further, the incidence of CIN can be as high as 50% for patients with multiple risk factors (Goldfarb et al., 2009). Incidence reports of CIN vary widely (Pattharanitima & Tasanarong, 2014). This is attributed to factors including a lack of consensus in definitions, assessments based on sCr levels rather than more direct measures of kidney function or glomerular filtration rate (GFR), differing patient samples such as inpatients versus outpatients, variations in iodinated contrast medium doses and routes (e.g., intra-arterial vs. intravenous), variations in preventive strategies and completeness of patient follow-up such as obtaining kidney lab values 48 to 72 hours post contrast exposure (Carstensen, Keer, Rempel, Jeon, & Barrett, 2012; Katzberg & Lamba, 2009).

A confounding variable relates to the route of contrast medium injection. Over the past two decades, much of the CIN literature includes all procedures using iodinated contrast mediums in calculating the overall incidence of CIN (American College of
Radiology, 2013). Although trials comparing intra-arterial (IA) (e.g., angiography) and IV administration are not available, the risk of kidney complications including CIN after IA administration of contrast is higher than after IV administration (Stacul et al., 2011). A major factor has to do with dosage; IV contrast for enhanced computed tomography is given in much lower doses than for angiography or arteriography, resulting in lower concentrations of contrast medium to the kidneys (Stacul et al., 2011). In the U.S., 80% to 90% of iodinated contrast is used for IV-CECT and 10% to 20% for cardiac and non-cardiac angiography and interventional procedures (Katzberg & Newhouse, 2010).

Similarly, Ahmed and Newhouse (2013) state kidney function in hospitalized patients is much different than outpatients; serum creatinine in inpatients may be inaccurate due to the non-steady state as a result of illness severity, comorbidities, and medications. Elevations and fluctuations will occur regardless of contrast exposure. Therefore, data from methodologies and inaccuracies may likely overestimate the incidence and risk for CIN in outpatients undergoing IV-CECT studies (American College of Radiology, 2013).

**Pathophysiology**

The pathophysiology of CIN is complex and underlying mechanisms are not completely understood (Andreucci, Solomon, & Tasanarong, 2014). Multiple factors appear to play a role in the acute deterioration of kidney function. Studies in vitro and in animals suggest that CIN is due to a combination of direct tubular toxicity, ischemic injury to the renal tubular cells, and the aggregation of red blood cells in the medullary circulation (Jorgensen, 2013). Proximal and distal tubular injury occurs upon contact with contrast medium (Jorgensen, 2013). Contrast mediums are thought to produce prolonged vasoconstriction of the arterioles leading to stasis of the contrast material in the renal
vasculature; this results in medullary ischemic injury, tubular toxicity, and death of proximal and distal renal tubular cells (Jorgensen, 2013). In addition, contrast mediums have an osmolality greater than that of plasma and appear to augment fluid viscosity, thereby increasing resistance to flow in renal tubules. Lower osmolar agents have an osmolality two to three times greater than the osmolality of plasma, whereas high osmolar agents and their osmotic effects can deform erythrocytes, thereby increasing stiffness and making the flow of red blood cells through capillaries difficult (Gupta & Bang, 2010). Further, red blood cells can become densely packed in the renal capillaries and blood flow through these vessels may cease.

The length of exposure of contrast medium in the renal vasculature is thought to have a direct influence on CIN development (Jorgensen, 2013). Low blood flow in the medulla causes an acceleration of the renal vasoconstrictive response and the release of vasoactive substances such as endothelin, nitric oxide, and adenosine (Isaac, 2012). Contrast mediums may trigger the release of endothelin and adenosine from the endothelial cells, further increasing vasoconstriction, and decreasing oxygen in the outer medulla (Gupta & Bang, 2010). Moreover, impairment in flow leads to hypoxia which causes an increase in the reactive oxygen species (nitric oxide), cytostructure breakdown and eventually cellular death (Isaac, 2012).

In summary, the pathophysiology and risk of CIN is related to both patient and procedure factors. As depicted in Figure 3, CIN likelihood is thought to be directly proportional to the severity of preexisting renal insufficiency and kidney vulnerability, as well as procedure related. Contrast medium accelerates the renal vasoconstriction
response leading to ischemic injury, hypoxia to the renal medulla and direct tubular cell death (Gupta & Bang, 2010; Isaac, 2012; Jorgensen, 2013).

**Figure 3.** Diagram showing proposed relationships in the development of CIN. Adapted from *Contrast Induced Nephropathy* [Webinar], by W. J. Weise, 2014), retrieved from https://www.youtube.com/watch?v=k1youa1EL0s.
Peripheral Arterial Disease

The prevalence of CKD and peripheral arterial disease (PAD) has increased significantly during the last decades as explained by the increasing numbers of people suffering from diabetes. Most of those affected will die or be disabled from vascular complications (Andersen, 2012). The prevalence of PAD also significantly increases with advanced age, CKD, smoking, and hypertension (Andersen, 2012).

For those with PAD and CKD, the risks for CIN are heightened. The combination of these two disorders can lead to progressive morbidity after advanced endovascular procedures, and are independently associated with all-cause mortality (Kougias, et al., 2014). Furthermore, PAD was found to be an independent predictor for development of CIN; in fact, the combination doubles the risk of its occurrence (Luders et al., 2012).

CIN is mostly associated with acute kidney injury after contrast enhanced studies through acute oxidative stress and other effects that promote renal medullary hypoxia. However, there is potential for chronic oxidative stress from a single or cumulative intravascular contrast exposure (Kougias et al., 2014). Endovascular aortic aneurysm repair (EVAR) is a common minimally invasive surgical procedure for those with abdominal aortic aneurysm (AAA). The prevalence of AAA is cited at 1.7% to 7.2% for men above 65 years and is a significant health problem for those with vascular disease (Saratzis et al., 2013). EVAR has easily replaced the open repair as first line treatment for AAA. Outcomes for this procedure are similar or superior to the open repair; however, patients are at an increased risk for post-procedure acute kidney injury, notably those with complex or ruptured AAA (Saratzis et al., 2013). In fact, 32% to 52% of patients will progress to CKD at 18 months, with CIN as an important risk factor for worsening
kidneys (Kougias et al., 2014). Patients undergoing EVAR repairs are at added risk for micro-embolization, plaque disruption and tubular necrosis from the insertion and manipulation of wires. They are also at added risk for CIN as EVAR repairs necessitate the administration of a considerable amount of contrast, for which IV hydration remains the cornerstone in CIN prevention (Saratzis et al., 2013). In addition, this repair comes with the standard of care requiring repeat IV-CECT for post monitoring and surveillance purposes (Kougias et al., 2014).

**Burden of Kidney Disease**

Chronic kidney disease is one of the most common serious medical conditions affecting U.S. adults. It is also a major cause of morbidity, mortality, and high medical costs (Hoerger et al., 2015). The Centers for Disease Control and Prevention (CDC) estimates more than 10% of U.S. adults, over 20 million people, have CKD. Recent data suggest that the number of deaths from CKD has doubled in the past two decades (Hoerger et al.). In addition to its burden on health, CKD requires substantial health care resources. In 2010, end stage renal disease (ESRD), the most severe stage of CKD, cost Medicare $32.9 billion, and those in earlier stages of CKD cost Medicare an estimated $48 billion (Hoeger et al., 2015; Honeycutt et al., 2013).

Patients are considered as having CKD when they have an eGFR of ≤ 60 mL/min/1.73m², transplantation, or one of any other less common reasons (e.g., electrolytes and other abnormalities due to tubular disorders, histologic abnormalities, structural abnormalities) (Department of Veterans Affairs & Department of Defense, 2014). Patients with CKD may suffer from varying levels of disease: mild illness without symptoms to severe illness associated with increased risk of death or progression to end-
stage kidney disease. The risk of developing CKD increases among people over 50 years of age and peaks after 70. In many patients the disease is caused by, or associated with other conditions including diabetes, hypertension, cardiovascular disease, malnutrition, and anemia (Department of Veterans Affairs & Department of Defense, 2014).

The prevalence of CKD in the Veteran population is estimated to be a third higher than the general population, due to demographic factors and the higher rates of comorbidities associated with CKD, such as diabetes and hypertension (Department of Veterans Affairs & Department of Defense, 2014; Hoeger et al., 2015). The Veterans Health Administration (VHA) currently cares for over 200,000 Veterans with moderate to severe kidney disease across multiple medical treatment facilities and outreach clinics (Department of Veterans Affairs & Department of Defense, 2014). Further, CKD is both a consequence of and a risk factor for acute kidney injury. Veterans Health Administration identifies CIN as a potentially preventable form of acute kidney injury, and the most well-described risk factor is the parenteral administration of iodinated radiocontrast agents (Department of Veterans Affairs & Department of Defense, 2014).

**Patient and Procedure-Related Risk for CIN**

Not all patients have the same risk or vulnerability for developing CIN after intravascular iodinated contrast administration (Au, Bruckner, Mohiuddin, & Hilleman, 2014; Joongyub et al., 2014; Moos et al., 2013; Schilp, de Blok, Langelaan, Spreeuwenberg, & Wagner, 2014). However, the most important patient related risk factor is pre-existing kidney disease (Owen et al., 2014). Other frequently mentioned risk factors are diabetes, hypertension, advanced age, cardiovascular disease, use of nephrotoxic medications, anemia, dehydration, malignancy, and gout (Moos et al., 2014).
The risk of death for high risk patients who develop CIN is 34% compared to 7% in those of low risk (Deek, Newton, Sheerin, Noureddine, & Davidson, 2014). Equally important is if CIN occurs after IV contrast administration, whether inpatient or outpatient, it tends to be in people with risk factors and multiple risk factors increase the risk exponentially (Carstensen et al., 2012).

Procedure—related risk factors include the high osmolality contrast medium, higher amounts of contrast medium, and multiple doses of contrast given within a short period of time (Moos et al., 2014). Iodinated contrast mediums are either ionic or non-ionic. Ionic mediums are older agents, higher osmolar (5-8 x human plasma), and considered first generation (Agency for Healthcare Research and Quality (AHRQ), 2016; Wood, 2012). While these agents produce quality images, they are associated with greater shifts of both solute and water within the kidneys, leading to greater nephrotoxic reactions (Wood; Deek, Newton, Sheerin, Noureddine & Davidson, 2013). The second generation, non-ionic agents decrease this risk as they have lower osmolality (2-3 x human plasma) (AHRQ, 2016; Deek et al., 2013). The latest agents are non-ionic and iso-osmolar, offering even lower osmolality (equal to human plasma) and therefore less risks for CIN, however costs are higher and per meta-analysis the benefits over the lower osmolar agents in clinical practice are observed to be only slight (AHRQ, 2016; Deek et al., 2013; Owen et al., 2014). Several guidelines, specifically those of the American College of Radiology (2013, 2015), recommend using the low osmolar contrast mediums (LOCM) as they are less nephrotoxic than the high osmolar contrast mediums (HOCM) especially in patients with underlying kidney disease. Most institutions (including this project site) use the non-ionic LOCM and reserve the non-ionic, iso-osmolar agent
(iodixanol) for higher risk procedures and highest risk patients. Despite this, all iodinated contrast media have higher osmolality than plasma and therefore, pose risks of CIN upon administration (Isaac, 2012; Katzberg & Newhouse, 2010).

Furthermore, there is a correlation between the volume and frequency of contrast medium administered (KDIGO, 2012). The use of large doses of contrast medium and multiple injections, notably within a 72 hour timeframe has been recognized as increasing risk for CIN (KDIGO; Andreucci et al., 2014). CIN is dose dependent; its risk increases with increasing volume of contrast medium administered during procedures. Larger volumes of contrast medium such as those used in coronary angiography and percutaneous coronary interventions place patients at much higher risk for CIN than smaller amounts used for IV-CECT (Andreucci et al.). With this being said, controversy remains concerning the risk of CIN after IV-CECT as historically the IA route has been studied and analyzed more extensively (Carstensen et al., 2012). Few studies have assessed the risk of CIN after IV administration, and most studies have not included a control group of patients who were not exposed to the IV contrast material (Davenport et al., 2013).

**Risk Stratification**

Kidney impairment can be expressed using several indices of kidney function. Despite widespread use, the serum creatinine (sCr) level is an unreliable indicator of kidney function as it is not a real-time biomarker and is influenced by gender, muscle mass, nutritional status, and age (Owen et al., 2014). Serum levels of creatinine provide a measure of filtration within the renal tubules and glomerulus, rising only after significant loss of functioning nephrons. An increase in sCr is relative to the amount of filtration
function loss; thus, sCr is not sensitive or specific for small alterations and can delay CIN diagnosis by an average of 48-72 hours (Jorgensen, 2013). Glomerular filtration rate (GFR) provides a better assessment of nephron function as it provides a more accurate account of working nephrons, estimating how much blood is passing through the glomeruli each minute. In most healthy adults the normal GFR is 90 mL/min/1.73 m² or higher (National Kidney Foundation). Patients with a GFR < 60 mL/min/1.73 m² have considerable loss of nephron units and are vulnerable to declines with renal injuries, such as those caused by contrast agents (Jorgensen, 2013). Even in people without kidney disease, GFR declines gradually with age (National Kidney Foundation (NKF)).

The National Kidney Foundation Kidney Disease Outcome Quality Initiative (KDOQI, 2013) recommends use of the estimated GFR (eGFR) for kidney risk stratification. Common equations for calculating eGFR are those developed by the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI), the Modification of Diet in Renal Disease (MDRD), and the Cockcroft-Gault Formula. These equations take into account predictive factors or “non GFR determinants” which affect sCr concentration (Inker & Levey, 2014). Predictive factors include age, gender, ethnicity (African, Asian, or Hispanic), nutritional status, muscle mass, extrarenal elimination, and tubular secretion (Inker & Levey, 2014). All three equations are validated for adults, widely used, and readily calculated by laboratories (Owen et al., 2014). Both the CKD-EPI and the MDRD are reported as mL/min/1.73m² and considered to be generally more accurate in measuring CKD while the Cockcroft-Gault is most commonly used for drug dosage adjustments and reported as mL/min (NKF, 2014).
These calculations all use sCr however, a newer biomarker is cystatin C, a serum protein freely filtered by the glomerulus and is showing promise to be an accurate marker of GFR (Bansai et al., 2016). Compared with sCr, cystatin C changes are not subject to confounding factors such as age, sex, gender, and muscle mass; changes are detected much earlier especially after contrast administration (Bansai et al.; Inker & Levey, 2014). Currently, cystatin C is being used as a marker of renal function in cardiac surgical patients.

The National Kidney Foundation (2014) stratifications assessing for kidney risks are often used when evaluating risk of CIN. These include five stages of CKD:

1 eGFR = ≥ 90 mL/min/1.73 m²: minimal risk for CIN
2 eGFR = 60-89 mL/min/1.73 m²: very low risk for CIN
3a eGFR = 45-59 mL/min/1.73 m²: low risk of CIN in the absence of risk factors
3b eGFR = 30-44 mL/min/1.73 m²: moderate to potential high risk for CIN
4 eGFR = 15-29 mL/min/1.73 m²: high risk for CIN
5 eGFR = < 15 mL/min/1.73 m²: approaching or on dialysis

**Prevention Guidelines**

Policies, like guidelines are based on evidence and translated so that best practices can be applied. Guidelines are systematic statements to assist providers and patients in their decisions about appropriate healthcare. Prevention guidelines on CIN have been published both in the U.S. and internationally since 1999 (Hiremath et al., 2013). There are multiple organizational and collaborative consensus statements and updates addressing CIN prevention (American College of Radiology, 2013; KDIGO, 2012; Levine et al., 2011; McCullough et al., 2006; Owen et al., 2014; Stacul et al., 2011).
Several clinical practice guidelines were reviewed for this project including those of the following organizations: American College of Radiology, Canadian Association of Radiologist, European Society of Urogenital Radiology, European Renal Best Practice, Kidney Disease: Improving Global Outcomes (KDIGO) Organization, American College of Cardiology Foundation and the Department of Veterans Affairs/Department of Defense management of CKD (American College of Radiology, 2013; Department of Veterans Affairs & Department of Defense, 2014; Fliser et al., 2012; KDIGO, 2012; Levine et al., 2011; Owen et al., 2014; Stacul et al., 2011). Synthesis of all guidelines consisted of three recommendations.

1. Baseline screening using eGFR, sCr, or a scoring system such as the RIFLE criteria (Risk, Injury, Failure, Loss, End-stage) as established by the Acute Dialysis Quality Initiative Group (2004) and KDIGO (Fliser et al., 2012) in all patients receiving contrast medium. Timeframes differed as to when to screen (immediately before, one week, to 30 days prior to administered contrast medium). The timeframes also differed in when to obtain kidney labs after contrast exposure: either at 12 or between 48 to 72 hours. Two guidelines had no recommendation in terms of timeframes, leaving this decision up to the provider who ordered the IV contrast image study (American College of Radiology, 2013; Department of Veterans Affairs & Department of Defense, 2014).

2. Risk factor assessment based on the laboratory value(s). Each guideline cites different risk factors, but all agree that baseline kidney impairment, older age and diabetes are the most important ones. All reviewed guidelines recommend
balancing the risk for CIN against the benefit of administering contrast, and recommend considering alternative imaging (not requiring contrast exposure) in patients at high risk for CIN, so long as images yield same diagnostic accuracy (Fliser et al., 2012).

3. Preventive strategies to minimize risks. Most guidelines recommend standard IV therapy both before and after administration of contrast medium if the eGFR is \( \leq 60 \text{ mL/min/1.73 m}^2 \) and the patient is diabetic; hydration is with isotonic IV solution (normal saline or lactated ringers) or sodium bicarbonate. Adequate extracellular volume expansion improves kidney blood flow, induces diuresis with dilution of contrast material within the tubules, and reduces the activation of the vasoactive response properties (Stacul et al., 2011). Sodium bicarbonate has been cited as better for patients undergoing angiocardiography and IA (vs, normal saline) in reducing the risk of CIN, but this has been challenged by findings from other meta-analyses, and currently is not considered by all guidelines, particularly for patients receiving IV iodinated contrast material (American College of Radiology, 2013). In addition, the guidelines vary in recommended timing, rate, and duration of IV fluids (1 hour, 2 hours, 6 hours, up to 12 hours) and volume (100mL/hour, 3mL/kg/hr, or 1 to 1.5mL/kg/hour, no exact recommendation) both before and after administration of the contrast medium. Wong and Irwin (2007) proposed that the sodium load of normal saline is crucial for its protective effect as it enables more effective volume expansion and inhibition of the renin-angiotensin vasoactive responses. They also state that IV hydration has the most benefit if the fluid load is given before
the contrast procedure (Wong & Irwin, 2007). This has practical importance as some outpatient settings may lack the resources to support prolonged infusions, and outpatients may not be willing to stay up to 6 hours post image study despite recommended orders.

To summarize, prevention guidelines recommend screening, identifying risk factors and hydration; however, many lack firm statements or clear evidence to help guide fluid choice, timing, rate and duration for CIN prevention. Isotonic fluids appear to have a better ability to expand intravascular volume than do sodium bicarbonate and half isotonic saline (Gupta & Bang, 2010; Ranji, Rennke, Magan, Moseson, & Wachter, 2015). In several reviewed guidelines, IV fluids are recommended to be started at least one hour prior to contrast exposure and continue at least two, and up to 12 hours both before and after IV-CECT image study.

Further, all guidelines reviewed favor volume expansion with IV fluid over oral hydration (American College of Radiology, 2013; KDIGO, 2012; Stacul et al., 2011). However, two recent meta-analysis looking at oral hydration protocols and safe cutoff points for IV intervention, especially for outpatients, were found (Cheungpasitporn et al., 2014; Hiremath et al., 2013). In both meta-analyses, multiple databases were searched (1947 to July 4, 2014, and 1947 to 3rd quarter 2011, respectively) for random controlled trials comparing oral versus IV route of volume expansion. Both sets of authors concluded that oral hydration is a potential protocol for logistical ease and lowered healthcare resource utilization. Further, they found the oral route was not any more risky and may be as effective as IV in the outpatient setting for CIN prevention. However, the oral route can be unreliable in some patients and adequately powered trials with hard
endpoints still need to be conducted. Limitations to the included studies were small sample sizes (N = 513 over six trials, median sample size 85 subjects), both oral and IV volume expansion protocols varied, samples included both IA and IV populations, and in general studies were of lower quality mainly due to lack of blinding (Cheungpasitporn et al., 2014; Hiremath et al., 2013).

Interesting enough, the updated European and Canadian guidelines (Fliser et al., 2012; KDIGO, 2012; Owen et al., 2014; Stacul et al., 2011) recommend the threshold need for IV hydration regimens at eGFR ≤ 30mL/min/1.73 m² regardless of risk factors (Fliser et al., 2012; Owen et al., 2014; Stacul et al., 2011; Stevens et al., 2013). They further recommend that when the eGFR is between 45 and 59 and additional risk factors are absent, patients receiving IV contrast medium require no specific prophylaxis or follow up. However, in those with an eGFR ≤ 45mL/min/1.73 m², recommendations can include either IV or an oral pre-procedural hydration as patients are considered at lower risk for CIN (Owen et al., 2014). An oral pre-procedural hydration protocol is not specifically specified in the guidelines or pre-defined other than general advice to avoid fluid restriction and encourage patients to drink fluids and salt (i.e., salty soup) for volume expansion before contrast studies when practical (Hiremath et al., 2013; Owen et al., 2014). There were no changes for patients who receive IA contrast medium; the recommendation remains IV hydration at eGFR ≤ 60mL/min/1.73 m².

Guidelines changes such as these validate the ever changing arena concerning prevention protocols for CIN and eventually may lead to additional changes or updated guidelines in the U.S.
Clinical Practice Guidelines Adherence

Clinical practice guidelines play an important role in the practice of clinical care (Lepanto, Tang, Murphy-Lavallee, & Billiard, 2011; National Quality Measures, 2009, 2014). Systematically developed statements, guidelines are intended to elevate the quality of clinical care by identifying those practices and processes that are supported by best available evidence.

Successful implementation of clinical practice guidelines should improve the quality of care by decreasing inappropriate variation and expediting the application of effective advances to everyday practice (Cabana et al., 1999). Despite the many different clinical practice guidelines available on the topic of CIN, CIN prevention remains a problem for many institutions (Yellen & Buffum, 2014). The guidelines, as published, make it difficult for practitioners to make clear informed decisions. Specifically, Gupta and Bang (2010) state that current CIN prevention guidelines lack detail and do not cover all aspects of patient management, such as who is responsible for guideline adherence, screening, hydration, and patient follow up (i.e., radiologist, hospital or clinic specialist, nephrologist, referring provider such as primary care). Recommended preventive measures may not be followed due to the lack of feasibility in local settings and lack of necessary resources which may dictate management choices (Goldfarb, McCullough, McDermott, & Gay, 2009). Follow up management is an essential part of an effective protocol and systems are required for patients with evidence of CI-AKI (Goldfarb et al., 2009).

In addition, computerized tools and aids such as standardized order sets and triggered alerts identifying high risk patients need to be developed, automatized, and
used. In an evaluation of the implementation of a computerized alert program in hospitalized patients, Cho et al. (2012) found an increased use of standardized prophylaxis and decreased risk of CIN by more than 50%. Further, Schilp et al. (2014) investigated the final year of a Dutch hospital safety program initiative looking at guideline adherence for CIN prevention. The study was conducted between November 2011 and December 2012; patient records \( n = 4297 \) were reviewed across 38 representative sample hospitals (Schilp et al., 2014). The authors found that 96% of high risk patients were identified, but subsequent preventive steps were performed less often; as only 60% of the high risk patients were hydrated before contrast administration, despite all hospitals having the same CIN prevention guideline. Possible reasons for the lack of hydration included staff perception of lack of time, deliberate misinterpretations of the guidelines, and miscommunications across departments (admission, emergency room, radiology, clinic, etc.).

Lastly, in a systematic review looking at physician adherence to clinical practice guidelines, Cabana et al (1999) listed barriers to guideline adherence. These include lack of awareness, familiarity, agreement, self-efficacy, and outcome expectancy, along with inertia of previous practice and external barriers (e.g., available resources). Therefore, before a clinical practice guideline can affect patient outcomes, physician barriers, attitudes, and behaviors need to be assessed as these can potentially interfere with implementation effectiveness.

In summary, significant gaps in knowledge and practice continue to exist with regards to the pathophysiology, incidence, significance of complications and prevention regimens related to CIN (Davenport, Cohan, & Ellis, 2015). Despite this, experts agree
that CIN remains a clinically significant problem with a substantial impact on patient outcomes. Iodinated contrast can cause acute kidney injury and is preventable. Continuing efforts to find ways to prevent CIN and interventions that attempt to reduce this risk are main challenges for delivering safe, efficient, quality care
METHODS

Data monitoring for this quality improvement project consisted of 6 months of ongoing chart reviews to determine if adherence to the implemented IV hydration protocol aimed at CIN prevention reliably occurred. The three specific project aims correspond with the following questions:

- What are the characteristics of vascular outpatients who presented as high risk for developing CIN?
- Were the pre and post IV hydration protocol ordered and implemented to those high risk vascular outpatients per the policy?
- In those vascular outpatients who received the IV hydration protocol, were there any pre and post protocol complications?

Ethical Consideration

All study procedures were approved by the Institutional Review Boards (IRB) of both the project site and California State University, Fullerton (CSUF). Patient records were reviewed using the Computerized Electronic Patient Record System (CPRS). All protected patient data were accessed following all VHA institutional policies regarding access to patient health information (PHI), and supported by use of password and public key infrastructure (PKI) software. Only de-identified data on patients who met the six month criteria as being at high risk for CIN were used. All collected hard copy data were destroyed after analysis. It was anticipated that no harm to patients would occur as this was a retrospective chart review and no patients were recruited.
Design

A retrospective chart review was used to evaluate the results of this quality improvement project at six months post implementation. The evaluation was aimed at adherence to the VHA Imaging Services Contrast Media policy for the following recommended practices: Identifying and stratifying patients at high risk for CIN, implementing a kidney protective IV hydration protocol for those who met criteria, and establishing the incidence of any complications resulting from the pre and post IV hydration protocols were determined.

Setting

This quality improvement project was conducted from the Surgical Healthcare Group Department of Vascular Surgery, in a 350 bed large, national teaching healthcare system serving both male and female Veterans in Southern California. The vascular clinics serve approximately 3,000 outpatients annually.

Sample

Male and female patients seen in any one of four outpatient vascular clinics (new, follow-up, post-op and vascular wounds) between January 1, to June 30, 2015 were included in the analysis. Patients were identified using sorted data from the Computerized Patient Record System (CPRS). The sample selection criteria were as follows:

- Outpatients seen in one of the four vascular clinics,
- IV-CECT image study ordered by a current vascular provider,
- eGFR ≤ 60mL/min and Diabetes,
- eGFR ≥ 30mL/min and ≤ 45mL/min and no other risks,
• eGFR between 45-60 mL/min with additional risk factors that include a cardiac history (cardiovascular disease), prior contrast within 72 hours, or dehydration (elevated BUN).

Records were excluded for the following criteria:

• eGFR > 60mL/min,

• Current hospitalized patients seen in the outpatient vascular clinics,

• Patients on or planning for dialysis, and

• Any patient presenting to clinic with obvious signs of CHF.

**Data Collection**

A data collection tool (Appendix F) developed by the Vascular Nurse Practitioner in collaboration with the interdisciplinary team was used. All patients were assigned an identification number for added patient identity protection and all rosters adhered to the institution’s Health Insurance Portability and Accountability Act (HIPAA) regulations.

The following variables were collected on all patients:

1. Demographics: Age, gender, ethnicity, primary reason for vascular consult, diagnostic study ordered, patient location, risk factors for CIN, pre and post IV-CECT image labs, use of concomitant nephrotoxic drugs (yes/no);

2. Policy adherence: Location of IV-CECT initiated, IV hydration protocol required (yes/no), use of electronic order set (yes/no), pre and post IV-CECT image labs ordered and obtained (yes/no), IV hydration protocol given (yes/no), location where IV hydration given, solution used for IV hydration, time delivery of pre-image, post image hydration;
3. Complications, unintended symptoms or events as a result of receiving the IV hydration protocol: Hospital admission at time or within one week after IV-CECT, any symptom or event complication particularly neurological (dizziness), cardiovascular (elevated or drop in blood pressure, heart rate changes), respiratory (changes in lung sounds or breathing pattern), skin (diaphoresis), and mental alterations (restlessness, anxiety), any fall or IV catheter malfunctions.

**Operational Definitions**

The operational definitions of the key variables for patient characteristics were as follows:

*Baseline kidney status* defined as having a sCr (normal range 0.7 to 1.3 mg/dL) and eGFR (≤ 60 mL/min) laboratory value within 30 days in the medical record prior to IV-CECT.

*CIN Criteria* defined as a transient rise in the sCr concentration of more than 25% or an absolute increase above baseline of 0.5 mg/dl within 48-72 hours after IV administration of contrast medium, and without any alternative etiology.

*Complications from the IV hydration protocol* defined as documentation at the time of or within 48 hours of the administration which includes any of the following:

- Dizziness
- Shortness of breath, tachypnea (observed or stated; > 20 breaths/min)
- Tachycardia (heart rate > 100 beats per min)
- Abnormal lung sounds (crackles, rales, wheezes, etc)
- Diaphoresis
• Anxiety
• Systolic change in blood pressure (> 10% higher or lower than baseline)
• Jugular venous distension
• IV malfunction
• Fall

Congestive heart failure (CHF) defined as resulting from the IV hydration protocol with patient symptoms of peri-procedural shortness of breath, abnormal lung sounds (crackles or rales), change in respiratory pattern, 3rd heart sound, restlessness and/or anxiety, hypotension, tachycardia, diaphoresis.

IV hydration defined as adhering to the modified vascular outpatient protocol (both pre and post IV-CECT procedure). The protocol is one liter of normal saline adjusted over 2-3 hours (converted to minutes) prior to and 250 mL normal saline over 30 minutes post contrast exposure.

Pre Image Labs defined as sCr (mg/dL), eGFR (institutionally calculated using Cockcroft-Gault formula and expressed in mL/min), and BUN (mg/dL) obtained immediately prior or within 30 days prior to IV-CECT image.

Post Image Labs defined as sCr and eGFR obtained within 14 days post IV-CECT image.

Risk factors defined as any captured documentation identified on the medical record problem list or by the ordering vascular provider verifying added patient risks for vulnerable kidneys and included:

• Baseline kidney disease defined as an eGFR ≤ 60mL/min
• Diabetes
- Advanced age (65 years and older)
- Cardiac history
- Nephrotoxic drugs: (> 5 year history nonsteroidal anti-inflammatory (NSAID) or COX 2 inhibitors, current use at time of IV-CECT: Chemistry agents, Lasix, or ACE inhibitor)
- Anemia
- Hypertension
- Dehydration (evaluated as elevated BUN)
- Prior contrast exposure within 72 hours of index procedure
- Gout
- Malignancy (concomitant active diagnosis at time of IV-CECT)

*Cardiac history* defined as prior myocardial infarction, congestive heart failure, valvular heart disease, coronary artery bypass surgery, percutaneous coronary interventions/stent placement, or cardiac pacemaker/automatic defibrillators.

*Vascular diagnosis* defined as:
- Peripheral arterial disease (carotid disease, intermittent claudication, any occlusions or narrowing of the peripheral arteries)
- Aneurysms of abdominal aorta or any lower extremity artery
- Vascular access construction and repair
- Vascular wound (arterial, venous ulcers, or diabetic foot)
- Vein disorders (varicose veins, thrombosis, malformations)
Measures

Demographic data (ethnicity, gender, diagnosis, diagnostic study, and patient location) were measured categorically. Age was measured in years. Biological markers sCr (mg/dL), eGFR (calculated per Cockcroft-Gault formula (mL/min), and the BUN (mg/dL), were measured using continuous data. The Vascular providers’ use of the electronic order set, whether or not the IV hydration pre and post protocol were given, solution given, and any resulting complications, were measured categorically. Lastly, the IV hydration pre and post protocol delivery times were measured in minutes.

Statistical Analysis

All data were entered and analyzed using the IBM Statistical Software Package for the Social Science (SPSS) version 23. Prior to analysis, data were examined for accuracy of data entry, missing values, frequencies and distributions. Descriptive statistics were used to analyze data in order to answer the three questions posed during the project.
RESULTS

The results of this project were aimed at assessing initial protocol adherence at six months post implementation. Initial data were collected January 1, to June 30, 2015 after implementation of the protocol in December 2014 (e.g., VHA Imaging Services Contrast Media policy was modified and adopted into local practice). Prior to implementation, all vascular providers were educated on the protocol and instructed on the use of an electronic order set. A data collection process was put in place. Baseline scorecard data indicated that approximately 19% of the patients seen in one of the four outpatient vascular clinics met the stratified high risk protocol criteria. Prior to implementation of this policy, patients at high risk for CIN were treated inconsistently, if at all; and did not receive standardized prevention. For this project, three questions were answered:

- What are the characteristics of the vascular outpatient population who are at high risk for developing CIN?
- What were the percentages of adherence to both the pre and post IV hydration protocol?
- In those vascular outpatients who received the IV hydration protocol, were there any pre and post-protocol complications?

Question 1: Patient Characteristics

A total of 1289 outpatient vascular clinic visits were reviewed from the following vascular clinics: new, follow up, post op and wounds. Patients were seen between January 1, to June 30, 2015. The 62 patients deemed high risk for CIN based upon the above criteria (4.8% of the total) are described in Table 4. The median age of the population was 73 years old, 93.5% were male and 98.4% were age 65 or older. Patient
ethnicities were 35.5% White, 25.8% Black, 19.4% Hispanic, 6.5% Asian, 1.6% American Indian or Alaskan, and 11.3% were other or declined to answer. All patients had vascular disease, 62.9% had PAD, 22.6% had aneurysmal disease and 14.5% had vascular wounds. Among this sample, 61.3% had diabetes mellitus, 71.0% had a cardiac history, 46.8% had prior cardiac surgery or a percutaneous coronary intervention, and 85.5% had hypertension.

Pre procedural IV-CECT imaging labs indicated a median pre sCr of 1.48, median pre eGFR of 47.2mL/min, and median pre BUN of 23. In 74.2% of patients who had post-procedural imaging IV-CECT labs, the median sCr was 1.46 and post eGFR was 47.0mL/min. Other characteristics include 35.5% had an elevated BUN prior to IV-CECT image, 29.0% had a concomitant malignancy, and 21.0% had anemia. Not quite one-third of patients (29.8%) presented with 2 or more risk factors for CIN, 39.7% had 3 or more risk factors, and 33.35% had 4 or more. Many patients were on nephrotoxic drugs at the time of the IV-CECT imaging: 25.8% on furosemide, 41.9% on an ace-inhibitors, and 16.1%, 2 or more concomitant nephrotoxic drugs.
Table 4

Characteristics of Patients at Risk for CIN (N = 62)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>73</td>
<td>63-98 years old</td>
</tr>
<tr>
<td>Pre sCr</td>
<td>1.48 mg/dL</td>
<td>1.2 to 2.20 mg/dL</td>
</tr>
<tr>
<td>Pre eGFR</td>
<td>47.2 mL/min</td>
<td>32.3 to 57.5 mL/min</td>
</tr>
<tr>
<td>Pre BUN</td>
<td>23 mg/dL</td>
<td>12 to 53 mg/dL</td>
</tr>
<tr>
<td>Post sCr</td>
<td>1.46 mg/dL</td>
<td>1.0 to 2.3 mg/dL</td>
</tr>
<tr>
<td>Post eGFR</td>
<td>47.0 mL/min</td>
<td>27.2 to 64.2 mL/min</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>58</td>
<td>93.5%</td>
</tr>
<tr>
<td>Female</td>
<td>4</td>
<td>6.5%</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>22</td>
<td>35.5%</td>
</tr>
<tr>
<td>Black</td>
<td>16</td>
<td>25.8%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>12</td>
<td>19.4%</td>
</tr>
<tr>
<td>Asian</td>
<td>4</td>
<td>6.5%</td>
</tr>
<tr>
<td>American Indian/Alaskan</td>
<td>1</td>
<td>1.6%</td>
</tr>
<tr>
<td>Other/Declined to answer</td>
<td>7</td>
<td>11.3%</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral Disease (PAD)</td>
<td>39</td>
<td>62.9%</td>
</tr>
<tr>
<td>Aneurysmal Disease</td>
<td>14</td>
<td>22.6%</td>
</tr>
<tr>
<td>Vascular Wound</td>
<td>9</td>
<td>14.5%</td>
</tr>
<tr>
<td>Risk Factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>38</td>
<td>61.3%</td>
</tr>
<tr>
<td>Cardiac History</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction, CHF</td>
<td>44</td>
<td>71.0%</td>
</tr>
<tr>
<td>Valvular Heart Disease</td>
<td>8</td>
<td>12.9%</td>
</tr>
<tr>
<td>CABG or PCI/cardiac stent</td>
<td>29</td>
<td>46.8%</td>
</tr>
<tr>
<td>Pacemaker or automatic defibrillator</td>
<td>6</td>
<td>9.7%</td>
</tr>
<tr>
<td>Dehydration (elevated BUN)</td>
<td>22</td>
<td>35.5%</td>
</tr>
<tr>
<td>Age &gt; 64 years old</td>
<td>61</td>
<td>98.4%</td>
</tr>
<tr>
<td>Anemia</td>
<td>13</td>
<td>21.0%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>53</td>
<td>85.5%</td>
</tr>
<tr>
<td>Gout</td>
<td>6</td>
<td>9.7%</td>
</tr>
<tr>
<td>Active Malignancy</td>
<td>18</td>
<td>29.0%</td>
</tr>
<tr>
<td>Chronic NSAID (&gt; 5 year history)</td>
<td>5</td>
<td>8.1%</td>
</tr>
<tr>
<td>Presented with 2 or more risk factors</td>
<td>18</td>
<td>29.8%</td>
</tr>
<tr>
<td>Presented with 3 or more risk factors</td>
<td>23</td>
<td>37.1%</td>
</tr>
<tr>
<td>Presented with 4 or more risk factors</td>
<td>19</td>
<td>30.6%</td>
</tr>
<tr>
<td>Nephrotoxic Drugs time of IV CECT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current use NSAIDS</td>
<td>6</td>
<td>9.7%</td>
</tr>
</tbody>
</table>
Current use chemotherapy agents 1 1.6%
Current use furosemide 16 25.8%
Current use ACE-I/ARB or both 36 58.0%
Current use of 2 nephrotoxic drugs 10 16.1%
Current use > 2 nephrotoxic drugs 3 4.8%

Note. ACE-I = angiotensin converting enzyme inhibitor, ARB = angiotensin II receptor blocker, NSAID = non-steroidal anti-inflammatory drug, sCr = serum creatinine, eGFR = estimated glomerular filtration rate, BUN = blood urea nitrogen, CABG = coronary artery bypass graft, PCI = percutaneous coronary intervention, CHF = congestive heart failure, IV-CECT = intravenous contrast enhanced computed tomography.

**Question 2: Adherence to the IV Hydration Protocol**

Of central interest, was whether or not the pre and post-procedural IV hydration protocols were received by those vascular outpatients identified as being high risk for CIN. In the 62 patients at high risk, 93.5% of IV-CECT imaging procedures were initiated by outpatient vascular providers who had received education on CIN, and instructed on the use of the electronic order set. However, only 64.5% of the patients received the IV hydration per the protocol as seen in Table 5. While all patients received pre-imaging labs (sCr, eGFR, and BUN), only 74.2% received post imaging labs (sCr and eGFR) within 14 days after the IV-CECT. Furthermore, because follow up is essential for ensuring post-procedural labs are complete and patients are without symptoms of CIN, post IV-CECT data were collected. In fact, 72.2% of post IV-CECT patients had appropriate post-procedural laboratories, and all were seen in the outpatient vascular clinics for follow up care. An additional finding was that 62.9% of providers used the electronic order set quick link to guide the correct ordering of the IV hydration protocol.

In the 40 patients who received the pre-procedure IV hydration as seen in Table 6, 62.5% received it at 120 minutes, 2.5% received at 150 minutes, 32.5% received at 180 minutes and 2.5% received at ≥ 240 minutes. For the post-procedure 82.5% received the
IV hydration at 30 minutes, 5.0% at 60 minutes, 2.5% at 180 minutes, and 10% received at ≥ 240 minutes.

There were a few patients admitted to the hospital for short stays or less than 24 hour admissions specifically for the IV hydration protocol. For three patients, this was planned, for one it was unplanned. The unplanned patient was admitted from the emergency room. Institutional practice permits patients who have significant comorbidities (e.g., fragility, older age, elevated sCr, lower eGFR) to be admitted for procedures such as those using contrast media. Patients may also be admitted if there are concerns for allergic reactions to the iodinated contrast media. All admitted patients received 5% dextrose with one half isotonic saline (D5 ½ NS) as the IV hydration solution at the rate of 125mL/hour (given upon admission and delivered continuously throughout their stay). The four admitted patients had pre-procedural delivery times of 180, 180, 240, and 180 minutes and post-procedural delivery times were greater than 240 minutes, therefore all hydration was considered adherent to policy.

One patient met criteria for the IV hydration protocol but orders were not written by the vascular provider. Therefore, the IV-CECT imaging study was done without CIN preventive measures. This patient required an emergent visit to his primary care provider the following day as the family reported confusion, disorientation, and low blood pressure. Laboratory values indicated that the patient had a significant rise in sCr. The patient was emergently admitted into the hospital for fluid resuscitation and was diagnosed as CI-AKI post endovascular aortic aneurysm repair (EVAR). Patient eventually recovered and was discharged home on day 22.
Table 5

*Protocol Adherence (N = 62)*

<table>
<thead>
<tr>
<th>Patients Screened and Hydrated</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location of IV-CECT initiated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular outpatient</td>
<td>60</td>
<td>96.8%</td>
</tr>
<tr>
<td>Emergency room</td>
<td>1</td>
<td>1.6%</td>
</tr>
<tr>
<td>Other (neurology outpatient clinic)</td>
<td>1</td>
<td>1.6%</td>
</tr>
<tr>
<td>IV hydration required</td>
<td>62</td>
<td>100%</td>
</tr>
<tr>
<td>IV hydration given</td>
<td>40</td>
<td>64.5%</td>
</tr>
<tr>
<td>Pre-image labs obtained per protocol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>sCr</td>
<td>62</td>
<td>100%</td>
</tr>
<tr>
<td>eGFR</td>
<td>62</td>
<td>100%</td>
</tr>
<tr>
<td>BUN</td>
<td>62</td>
<td>100%</td>
</tr>
<tr>
<td>Post-image labs obtained per protocol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>sCr</td>
<td>46</td>
<td>74.2%</td>
</tr>
<tr>
<td>eGFR</td>
<td>46</td>
<td>74.2%</td>
</tr>
<tr>
<td>Used electronic order set to order IV hydration</td>
<td>39</td>
<td>62.9%</td>
</tr>
<tr>
<td>Follow up visit with vascular clinic</td>
<td>62</td>
<td>100%</td>
</tr>
</tbody>
</table>

*Notes. sCr = serum creatinine, eGFR = estimated glomerular filtration rate, BUN = blood urea nitrogen.*
Table 6

*Protocol Adherence (N = 40) in those receiving the IV Hydration*

<table>
<thead>
<tr>
<th>Patients Who Received Hydration</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location where IV hydration given</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infusion Center</td>
<td>35</td>
<td>87.5%</td>
</tr>
<tr>
<td>ER</td>
<td>1</td>
<td>2.5%</td>
</tr>
<tr>
<td>Admitted to the hospital (planned)</td>
<td>3</td>
<td>7.5%</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>2.5%</td>
</tr>
<tr>
<td>Solution used for hydration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal saline</td>
<td>36</td>
<td>90%</td>
</tr>
<tr>
<td>D5 1/2NS</td>
<td>4</td>
<td>10%</td>
</tr>
<tr>
<td>Time delivery hydration pre-procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>120 minutes</td>
<td>25</td>
<td>62.5%</td>
</tr>
<tr>
<td>150 minutes</td>
<td>1</td>
<td>2.5%</td>
</tr>
<tr>
<td>180 minutes</td>
<td>13</td>
<td>32.5</td>
</tr>
<tr>
<td>240 minutes or longer</td>
<td>1</td>
<td>2.5%</td>
</tr>
<tr>
<td>Time delivery hydration post-procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 minutes</td>
<td>33</td>
<td>82.5%</td>
</tr>
<tr>
<td>60 minutes</td>
<td>2</td>
<td>5.0%</td>
</tr>
<tr>
<td>180 minutes</td>
<td>1</td>
<td>2.5%</td>
</tr>
<tr>
<td>240 minutes or longer (admitted)</td>
<td>4</td>
<td>10%</td>
</tr>
</tbody>
</table>

**Question 3: Protocol Complications**

Data for both pre and post protocol complications were collected to determine if patients safely received the IV hydration. As seen in Table 7, of the 40 patients who received the IV hydration protocol, 27.5% had a complication: increase in blood pressure, 7.5%: shortness of breath with an increase in respiratory rate, 7.5%: diaphoresis, 15%: anxiety and restlessness, 2.5%: dizziness, and 2.5% complained of hunger. One patient, had both shortness of breath and an increase in blood pressure. No patient had abnormal lung sounds (crackles/rales), jugular venous distention, IV malfunction, or an inadvertent fall. There were no sentinel events. None of the patients required termination of the IV hydration protocol. Further, no patient suffered a complication requiring an unplanned hospital admission or emergency room visit. None of the patients who received the IV
hydration protocol were subsequently determined on follow up to have signs or symptoms of CIN. All patients received the required IV-CECT without incidence and were discharged as planned.

Table 7

*Patient Complications (N = 40) from the IV Hydration Protocol*

<table>
<thead>
<tr>
<th>Complication</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications blood pressure, increase</td>
<td>11</td>
<td>27.5%</td>
</tr>
<tr>
<td>Anxiety/restless</td>
<td>6</td>
<td>15%</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>3</td>
<td>7.5%</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>3</td>
<td>7.5%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1</td>
<td>2.5%</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>1</td>
<td>2.5%</td>
</tr>
<tr>
<td>Other (hunger)</td>
<td>1</td>
<td>2.5%</td>
</tr>
<tr>
<td>Abnormal lung sounds (crackles/rales)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Jugular venous distension</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Intravenous complication</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fall</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CIN</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Note. CHF = congestive heart failure.*
DISCUSSION

This is the first known description of the implementation of a modified VHA Imaging Services policy for iodinated contrast media within a Veteran’s Affairs Healthcare System. Findings of this initial six-month evaluation conducted in a single outpatient vascular clinic, revealed that the modified policy was appropriately implemented for most outpatients screened to be at high risk of developing CIN. Policy implementation led to no unexpected or severe complications beyond those that accompany procedures using iodinated contrast media. None of the 62 patients who received the recommended screening and follow up care were found to have CIN. Of the 1,289 charts reviewed, 62 charts met the inclusion criteria which focused on screening and stratifying patients at risk for developing CIN.

Patient Characteristics

The number of patients in the 6 month initial evaluation was over 1,000 but only 62 met the inclusion criteria of high risk for developing CIN. Among the 62 patients, aside from an eGFR ≤ 60 mL/min, all had independent risk factors over and above those characteristics that made them eligible for the protocol. For example 98.4% were 65 years or older. Several sources cite advanced age as being 65 years and older (Bansai et al., 2014; KGIGO, 2012; Moos et al., 2013). Advanced age is associated with age-related changes such as a reduction in renal mass, function, and perfusion. Other age changes include renovascular disease, a defective prostaglandin synthesis, and hypovolemia especially when undergoing diagnostic procedures (Toprak & Cirit, 2007). The majority of the sample (93.5%) were male. The National Kidney Foundation reports being female as an independent risk factor for CIN, given that hormones affect the renin-angiotensin-
aldosterone system (RAAS) and renal blood flow (Johnson, 2011); however, it is unclear the magnitude of risk attributed to gender due to confounding variables (older, postmenopausal, comorbidities, contrast medium dosages, etc). Ethnicity has not been found to be a risk factor for CIN, although blacks with diabetic neuropathy have a faster acceleration of ESRD (Bansai, et al., 2014). Owen et al. (2014) also found that First Nation people had a higher prevalence for CIN versus other ethnicities.

Other significant independent risk factors for many patients in the sample, include pre-existing kidney disease, diabetes, and cardiovascular disease. The patient sample was drawn from among those with an eGFR at less than 60 mL/min. Patients with such a low eGFR have a reduced number of nephrons, decreased glomerular filtration, vulnerable kidneys and associated vasodilatory responses. This results in a slower clearance of contrast media and therefore, an added risk for CIN. When seen in patients with CKD, diabetes is associated with a dramatic increased (as high as 50%) risk of developing CIN compared to those observed with CKD alone, as diabetes alters the nitric-oxide dependent kidney vasodilatory responses (Andreucci et al., 2014). Patients with diabetes and CKD suffer endothelial dysfunction and are more likely to experience oliguria, kidney failure, and require dialysis compared with nondiabetics especially among those with azotemia (Gupta & Bang, 2010; Toprak & Cirit, 2007).

Further, this patient sample had a high prevalence of cardiovascular (at least 71%) and peripheral vascular disease (63%), as well as hypertension (86%); all associated with accelerated or diffuse renal artery atherosclerosis and linked to the development of CIN (Au, et al., 2014). Hypertension is an independent risk factor for CIN as it alters the intrarenal expression of vasoactive mediators, notably the RAAS (Toprak & Cirit, 2007).
The protocol identifies patients with a cardiac history and an eGFR between 45 and 60 as having potential high risk for CIN, and IV hydration should be considered. The literature is inconsistent in that guidelines do not always identify cardiovascular disease as an added risk factor (KDIGO, 2012). Others cite advanced congestive heart failure (New York Heart Association Class III or IV), compromised left ventricular systolic performance, and post intra-arterial cardiovascular imaging procedures as additional cardiovascular risk factors (Andreucci et al., 2014; Goldfarb, et al., 2009; Laville & Julliard, 2010). The American College of Radiology (2015) cites cardiovascular disease as being only a proposed CIN risk factor for IV-CECT, as it has not been rigorously confirmed nor with consensus agreement. It seems as those with a lowered ejection fraction, intravascular cardiac volume depletion, and hypovolemia would be at a much higher risk for CIN than what the protocol criteria identified as “cardiac history.” In this sample, of the 40 patients who received the IV hydration protocol, 38 had the diagnosis of diabetes and all 38 received the protocol. Since the literature is not consistent, it is conceivable that providers and radiologists may have decided against the IV hydration protocol in these healthier outpatients with cardiac histories, as most likely they did not present with the severity of volume depletion seen in advanced heart failure. It is also conceivable that providers may have chosen an alternative prophylaxis such as oral hydration and this was not captured. Still, it remains that CIN is an independent risk factor for increased morbidity and mortality in the cardiac patient, and all efforts to decrease its incidence should be pursued (Patel, King, & Jovin, 2011).

Other characteristics of the sample include the concomitant usage of nephrotoxic drugs such as the non-steroidal anti-inflammatories (NSAIDs) and the loop diuretic
furosemide. NSAID drugs are important risk factors for CIN because they inhibit the vasodilatory effects of prostaglandins rendering the kidney vulnerable to contrast media (Toprak & Cirit, 2007). Loop diuretics are risk factors for CIN because they cause further volume depletion in an already volume depleted kidney. Overall, the independent usage of chronic NSAID drugs in this sample were low (8%). However, the concomitant use of angiotensin-converting enzyme inhibitors (ACE-I) and or angiotensin receptor blockers (ARBs) were high. In CIN, the RAAS controls renal homeostasis and plays an important role as renal vasoconstriction occurs after the administration of contrast media (Patel, King, & Jovin, 2011). Although controversial, it remains unclear the effect ACE-I and/or ARBs have on the RAAS, especially among the elderly, because these drugs have the potential to reduce renal function and vasoconstriction by inhibiting angiotensin II (Andreucci et al., 2014; Patel, King, & Jovin, 2011).

Finally, more than 70% of the high risk sample had three or more additional risk factors for CIN. This is critical because it is believed that multiple risk factors contribute to the development of CIN (Mohammed, et al., 2013; Owen et al., 2014).

In summary, both the level of kidney function at the time of contrast media exposure and the independent patient specific risk factors, impact the level of kidney vulnerability for CIN. The characteristics for CIN risks in this patient sample are consistent with those documented in the literature; therefore a CIN prevention policy with an IV hydration protocol to reduce kidney injury seems warranted.

**Adherence to the IV Hydration Protocol**

In this sample, all 62 outpatients met the stratified criteria of being at high risk for developing CIN and thus, met the criteria for the IV hydration protocol. Of these
outpatients, only 64.5% received the protocol. While use of IV hydration is a positive change, there is still room for improvement. Prior to implementation of this policy, high risk outpatients did not receive standardized care; preventive treatments were inconsistent. The initial goal for this project was aimed at a 20% IV hydration protocol adherence rate and from this initial data, this goal was exceeded.

One possible reason for the IV hydration protocol adherence rate includes the resident provider staff who attended to this patient sample. The vascular clinics serve a large population of patients within a large teaching institution and resident staff rotates into outpatient clinics every four weeks. It is challenging to ensure that all providers have the knowledge on protocols and processes. According to Cabana et al. (1999), barriers to protocol adherence include lack of awareness and familiarity. This initial adherence rate could be a reflection of the time lag before all providers were on board with this practice change.

Another possible reason for the IV hydration adherence rate were the challenges required to schedule patients and to coordinate with all involved (vascular, radiology, infusion center, and patient). Change theory stresses the importance of adequate communication and peer networking within the adoption process; therefore, change agents were needed in each of the departments (Rogers, 2003). For all three departments, the most effective change agents turned out to be members of the clerical staff as they were best able to network with one another and worked out a complex coordinated patient scheduling system. Specific time slots needed to be identified and agreed to between the radiology department and the infusion center. When patients required the IV hydration protocol, they were offered an available appointment slot in the infusion center.
This coordination required new work processes, took time, and may have led to initial miscommunications. Miscommunications across and within departments have been cited as possible reasons for patients not receiving preventive IV hydration (Schilp et al., 2014).

In considering the 65% adherence rate, it is plausible that providers or radiologists may have considered ordering the IV hydration but decided against it as 34% did not place orders. The project team radiologist reported that many factors go into a radiologist decision-making and as final decision makers, they may have consciously ordered no contrast or an iso-osmolar contrast and no peri-procedure IV hydration. Also, providers may have chosen different individualized treatment plans since all patients did receive the pre-imaging laboratories. Policies are based on evidence, and guidelines are starting points which have to be adapted to individual patients. Critical is knowing the risk factors and available evidence-based preventive interventions in order to prevent scenarios such as the one in this project where a patient was given an IV-CECT image, no preventive treatment and suffered a possible iatrogenic event requiring a 22 day hospital stay.

Lastly, of the 62.9% providers who did use the electronic order sets for ordering the IV hydration protocol, 87.5% correctly ordered the procedure to be done in the infusion center, 90% ordered the correct solution, 97.5% ordered and their patients received the correct rate of the pre-procedure solution, and over 82% ordered and their patients received the correct post procedure solution. These outcomes were most likely due to the computerized tools which helped to standardize the correct care process.
Pre and Post Protocol Complications

In this sample of 40 patients, 73% who received the IV hydration protocol did not develop any significant adverse effects. Twenty-seven percent had an isolated complication of increased blood pressure (BP). One patient had both increased BP and shortness of breath (SOB), and 15% of the sample had anxiety and restlessness. For this protocol, the most potentially dangerous complication is the risk of volume overload with the concern for congestive heart failure. Patients requiring hydration are compromised and at risk for over-hydration because of their advanced age and multiple comorbidities. Symptoms of volume overload include SOB, anxiety, restlessness, and elevated blood pressure. There is the possibility that these outpatients may have been experiencing early signs of volume overload, but still, no patient required additional interventions for SOB or diuresis (e.g., supplemental oxygen or diuretic).

This modified protocol calls for a rapid amount of volume load (1000 mL over 2 to 3 hours). The protocol permits nurses to adjust the rate and prolong the time delivery per clinical judgement. The nursing staff in the infusion center all received specialty training by the Vascular Nurse Practitioner on monitoring patients for volume overload. Further, the Vascular Nurse Practitioner was accessible for questions or any nursing concerns. It appears that the nursing staff may have slowed the pre-procedural IV hydration rate to favor the 3 hour versus the 2 hour, which accounts for the longer pre-procedure hydration time deliveries seen in 34.5% of patients.

There is general acceptance that fluid-loading is the single most important intervention that can prevent CIN, as this approach is advocated in all guidelines (American College of Radiology, 2015; Gupta & Bang, 2010; KDIGO, 2013; Owen et
Further, guidelines agree that the use of normal saline is superior over one half isotonic saline, sodium bicarbonate, mannitol and oral fluids (Owen et al.; Rudnick, 2016). Normal saline is safe, carries few side effects, and is cost-effective as IV fluids increase urine flow rates, reduces the concentration of contrast medium in the tubule, and expedites the excretion of contrast medium; this hydration reduces the length of time that tubular cells are exposed to the toxic effect of contrast medium (Gupta & Bang, 2010).

Despite agreement across guidelines about pre-procedural hydration, lacking are data that point to the optimal fluid regimen for both pre and post-procedure hydration. According to the adopted contrast media policy, the minimal recommendation for a pre-infusion delivery time is 3 hours since “fewer than 3 hours may not be effective.” Traub, et al. (2013) found a significant association between receipt of at least one liter of intravenous fluids and a marked decrease in the rate of CIN. Even further, in the VA/DoD 2014 clinical practice guidelines for the management of patients with CKD, recommends offering oral hydration for CIN prophylaxis to patients in which IV hydration is not feasible.

For this specific IV hydration protocol regimen, there were few adverse events, all of which were self-limited. None of the 40 patients who received the IV hydration protocol required termination.

Although only 64.5% of the high risk patients appropriately received the pre and post-procedural IV hydration protocol, clinical outcomes were improved. Aside from the self-limited complications, none of the patients developed an unintended consequence or suffered any known new harm from the IV hydration protocol or a sentinel event.
Further, all patients were screened appropriately for CIN risks as all patients received the appropriate laboratories prior to the IV-CECT image study. The majority of the patients 74.2% completed post kidney labs and all received follow up care. Based on the literature and the findings of this project, the use of an IV hydration protocol to protect patients at risk for CIN seems to be safe and can lead to better patient outcomes (ACR, 2015; Mohammed, et al., 2013; Owen, et al., 2014).

**Strengths of the Project**

The strength of this project was the use of an integrative framework to adopt an innovation aimed at preventing kidney harm in ambulatory patients. The Johns Hopkins Quality and Safety Framework, a collaborative implementation model for knowledge translation, was well suited for this project. The model encouraged engagement of stakeholders, involvement of an interdisciplinary work team, and local collaboration. Translating evidence into healthcare organizations is complex and can be challenging.

Another strength of the project was the use of team facilitators. Elnitsky et al. (2015) state that internal facilitators engage the multiple disciplines and multiple levels of leadership for implementation. IV-CECT imaging studies are ordered by multiple providers and by providers in multiple disciplines. Per current radiology policy ordering providers remain responsible for all procedural laboratory testing and IV hydration prior to contrast administration. The facilitators of this project team used the Johns Hopkins framework to engage and gather multilevel stakeholder support. The two facilitators physically took the walk several times with stakeholders to help identify barriers and generate enthusiasm. In addition, negotiations with nursing leadership had to be successful in order to secure a place to do the infusions, not to mention accountably for
the staff nurses to provide this extra care. A win-win occurred when the hospital’s infusion center and nursing staff were finally secured. The two facilitators conducted multiple education opportunities, heightening awareness and promoting this project to providers and nursing. Knowing the organizational culture, being excellent communicators, being experts in the field, and having persistence were critical to this process. Facilitator skills like these, helped moved the project along and increased the adoption of this best practice change.

Lastly, a strength of the project was piloting change on a smaller scale before considering hospital wide implementation. The interdisciplinary work team had to systematically make the interventions of screening, stratifying and IV hydrating high risk patients a part of the work process by identifying barriers and building bridges. Barriers included the nursing staff in the infusion center as they felt already busy and adding another group of patients was overwhelming. They resisted by not cooperating with the scheduling. The nurses viewed the ownership of hydrating patients belonged to radiology. The team invited several key nursing staff members and the leadership of the infusion center to a team meeting and shared perceptions and viewpoints. Bridges were built when it was agreed that the Vascular Nurse Practitioner would assist with any concerning issues. It was also agreed that the radiology department technicians would insert the IV so that nurses would only be responsible for monitoring the patient during the pre and post IV-CT infusions. It was further agreed that the interdisciplinary team would ask leadership to purchase reclining chairs for patients versus occupying one of the infusion center’s beds, as they already ran a full schedule and space was limited. Teaming with the nursing staff by providing a supportive, nonjudgmental atmosphere improved
communications and trust. By implementing this project on a pilot scale, the interdisciplinary team was able to listen to end users feedback, evaluate feasibility, work with resistors, and make gradual changes while building networks to maintain the momentum for success.

**Implications for Nursing Practice and Research**

A key component in preventing the increased morbidity and mortality associated with CIN is the role of the nurse. Nurses are at the forefront of risk stratification, prevention, follow up, and education. Implications for nursing practice as a result of this project are threefold: nurses need to be educated of the potential risks of CIN, nurses need to be liaisons between the radiology department and the referring clinician, and nurses need to advocate for the use of appropriate preventive strategies, to help providers standardize safe practice in order to improve outcomes for those at risk for CIN.

Knowledge of current evidence is essential in the care of patients undergoing procedures which have the potential to cause harm (Hallquist, 2009). Nurses have vital roles in assessing patients for appropriate therapy and for providing timely interventions which may reduce procedure-associated complications. It is critical for nurses to know the risk factors for CIN and how to use criteria for risk stratifications. Nurses need to know the current evidence for pre and post procedure hydration. Additionally, nurses have a responsibility to provide patient education regarding prevention, and to facilitate understanding so that patients adhere to the recommended therapies. By nurses having knowledge, they become empowered to plan appropriate, safe care. Unfortunately, studies show patients at risk for CIN continue to receive IV-CECT without prophylaxis or follow up, despite multiple studies supporting the role of volume expansion for pre and
post hydration (Brown, 2014). Furthermore, nurses need to be part of the team and engage providers concerning CIN as multiple studies continue to show that among providers there remains wide variability in their knowledge of CIN (Jasuja et al., 2009; Weisbord et al., 2009).

A lesson learned from this project was the importance of empowering and engaging specific nurses to be liaisons. The clerical staff helped in many ways to facilitate the process between radiology department, the infusion center, and the referring clinician. However, liaison nursing staff who were empowered and took ownership of preventive protocols would have ensured that orders were written, laboratories obtained, patients educated on the processes, and departments coordinated ahead of time. Only then, would patients not be at risk for cancellation or rescheduling. For example, if the patient was delayed or required a slower pre-procedure infusion, (e.g., 3 hours versus 2 hour), radiology staff needed to be informed and the patient accommodated. Goldfarb et al. (2009) state despite best efforts preventive measures may not be followed due to the lack of feasibility in local settings and the lack of necessary resources. Miscommunications among staff have been identified as possible reasons for lack of pre-procedure hydration and guideline adherence (Schlip, et al., 2014). For this project site, resources for IV hydration (structure and RN staff) in the radiology department were not available, so the hospital’s infusion center assumed the workload for the pre and post-procedure IV hydration. Interdepartmental nurse liaisons would have greatly improved patient processes and guideline adherence.

A final implication is the need for nurse champions to take ownership of CIN prevention policies. Nurses could help providers change behavior and move towards a
consistent and safer practice. In general, adherence to recommended guidelines is low among providers, causing omission of therapies and contributing to preventable harm (Pronovost, 2013). Provider adherence is critical in translating recommendations into improved outcomes. Providers often lack awareness of specific interventions or rely on memory or checklists to ensure all interventions to prevent harm are addressed (Moos, et al., 2013; Pronovost, 2013). This project demonstrated that the use of a CIN prevention policy which bundled four specific strategies (screening, risk stratifying, and pre and post hydration), led to an initial adherence rate of 65%. According to AHRQ (2015), nurses play a critical role in ensuring patient safety by detecting errors and near misses, understanding care processes and weaknesses, and by performing countless other tasks to ensure patients receive high quality care. By being champions and endorsing CIN prevention guidelines, all providers become part of a system rather than individuals, working together to ensure all patients receive the best evidence.

Several implications for nursing research were identified while conducting this project, as CIN prevention is still not fully understood (Deek, et al., 2014). Numerous strategies to prevent CIN have been trialed and include oral hydration; volume expansion with several choices of fluids (sodium chloride, bicarbonate, or a combination of both), the administration of an antioxidant N-acetylcysteine, and the use of oral statins (AHRQ, 2016). Multiple clinical studies and national guidelines support the use of intravenous hydration to prevent CIN, but as of yet, there are no sufficiently powered, prospective trials examining the minimally effective length of time, rate, optimal solution, nor timing of the peri-procedural hydration. Specifically, there are no published consensus recommendations for ambulatory patients. Given that fluid administration is the most
important means of prevention, nursing research in this area looking at different or combination of strategies would be of great benefit.

Another researchable area is to evaluate the cut off values for deciding when to consider IV hydration prophylaxis. Recent European guidelines have been updated and recommend lower cut off values than guidelines in the U.S. In Europe, patients are considered at high risk for CIN when presenting with pre-existing eGFR < 40 ml/min/1.73m² or an eGFR < 45 ml/min/1.73m² in combination with other risk factors such as diabetes mellitus and advanced age (Owen et al., 2014).

Still, another area for future research include evaluating the use of oral hydration outpatient protocols. This would build on patient risk stratifications, similar to the one conducted by Yellen & Buffum (2014); however include a control group and on a large scale.

Testing a risk scoring tool to prevent CIN in outpatients undergoing IV-CECT is still another area for future research. Currently all validated tools (Mehran, RIFLE, and AKIN) are for those undergoing intra-arterial cardiac procedures or inpatients. A scoring tool for outpatients may help to standardize preventive treatment.

Lastly, testing the development of computerized tools and aids which standardize and automatize order sets and processes need to be conducted. In addition to “view alerts” and “triggers” a full alert program such as the one developed by Cho et al. (2012) could be evaluated on a large scale. These types of alerts remind providers that their patient is at risk for CIN. Prophylactic orders links not only offer provider guidance, but help ensure the proper ordering of preventive measures. In Cho et al.’s study, with the use
of a computer alert program, a markedly increased use of CIN prophylaxis (>50%) with an overall decreased incidence of CIN occurred in hospitalized patients.

Future Research

Alternatives to the current use of iodinated contrast to prevent CIN are on the horizon. The radiology department at this institution is investigating the use of iso-osmolar contrast media (IOCM) for IV-CECT in high risk patients with multiple risk factors, including those with contrast allergy. The only available IOCM iodixanol, is very expensive and historically reserved for higher risk patients undergoing intra-arterial procedures. IOCMs may have a future role as an alternative for intravenous procedures, but at this time they are not without controversy, as the literature cites the advantages of using IOCM for IV-CECT are small and not clinically seen over the LOCM agents.

Another treatment on the horizon is the use of carbon dioxide (CO2) as an adjunct to iodinated contrast medium for peripheral endovascular procedures in high risk patients. Thulasidasan et al. (2016) are reporting the use of CO2 in combination with smaller dosages of iodinated contrast medium for evaluating critical limb ischemia. The authors reported a 90% reduction in the volume of iodinated contrast use with an incident rate of CIN at 14% compared to a standard dose of contrast media with a CIN rate of 29% for this procedure. Currently, this institution is using CO2 as a diagnostic for evaluating patency of dialysis access devices (fistulas and grafts). The smaller doses of iodinated contrast protects the end stage kidney failed patient from potential iatrogenic kidney harm. Prasad (2015) states safety is a main concern with the use of CO2 especially above the diaphragm because of the risk of gas embolism of the spinal, coronary, and cerebral arteries.
Finally, hydration regimens such as the product Renal Guard® is a novel high urine flowrate device designed to prevent CIN in high risk patients. This device creates and maintains a high peri-procedural urine output, allowing the body to rapidly eliminate the contrast medium and thereby reducing its toxic effects. Currently, this product is being trialed in the U.S. and reserved for use with intra-arterial catheter procedures such as cardiac, aortic and possibly peripheral vascular disease.

Conclusions

Contrast induced nephropathy remains the third most common cause of all hospital acquired acute kidney injury and carries significant morbidities and mortalities, especially among patients with vascular disease. CIN continues to be a topic of intense interest, in large part because of the ever increasing number of patients who receive IV-CECT. However, CIN cannot be viewed as a treatable or acceptable complication of iodinated contrast procedures as it has been determined that even mild, reversible kidney injury conveys the risk of persistent tissue damage. This type of persistent damage can result in an irreversible decline of kidney function (KGIGO, 20102). Yet, fear of kidney injury should not dictate avoidance of diagnostics and optimal treatment, but rather good clinical judgement, knowledge of the risks, and effective preventive measures.

A pilot project to study the processes, appropriateness, and feasibility of adopting a modified CIN prevention policy for patients who require IV-CECT in the clinical context turned out to be an excellent strategy, prior to recommending such a policy for outpatients on a larger scale. Opportunities for improving CIN prevention definitely exist, as studies continue to show that appropriate and proven prophylactic interventions are not universally applied (Moos et al., 2014). Studies have found that volume expansion is used
in less than 60% of high risk patients undergoing IV-CECT image studies despite it being relatively inexpensive, low risk and considered the minimum standard of care for patients at high risk for developing CIN (Davenport et al., 2015; KDIGO, 2012; Ranji et al., 2015; Schilp et al., 2014).

This Doctor of Nursing Practice change project heightened awareness within the institution of the risk factors associated with CIN and appropriate pre and post procedure hydration needs. Implementation of the hydration protocol was noted to be a safe therapy and improved practice within the outpatient vascular clinic. Continuing efforts to prevent CIN and interventions that attempt to reduce the risks are the main challenges for protecting kidneys, protecting lives.
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doi:10.1001/jama.1996.03530430033035


Moos, S. I., van Vemde, D. N., Stoker, J., & Bipat, S. (2013). Contrast induced nephropathy in patients undergoing intravenous (IV) contrast enhanced computed
tomography (CECT) and the relationship with risk factors: a meta-analysis.


Owen, R. J., Hiremath, S., Myers, A., Fraser-Hill, M., & Barrett, B. J. (2014). Canadian Association of Radiologists consensus guidelines for the prevention of contrast-


APPENDIX A

VHA (VISN 22) IMAGING SERVICES POLICY ON CONTRAST MEDIA

Iodinated Contrast Media Screening Procedures

**Allergy Assessment:**
- Prior iodinated contrast reaction
- Asthma
- Consider shellfish allergy

**Pre-Treatment:**
- Methylprednisolone 32mg po, OR Hydrocortisone 200mg IV if NPO;
- 12 and 2 hours prior to contrast
- Benadryl 25-50mg IV within one hour of contrast

If patient is taking metformin, discontinue at the time of procedure. Scr will be re-evaluated at 48 hrs by the radiologist to determine if metformin should be restarted.

**Dialysis Patients:** Very High Risk category. Contrast may jeopardize renal recovery (if acute RF) or impair residual renal function (if chronic RF). The volume of contrast as well as hydration may add to fluid overload in these patients especially with heart failure. Consider Nephrology consult.

**Intra-Venous**

- **Low Risk**
  - eGFR >60ml/min

- **High Risk**
  - eGFR <60ml/min and Diabetes
  - eGFR >30 and <45 ml/min

- **Potential High Risk**
  - eGFR 45-60 ml/min + Risk Factors:
    - Risk factors:
      - Cardiac History
      - Prior Contrast within 72 hrs
      - Dehydration

- Consider Hydration

- No IV Hydration
  - Encourage PO Fluids

- IV Hydration
  - NaCl 0.9% @ 250 ml/h for 4 hr before and 4 hr after contrast

- Iohexol 300
  - (Omnipaque)

- Very High Risk
  - Intra-venous and Intra-arterial
  - eGFR <30 ml/min

- Consider alternative imaging w/o contrast

**Intra-Arterial**

- **Low Risk**
  - eGFR >60ml/min

- **High Risk**
  - eGFR <60 ml/min

- Iodixanol 320
  - (Visipaque)

- IV Hydration
  - NaCl 0.9% @ 250 ml/h for 4 hr before and 4 hr after contrast
APPENDIX B

PERMISSION TO USE MODIFIED MODEL IN PUBLICATION

Yvonne Gallegos <yvonnegallegos@csu.fullerton.edu> 9/19/15

Dr. Pronovost, I am a Doctoral Nursing Student and am asking permission to modify and use the John Hopkins Quality and Safety Research Group: strategy for translating evidence into practice diagram in my capstone publication. I am using this model as a framework to implement a hospital protocol to reduce the incidence of contrast induced nephropathy in at risk patients.

The diagram is attached with my modifications.

Thank you,

Yvonne Gallegos NP
Vascular Nurse Practitioner
VA Healthcare Systems, Long Beach CA 90822

Peter Pronovost <ppronovo@jhmi.edu> 9/21/15

Sure, no problem.

Best of luck, would you share with me how you revise it. Would love to learn from you how others are using model.

Warm regards,

peter
APPENDIX C

KNOWLEDGE-CHECK: CONTRAST INDUCED NEPHROPATHY

Needs Assessment for Vascular Providers

1. What is your title?
   a. Attending
   b. Resident
   c. Nurse Practitioner
   d. Radiologist
   e. Other

2. How much training have you received on the prevention of contrast induced acute kidney failure or nephropathy?
   a. None
   b. A little bit of training
   c. A moderate amount of training
   d. A lot of training

3. How many patients have you taken care of who developed contrast induced nephropathy at any time in the past?
   a. None
   b. One to three
   c. Four or more
   d. Ten or more

4. Our Radiologist has published a document titled “Iodinated Contrast Media Screening Procedures.” Are you aware of this document?
   a. Yes
   b. No

5. Which of the following conditions are independent risk factors for contrast induced nephropathy? (circle all that apply)
   a. Hypertension
   b. Chronic kidney disease
   c. Allergy to contrast media
   d. Chronic obstructive lung disease
   e. Coronary artery disease
   f. Diabetes mellitus
   g. Anemia
   h. Congestive heart failure
   i. Atrial fibrillation
6. At what cut off level of estimated glomerular filtration rate (eGFR) does the risk for contrast induced nephropathy increase? (choose the best answer)
   a. eGFR > 60ml/min
   b. eGFR > 30 and < 60 ml/min
   c. eGFR < 60 ml/min and Diabetes
   d. Not sure or I don’t know

7. Which patients are at higher risks for CIN?
   a. Those undergoing intra-arterial iodinated contrast studies
   b. Those requiring intravenous iodinated contrast studies
   c. Not sure or I don’t know

8. What do you perceive as the most important barrier in screening patients for risk factors and ordering the IV hydration preventive protocol as recommended by radiology?
   a. Clinical time constraints
   b. Processes unclear
   c. Screening and giving IV hydration to high risk patients is controversial and not necessary
   d. None of the above
   e. Not sure
## APPENDIX D

### PROJECT TIMELINE

<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>February 2015</td>
<td>Purpose statement 3/8</td>
<td>Methods, Evaluation Plan 4/5</td>
<td>Review of literature 4/26</td>
<td>Present project proposal</td>
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<tr>
<td></td>
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<td>Initial TOE and topics 3/22</td>
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<td>Present plan to SHCG, get approval for data collection tool</td>
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<td>Team start SOP for vascular clinic</td>
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<td>Education needs of providers</td>
<td>Met/w DSS, develop computer database scorecard</td>
<td>Meet with librarian, ROL</td>
<td>Present project to N695 class</td>
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<td>In-service staff on CIN/ policy and best practice</td>
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<tr>
<td>Educate infusion center staff</td>
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<tr>
<td>Fall semester begins</td>
<td>Fall semester ends</td>
<td>Finish manuscript and submit to American Journal of Nursing on CIN</td>
<td>Present project to CPC, get approval for SOP</td>
<td>Prepare abstract for National Kidney Foundation (NKF) for project dissemination</td>
<td>Complete 6 month data analysis</td>
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<tr>
<td></td>
<td></td>
<td>Obtain permission from authors to use adapted framework model and images for publication</td>
<td>QI poster on CIN protocol. Present to VISN and at PI fair</td>
<td>Write up analysis of data</td>
<td>Write up analysis of data</td>
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<td>Create data tables showing initial implementation, and current outcomes</td>
<td>Create data tables showing initial implementation, and current outcomes</td>
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<td>Abstract to NKF</td>
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<tr>
<td>Findings and Discussion</td>
<td>Create poster WIN</td>
<td>Project defense with full committee</td>
<td>Create poster for NKF</td>
<td>Graduation!</td>
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<tr>
<td>Write full doctoral project paper</td>
<td>Have images for poster finalized</td>
<td>PowerPoint completed for defense</td>
<td>Poster presentations to both WIN conference and to NKF</td>
<td>Podium presentation of CIN project to VISN 22 APRN 2016 conference</td>
<td></td>
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<tr>
<td></td>
<td>Accepted manuscript to AJN for future publication</td>
<td>Defend project</td>
<td>Education to medical staff</td>
<td></td>
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</tbody>
</table>
# APPENDIX E

## DATA COLLECTION TOOL

<table>
<thead>
<tr>
<th>Quarter/year of visit to vascular Clinic/location if not clinic</th>
<th>Quarter/year</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Age:</td>
<td>1. Male 2. Female</td>
</tr>
<tr>
<td>Diagnosis for vascular consult (vascular DX)</td>
<td>1. Peripheral vasc disease (carotid, claudication) 4. Vascular wound (arterial/venous)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. Aneurysm (abdominal, iliac) 5. Vascular access</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Varicose veins/venous disease 6. Other</td>
<td></td>
</tr>
<tr>
<td>Diagnostic Study ordered</td>
<td>1. CTA aortic ileofemoral w/contrast 4. CT(A) pelvis w/contrast</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. CT(A) lower extremities w/contrast 5. CTA neck w/contrast</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. CT(A) abdomen w/contrast 6. MRI w/contrast</td>
<td></td>
</tr>
<tr>
<td>Did vascular initiate IV-CECT?</td>
<td>1. Yes 2. No</td>
<td></td>
</tr>
<tr>
<td>If not, Who ordered IV-CECT? (Initiated_other)</td>
<td>1. ER 2. Inpatient acute areas 3. Outside hospital 4. CLC 5. SCI 6. Other</td>
<td></td>
</tr>
<tr>
<td>Patient Location</td>
<td>1. Inpatient 2. Outpatient</td>
<td></td>
</tr>
<tr>
<td>Documented reason for “no hydration” if met criteria</td>
<td>1. Yes 2. No 3. n/a (gave hydration) Reason:</td>
<td></td>
</tr>
<tr>
<td>Hydration protocol required</td>
<td>1. Yes 2. No</td>
<td></td>
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<tr>
<td>Hydration done</td>
<td>1. Yes 2. No</td>
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<tr>
<td></td>
<td>2. eGFR &gt;30, &lt;45</td>
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<tr>
<td></td>
<td>3. eGFR 45-60 + risk factors</td>
<td></td>
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<tr>
<td></td>
<td>(cardiac hx MI, CABG, pacemaker, CHF), dehydration (↑BUN)</td>
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<tr>
<td></td>
<td>6. Chronic NSAID 7. Cardiac Hx (CHF, MI, CABG, pacemaker, valvular dx, etc.)</td>
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<tr>
<td></td>
<td>8. Dehydration (↑ BUN) 9. 2 Risks 10. 3 Risks 11. 4 or &gt; Risks</td>
<td></td>
</tr>
<tr>
<td>sCr/eGFR/BUN pre image obtained</td>
<td>1. Yes 2. No</td>
<td></td>
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<tr>
<td>Pre sCr</td>
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<td></td>
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<tr>
<td>Pre eGFR</td>
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<td></td>
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<tr>
<td>Pre BUN</td>
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<tr>
<td>sCr/eGFR post image obtained</td>
<td>1. Yes 2. No</td>
<td></td>
</tr>
<tr>
<td>Post sCr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post eGFR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIN criteria?</td>
<td>1. Yes 2. No sCr &gt;25% or &gt;0.5 mg/dl baseline</td>
<td></td>
</tr>
<tr>
<td>Dialysis</td>
<td>1. Yes 2. No</td>
<td></td>
</tr>
<tr>
<td>Nephrotoxic drugs at time of image study</td>
<td>1. None 4. Lasix 2. NSAIDs (&gt; 5 years) 5. Ace Inhibitors 3. Outpatient chemotherapy drugs 6. 2 drugs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7. 3 or more drugs</td>
<td></td>
</tr>
<tr>
<td>Location protocol given</td>
<td>1. Infusion center 2. SDS 3. Radiology 4. ER 5. Other</td>
<td></td>
</tr>
<tr>
<td>Solution given</td>
<td>1. Normal Saline</td>
<td>2. LR</td>
</tr>
<tr>
<td>---------------</td>
<td>-----------------</td>
<td>------</td>
</tr>
<tr>
<td>Hours for pre-procedure</td>
<td>1. 2 hours</td>
<td>2. 3 hours</td>
</tr>
<tr>
<td>Hours for post-procedure</td>
<td>1. 30 mins</td>
<td>2. 60 mins</td>
</tr>
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<td>Did use electronic order set?</td>
<td>1. Yes</td>
<td>2. No</td>
</tr>
<tr>
<td>Hospital admission at time or w/in 1 week after contrast image study</td>
<td>1. Yes</td>
<td>2. No</td>
</tr>
<tr>
<td>Admitted for hydration protocol?</td>
<td>1. Yes</td>
<td>2. No</td>
</tr>
<tr>
<td>sCr complication</td>
<td>1. Yes</td>
<td>2. No</td>
</tr>
<tr>
<td>eGFR complication</td>
<td>1. Yes</td>
<td>2. No</td>
</tr>
<tr>
<td>Neuro complication</td>
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<td>2. No</td>
</tr>
<tr>
<td>CV complication</td>
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<td>2. No</td>
</tr>
<tr>
<td>Pulmonary</td>
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<td>2. No</td>
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<tr>
<td>Renal complication</td>
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<td>2. No</td>
</tr>
<tr>
<td>GI complication</td>
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<td>2. No</td>
</tr>
<tr>
<td>Skin complication</td>
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<td>2. No</td>
</tr>
<tr>
<td>Follow up visit w/vascular?</td>
<td>1. Yes</td>
<td>2. No</td>
</tr>
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</table>
APPENDIX F

IRB APPROVAL (CSUF)

IRB APPROVAL HSR-15-0483
Del Rio, Natalie <ndelrio@exchange.fullerton.edu>  12/4/15

Re: Contrast Induced Nephropathy: Protecting Kidneys, Protecting Lives

The application you submitted to the IRB office has been initially reviewed and has been approved. Please pick up the approval letter and consent form if applicable from your faculty advisor, Dr. Asma Taha. It will be sent via campus mail (EC-190). If you have any questions, please feel free to contact me.

Natalie Del Rio

Regulatory Compliance, MH-103

Institutional Review Board/IACUC

California State University Fullerton

Tel: 657-278-7640/Fax: 657-278-7238
APPENDIX G

IRB APPROVAL (VA-LONG BEACH HEALTHCARE)

Research & Development Committee
Long Beach VAMC Research Health Care Group (151)
5901 E. 7th St. • Long Beach, CA 90822 • 362-826-5801 • Fax: 362-826-5875

APPROVAL - Initial Review

Date: November 9, 2015
From: Christopher Reist, M.D., ACOS/R&D
Investigator: Ian L. Gordon, M.D., Ph.D.
Protocol: Protecting Kidneys From Contrast Induced Nephropathy
ID: 01386

The following items were reviewed and approved at the 11/05/2015 meeting:

• IRB Coord Memo
• SRS memo

This project has been reviewed and approved by the appropriate subcommittees and has been granted approval by the Research and Development Committee.

Approval by each of the following is required prior to study initiation:

IRB (Subcommittee on Human Studies) [Approval Granted 09/29/2015]
Subcommittee on Research Safety [Approval Granted 10/07/2015]
Research & Development Committee

Christopher Reist, M.D., ACOS/R&D

This project has been reviewed and approved by the appropriate subcommittees and has been granted approval by the Research and Development Committee.
APPENDIX H

RESULTS: PROJECT MANUSCRIPT

Maureen Shawn Kennedy <em@editorialmanager.com>

Feb 25 (2 days ago)

Ref.: Ms. No. AJN6217R1
Protecting Kidneys, Protecting Lives: Prevention of Contrast-Induced Nephropathy
American Journal of Nursing

Dear Yvonne

6217R1

Yvonne,

Thank you for the revisions. We are ready to accept but there are two issues that need to be addressed first:

1/ use of secondary sources (e.g., articles in Critical Care Nurse) – you need to cite the original source for the data/information – not a review article. Please review your sources and replace secondary sources with the primary source.

2/ Cross-check plagiarism software came back at 10%, largely from too close wording to the Jorgenson article in Critical Care Nurse, http://www.acr.org/~/media/37D84428BF1D4E1B9A3A2918DA9E27A3.pdf the ACR Manual on Contrast Media (http://www.acr.org/~/media/37D84428BF1D4E1B9A3A2918DA9E27A3.pdf) and the Deek article in Australian Critical Care. Please review and reword these sections. I will send the report in a separate email. The colored numbers indicate the passages that are word for word/too close wording. Some I realize are inevitable and ordinary terms – fix those that are a few lines.

Once you fix these two items, we will gladly accept. Then it will go through clinical review and fact-checking (we check all references). Once the clinical editor signs off, it will get scheduled for a future issue. I put the reviewers' final comments below.

REVIEWER COMMENTS
R1: Thank you for revising (and strengthening) the submission. The article is more focused and provides numerous resources for further reading.
The discussion of hydration is good - I encourage you to include the recommendation of KGIGO that hydration to achieve a minimum of 150cc/hr urine flow is desirable (it is not uncommon for nephrology to suggest an endpoint (e.g. urine flow needed)

R3: The revision is stronger and more detailed. Authors have incorporated most/all reviewer suggestions. New intro paragraphs provide a stronger opening.

I would suggest dropping all or most of "Nursing Publications on CIN" on page 5. The very good intro makes clear why we need to know about it. A lack of articles on the subject in the nursing literature is not a reason to learn more about an important clinical topic. If this was a lit review, then would have a place.

Table 3 includes no patient teaching. Would retitle "nursing considerations" or something similar or reword. [Editors can work with you to do this.]

Do you have permission for Table 1. Figures 1 and 3 or are they original (yours) and never have been published elsewhere? Nice job on making the manuscript "meatier" and in reorganizing for better flow

IMPORTANT: WHEN YOU REVISE YOUR MANUSCRIPT, MAKE ALL CHANGES AND ADDITIONS IN RED OR USE THE HIGHLIGHT FUNCTION IN WORD, SO EDITORS CAN READILY IDENTIFY THE REVISIONS. DO NOT USE TRACK CHANGES.

When submitting your revision, go to http://ajn.edmgr.com/ and log in as an Author. You will see a menu item call Submission Needing Revision. There you will find your submission record and opportunity to submit your revision.

Please send your revision within one month or contact us to arrange another date. If we don't receive your revision or hear from you, we will consider your manuscript withdrawn.

We look forward to receiving your revision and to working with you to disseminate your work.

Sincerely, Shawn

Maureen "Shawn" Kennedy, MA, RN, FAAN
Editor-in-Chief, American Journal of Nursing
Wolters Kluwer Health
Lippincott, Williams & Wilkins
Ovid Technologies
333 Seventh Ave, 19th floor, NY, NY 10001
shawn.kennedy@wolterskluwer.com
AJN, the leading voice of nursing since 1900
On the Web at www.ajnonline.com
APPENDIX I

MANUSCRIPT SUBMITTED TO AMERICAN JOURNAL OF NURSING

Protecting Kidneys, Protecting Lives: Prevention of Contrast-Induced Nephropathy

Radiographic imaging scans using intravascular iodinated contrast media are an important part of the clinical management of many patient conditions, yet these scans are not without complications (Hiremath, Akbari, Shabana, Fergusson, & Knoll, 2013). With approximately 80 million annual doses of contrast media safely given worldwide, intravascular iodinated contrast media has the potential to cause acute kidney injury (Hiremath et al., 2013). Contrast-induced acute kidney injury (CI-AKI) or nephropathy (CIN) impacts healthcare cost and affects patient morbidities and quality of life (Brown et al., 2014). Disturbingly, once CIN develops, management is primarily supportive as there are no current treatments which can reverse its effects. Prophylactic strategies need to be considered in order to protect the kidneys and prevent injury (Mohammed, Mahfouz, Achkar, Rafie, & Hajar, 2013). The aims of this article are to discuss (1) CIN along with its epidemiology, complications, and clinical effects, (2) screening methods for at risk patients; (3) early diagnosis of CIN complications, and (4) nursing implications related to prevention and patient education.

**Contrast-Induced Nephropathy**

Radiographic procedures utilizing intravascular iodinated contrast media include computed tomography (CT), computed tomography angiography (CTA), angiography and other related studies (see Table 1). Intravascular iodinated contrast media contain iodine which is the isotope element that enhances the radiopaqueness of vascular structures, organs and soft tissue (Wood, 2012). Such media are either ionic or non-ionic agents. Ionic agents are older, higher osmolar, and considered first generation as the osmolalities of these agents are higher than that of plasma (Wood). While these agents produce good quality images, they are associated with greater shifts of both solute and water within the kidneys, leading to greater nephrotoxic reactions (Wood; Deek, Newton, Sheerin, Noureddine & Davidson, 2013). The non-ionic or second generation agents decrease this risk as they have lower osmolality (Deek et al.). The latest agents are non-ionic and iso-osmolar, offering even lower osmolalities and less incidence of CIN, although costs are higher (Deek, et al.). Currently, most institutions use the non-ionic lower osmolar iodinated contrast agents; however, all contrast media still have higher osmolality than plasma and therefore pose risks of CIN upon administration (Isaac, 2012).

Contrast induced nephropathy is the occurrence of acute kidney failure after the administration of an iodinated contrast agent that is not attributable to other causes (Gupta & Bang, 2010; Rose & Jung, 2015). It is the third most common cause of hospital-acquired acute kidney failure, behind decreased kidney perfusion secondary to hypotension and nephrotoxic medications (Jorgensen, 2013). Contrast induced nephropathy is responsible for one in six patients in intensive care units experiencing either decreased kidney function, prolonged hospital length of stay or need for dialysis after contrast media exposure (Deek, Newton, Sheerin, Noureddine, & Davidson, 2014). In addition, CIN can occur in as many as 10% or more of ambulatory patients who
receive contrast media and is associated with a significant risk for severe kidney failure and death (Carstensen, Keer, Rempel, Jeon, & Barrett, 2012; Mitchell, Jones, Tumlin, & Kline, 2010). Patients who require dialysis as treatment for CIN suffer dramatic increased mortality rates at one year, and have a projected median two-year survival rate of only 19% (Owen, Hiremath, Myers, Fraser-Hill, & Barrett, 2014).

Typically, CIN involves an increase in the serum creatinine (sCr), peaking over two to five days, and in most cases, normalizing within one to three weeks after iodinated contrast exposure (Stacul et al., 2011). CIN adversely affects kidney structure and function. Recent evidence supports the notion that even mild, transient AKI changes can lead to persistent damage, and severe AKI can lead to an irreversible decline of kidney function with progression to end-stage kidney failure (Fliser et al., 2012).

Intravascular iodinated contrast media can be administered both intravenously (IV) and intra-arterially (IA). Much of what is known about CIN has been studied with patients undergoing coronary angiography or percutaneous coronary interventions (KDIGO, 2012; Owen et al., 2014). Coronary angiography differs from IV iodinated contrast administration in three major ways: (a) administration of the contrast is intraarterial and supra-renal, (b) the injection requires a catheter procedure that can dislodge atheroemboli, and (c) the contrast medium dose via the renal arteries is more abrupt and of high concentration (American College of Radiology Committee on Drugs and Contrast Media, 2015). Therefore, the overall incidence of CIN in patients receiving cardiac angiography is higher than in patients who receive IV iodinated contrast medium; the reported data (coming primarily from IA administration studies) likely over-estimate the risk of CIN for patients undergoing IV contrast-enhanced studies as well as contribute to the lack of universally accepted prevention guidelines (Bansai et al., 2014; Brown et al, 2014; Katzberg & Newhouse, 2010).

In the general population of patients receiving IV contrast enhanced radiographic imaging scans, the risk of developing CIN is low (Andreucci et al., 2014). In a recent meta-analysis, the mean incidence of CIN was cited as 5% and associated with pre-existing kidney impairment, diabetes, presence of malignancy, advanced age, and chronic use of non-steroidal anti-inflammatory drugs (Moos et al., 2013). However, when focused specifically on high risk patients including those with pre-existing kidney impairment and diabetes, the incidence of CIN can be 25% or higher (Katzberg & Lamba, 2009; J. McDonald et al., 2013; R. McDonald et al., 2013; Moos et al., 2013; Pattharanitima & Tasanarong, 2014; Wong & Irwin, 2007). Hospitalized patients tend to have higher rates of CIN than outpatients (Ahmed & Newhouse, 2013), probably reflecting their diminished kidney function (in aggregate). Paradoxically, even critically ill patients with normal kidney function have an elevated rate of CIN (up to 25%) (KDIGO, 2013).

Pathophysiology of CIN

Not completely understood, CIN involves multiple factors playing a role in the acute deterioration of kidney function (Jorgensen, 2013). Studies in vitro and in animals suggest that CIN is due to a combination of direct tubular toxicity, ischemic injury to the renal tubular cells, and aggregation of red blood cells in the medullary circulation (Gupta & Bang, 2010). At the moment of contact with contrast, tubular injury (both proximal and distal) occurs (Jorgensen, 2013). Contrast media are thought to produce prolonged arteriolar vasoconstriction leading to stasis of contrast material in the renal vasculature;
this results in medullary ischemic injury, tubular toxicity, and tubular cell death (Jorgensen, 2013). In addition, the high osmolality of the contrast media appears to augment the fluid viscosity, increasing resistance to flow in the renal tubules. In fact, the effects of high osmolar agents such as those used in IA administration can actually deform erythrocytes, increasing their stiffness and making flow through the capillaries difficult (Gupta & Bang, 2010). Further, red blood cells can become densely packed in the renal capillaries stopping blood flow completely.

The length of exposure of the contrast media in the kidney vasculature is thought to have a direct influence on CIN development (Jorgensen, 2013). Contrast media may trigger the release of endothelin and adenosine from endothelial cells, increasing vasoconstriction and decreasing oxygen in the outer medulla (Gupta & Bang, 2010). Moreover, impairment in flow leads to hypoxia which causes an increase in the reactive oxygen species (nitric oxide), cytostucture breakdown, and eventually cell death (Isaac, 2012).

In summary, both patient and procedure related factors contribute to CIN. As depicted in Figure 1, CIN likelihood is thought to be directly proportional to the severity of preexisting kidney impairment and is mediated by procedure-related factors. Contrast media may accelerate the renal vasoconstriction response leading to ischemic injury, hypoxia to the renal medulla, and direct tubular cell death (Gupta & Bang, 2010; Isaac, 2012; Jorgensen, 2013).

**Nursing Publications on CIN**

Despite the high incidence of CIN, little published information has been disseminated specific to nurses. In July 2015, a search of the Cumulative Index of Nursing and Allied Health Literature (CINAHL) database using the unrestricted search term “contrast induced nephropathy” led to the discovery of 354 sources, only 12 of which came from 7 nursing journals. A concurrent search in PubMed of “contrast induced nephropathy” AND “nurs*” led to the discovery of only 7 sources, 3 of which were in the 12 found in CINAHL and 2 from older pertinent articles (2003, 2004) from Critical Care Nurse that did not have CIN in the title. Given this minimal coverage, a possibility exists that nurses may not be fully aware of CIN as a potential contrast exposure complication. It is essential for nurses to have up-to-date knowledge of CIN prevention, as they have vital roles in suspecting and identifying patients at risk, as well as in employment of preventive strategies.

**Patient and Procedure-Related Risk for CIN**

Not all patients have the same vulnerability for developing CIN after iodinated contrast administration (Au, Bruckner, Mohiuddin, & Hilleman, 2014; Joongyub et al., 2013; Moos et al., 2013; Schilp, de Blok, Langelaan, Spreeuwenberg, & Wagner, 2014). The most important patient-related risk factor is pre-existing kidney disease (Owen et al., 2014). Other risk factors are diabetes, hypertension, advanced age, cardiovascular disease, nephrotoxic medication use, anemia, dehydration, malignancy, and gout (Moos et al., 2014). The risk of death for high risk patients who develop CIN is 34% compared to 7% in those of low risk (Deek et al., 2014).

Factors which can increase procedure-related risk include high osmolar contrast medium, higher amounts of contrast medium, and multiple doses of contrast given within a short period of time (Moos et al., 2014). Among procedures requiring contrast agents, coronary angiography and percutaneous coronary interventions are associated with the
highest CIN rates (R. McDonald et al., 2013). These rates are attributed to higher dosage and amounts of contrast media, IA administration route, and the overall higher morbidity of patients requiring these procedures.

**Risk Stratification**

Kidney impairment can be expressed using several indices of kidney function. Despite widespread use, the serum creatinine (sCr) level is an unreliable indicator of kidney function as it is not a real-time biomarker and is influenced by gender, muscle mass, nutritional status, and age (Owen et al., 2014). Serum levels of creatinine provide a measure of filtration within the renal tubules and glomerulus, rising only after significant loss of functioning nephrons. An increase in sCr is relative to the amount of filtration function loss; thus, sCr is not sensitive or specific for small alterations and can delay CIN diagnosis by an average of 48-72 hours (Jorgensen, 2013).

Glomerular filtration rate (GFR) provides a better assessment of nephron function as it provides a more accurate account of working nephrons, estimating how much blood is passing through the glomeruli each minute. Glomerular filtration rates can be estimated from sCr levels and includes some or all of the following variables: age, gender, weight, and race. Since kidney function is proportional to the kidney size, adjustments for body surface areas are necessary when comparing the estimated GFR (eGFR) to normal values or to the levels defining the categories of chronic kidney disease (National Kidney Foundation, 2014). In most healthy adults, the normal eGFR is 90 mL/min/1.73 m² or higher (National Kidney Foundation). Patients with an eGFR < 60 mL/min/1.73 m² have considerable loss of nephron units and are vulnerable to declines with renal injuries, such as those caused by contrast agents (Jorgensen, 2013). Glomerular filtration rates decline gradually with age, even in people without kidney disease; however, is substantial variation among individuals and the reasons for decline are not known (National Kidney Foundation).

Members of the National Kidney Foundation Kidney Disease Outcome Quality Initiative (KDOQI, 2013) recommend use of the eGFR for kidney risk stratification. Commonly used equations for eGFR are those developed by the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) and the Modification of Diet in Renal Disease (MDRD), both validated in adults (see Figure 2). These predictive equations take into account sCr and factors predictive of muscle mass including age, gender, ethnicity (African, Asian, or Hispanic), extremes of muscle mass, and nutritional status; they can be readily calculated by laboratories (Owen et al., 2014) and are often reported in medical records. Evidence supports use of formulas that include cystatin C, a neuroendocrine basic polypeptide, as these better predict clinical outcomes (KDIGO, 2013).

The National Kidney Foundation stratifications assessing for kidney risks (KDIGO, 2013) are often used when evaluating risk of CIN. These include five categories of chronic kidney disease estimated from sCr. The categories are reported as rounded to the nearest whole number relative to the average body surface area of 1.73 m² in adults, using the units mL/min/1.73 m² (see Figure 3):

- Category 1 eGFR = ≥ 90 mL/min/1.73 m²: minimal risk for CIN
- Category 2 eGFR = 60-89 mL/min/1.73 m²: very low risk for CIN
- Category 3a eGFR = 45-59 mL/min/1.73 m²: low risk of CIN absence of risk factors
- Category 3b eGFR = 30-44 mL/min/1.73 m²: moderate to potential high risk for CIN
- Category 4 eGFR = 15-29 mL/min/1.73 m²: high risk for CIN
Category 5 eGFR = < 15 mL/min/1.73 m²: approaching or requiring dialysis

**Prevention Guidelines**

Prevention guidelines for CIN have been available since 1999 (Hiremath et al., 2013). In fact, many organizational and collaborative consensus statements and updates currently address CIN prevention (American College of Radiology Committee on Drugs and Contrast Media, 2015; KDIGO, 2012; Levine et al., 2011; Owen et al., 2014; Stacul et al., 2011). A synthesis of these guidelines led to the delineation of a 3-step process for CIN prevention. Table 2 summarizes key nursing recommendations related to CIN prevention from published guidelines, and indicates the strength of the evidence base.

The three steps are as follows:

4. **Baseline screening** in all patients receiving contrast medium using eGFR, sCr, or a scoring system such as the RIFLE criteria (Risk, Injury, Failure, Loss, End-Category) as established by the Acute Dialysis Quality Initiative Group (Wahrhaftig, Correia, Matias, & De Souza, 2013) and KDIGO (Fliser et al., 2012). Screening may occur immediately before the procedure or up to 30 days prior to contrast medium administration. Post-procedure kidney assessment can be done between 12 to 72 hours afterward.

5. **Risk factor assessment and stratification** based on laboratory values and pre-existing factors. Each guideline lists different CIN risk factors; baseline kidney impairment, older age, and diabetes are noted as the most sensitive (see Table 2). All guidelines include recommendations for balancing the risk for CIN against the benefit of administering contrast, recommending that alternative imaging (not requiring contrast exposure) be considered in patients at high risk for CIN. Further, all recommend minimizing the exposure to contrast media by using the lowest possible dose and volume necessary to obtain diagnostic accuracy.

6. **Preventive strategies** to minimize risks based upon risk factor stratification (see Table 2).
   a. *Hydration protocol: IV fluids.*
      i. Most guidelines recommend standard IV fluid therapy with isotonic IV solution (normal saline or lactated ringers) both before and after administration of contrast medium when eGFR is ≤ 60 mL/min/1.73 m² and the patient is a diabetic. Sodium bicarbonate (vs. normal saline) may reduce CIN risk more effectively for patients receiving IA contrast (American College of Radiology Committee on Drugs and Contrast Media, 2015).
      ii. Guideline recommendations vary in timing, rate, duration and volume of IV fluids both before and after administration of the contrast medium (see Table 2). The sodium load of normal saline, especially pre-procedure, may be crucial for its protective effect; it enables more effective volume expansion and inhibition of the renin-angiotensin vasoactive responses (Wong & Irwin, 2007). This has practical importance as some outpatients may want to leave and not stay for the post hydration infusion despite recommended orders.
b. *Hydration protocol: Oral fluids.* Guidelines favor volume expansion with IV fluids over oral hydration (American College of Radiology Committee on Drugs and Contrast Media, 2015; Stacul et al., 2011), especially with patients who have any kidney dysfunction (KDIGO, 2012). However, in two recent meta-analyses looking at oral hydration protocols and safe cutoff points for IV intervention, especially for outpatients (Cheungpasitporn et al., 2014; Hiremath et al., 2013), authors concluded that oral hydration may be more acceptable in clinical settings due to its feasibility and lowered healthcare resource utilization. Further, evidence supports that for CIN prevention, oral fluids were no more risky and may be as effective as IV hydration in outpatient settings. However, the oral route can be unreliable in some patients and adequately powered trials with hard endpoints have not been conducted (Cheungpasitporn et al., 2014; Hiremath et al., 2013).

To summarize, recommendations from CIN prevention guidelines include screening, identification of known CIN risk factors, and hydration. Adequate extracellular volume expansion improves kidney blood flow, induces diuresis with dilution of contrast material within the tubules, and reduces activation of the vasoactive response (Stacul et al., 2011). Isotonic fluids appear to better expand intravascular volume than do sodium bicarbonate and half isotonic saline (Gupta & Bang, 2010; Ranji, Rennke, Magan, Moseson, & Wachter, 2015). However, many guideline recommendations are not clear in terms of actual practice strategies; little evidence is available to help guide specific fluid choice, timing, rate, and hydration duration. For example, KDIGO guidelines (2012) suggest – but do not recommend - use of oral N-acetylcysteine (potent antioxidant with vasodilatory properties) with IV isotonic crystalloids for patients at high risk of CIN but base this on low quality, inconsistent evidence. Contrast this with the European Renal Best Practice Guideline suggestion to only use oral N-acetylcysteine in patients receiving adequate fluid and salt loading (2D) and not as the sole method of CIN prevention (Fliser et al., 2012).

Interestingly, updated recommendations from European and Canadian guidelines recommend IV hydration only for high risk patients, setting the threshold for IV hydration regimens as eGFR ≤ 30mL/min/1.73 m² regardless of risk factors (Fliser et al., 2012; Owen et al., 2014; Stacul et al., 2011; Stevens et al., 2013). Furthermore, in patients with eGFRs between 45 and 59 and no additional risk factors, preparation for IV contrast medium requires no specific prophylaxis or follow up. However, in patients with eGFR ≤ 45mL/min/1.73 m², receipt of either IV or oral pre-procedural fluids can be given (Owen et al., 2014). No specific oral pre-procedural hydration protocol is given; the general advice is to avoid fluid restriction and encourage patients to drink fluids containing salt (i.e., salty soup) for volume expansion before contrast studies when practical (Hiremath et al., 2013; Owen et al., 2014).

**Use of Clinical Practice**

Despite the many different clinical practice guidelines available, CIN prevention is not consistently done (Yellen & Buffum, 2014). Current guidelines are inconsistent making it difficult for nurses and other providers to develop institutionally appropriate protocols and to make clear informed decisions. Gupta and Bang (2010) note that current CIN prevention guidelines lack detail and do not cover all aspects of patient management,
such as who is responsible for guideline adherence, screening, hydration, and patient follow up (i.e., radiologist, hospital or clinic specialist, nephrologist, referring provider). Recommended preventive measures may not be followed due to the lack of feasibility in local settings and lack of necessary resources which may dictate management choices (Goldfarb, McCullough, McDermott, & Gay, 2009). Also, many health care settings lack appropriate follow-up management protocols and systems required for patients who may develop CIN (Goldfarb et al., 2009).

In addition, computerized tools and aids such as standardized order sets and triggered alerts identifying high risk patients must be developed and used. In an evaluation of a computerized alert program in hospitalized patients, Cho et al. (2012) found an increased use of standardized prophylaxis and > 50% decreased risk of CIN. In the final year of a Dutch hospital CIN prevention initiative across 38 representative sample hospitals and ~5000 patients (Schilp et al., 2014), 96% of high risk patients were identified, but only two thirds received hydration before contrast administration (which was part of the CIN prevention guideline). Possible reasons for lack of pre-procedure hydration included staff issues (e.g., lack of time), deliberate guideline misinterpretation, and miscommunications across departments (admission, emergency room, radiology, clinic, etc.).

Barriers to CIN prevention will vary by institution. Nurses describe overcoming multiple barriers in a large hospital as one radiology staff nurse initiated an evidence-based CIN protocol (which included oral hydration for moderate risk patients) (Yellen & Buffum, 2014). Barriers to implementation were multiple:

- Radiology technologist resistance due to turf protection
- Radiologist fear of lifting the rule for pre-procedural fasting (thought to lead to vomiting)
- Lack of communication across departments
- Fears of changing practice
- The need for ongoing education across members of several professions/disciplines.

Sharing evidence about the recommended practices proved to be the most important strategy used in implementation of the new practice protocol for CIN prevention. Once successful, protocol implementation led to substantial cost savings due to fewer IV bicarbonate infusions (for highest risk patients) and less patient time spent at the ambulatory facility post-procedure (a patient satisfier) (Yellen & Buffum, 2014).

**Nursing Implications in CIN prevention**

Nurses need to be proactive as they play an important role in CIN prevention. They need to monitor patients for risk factors that can be modified and communicate concerns between providers and radiologists. Ideally, they should be sure all patients scheduled for radiographic image studies requiring intravascular iodinated contrast have a pre-procedure GFR, eGFR, or at least, creatinine to evaluate CIN risk level (e.g., using the National Kidney Foundation categories). They should assess patients for medical and other risk factors (e.g., diabetes, advanced age, other conditions) and recent radiographic contrast administration (computed tomographic scan or interventional contrast media studies) so that an appropriate hydration protocol can be determined (see Table 2). Nurses should educate patients about their personal risks of CIN and potential signs and symptoms to watch for post-procedure. See Tips for Patient Teaching, Table 3.
Nurses will also assist patients as they take part in preventive procedures. With medical approval, diuretics may be withheld the day of the procedure to prevent dehydration. Medications such as non-steroidal anti-inflammatory agents should be discontinued (see Table 2); however, there is insufficient evidence to support the routine discontinuation of all nephrotoxic types of medications such as angiotensin-converting enzyme inhibitors (ACE-I) or angiotensin receptor blockers (ARBs) in stable patients and should be considered on an individual patient basis (Oliver-McNeil & Grines, 2010).

While not a risk factor for CIN, the oral hypoglycemic medication metformin and metformin-containing medications are often held prior to IV contrast administration as they have been thought to cause severe and even fatal lactic acidosis in the presence of acute kidney failure from contrast media (American College Radiology, 2015; Owen et al., 2014; Stacul et al., 2011). Looking back, the American College of Radiology in 1998 updated the older recommendation from discontinuing metformin 48 hours prior to IV contrast to discontinuing at the time of the contrasted procedure. The 1998 guideline also includes the recommendation to withhold metformin for 48 hours following the procedure, with resumption only after the kidney status has been reevaluated and found to be normal (Bush & Bettman, 1998). This recommendation is still included in all current metformin package inserts. Moving forward, the 2015 recommendation states that patients taking metformin are not at any higher risk for post contrast AKI and support not discontinuing it in those with an eGFR ≥ 30mL/min/1.73 m², nor is there a need to reassess the patient’s kidney status following the test or procedure (American College of Radiology). Changes like these highlight the complexities and challenges for nurses to stay current with new guidelines.

Further, on the day of the procedure, nurses will implement, evaluate, and document the hydration protocol (e.g., oral or IV fluids) and amount of fluids taken. Nurses need to monitor patients for fluid overload as many patients requiring hydration are older and have pre-existing comorbidities, such as reduced left ventricular function, making them vulnerable to pulmonary edema (See Figure 4). They will probably be involved in scheduling post-procedure follow ups, and need to be able to give patients anticipatory guidance for things to watch for post-procedure. Likely post-procedure symptoms of CIN would be fatigue, anorexia, conditions related to fluid retention (e.g., swelling of feet and ankles, puffiness around eyes), dry and itchy skin (National Kidney Foundation, 2015).

Conclusions

In view of the increasing number of patients who receive and benefit from iodinated IV contrast media for computed tomography and angiography studies, nurses need to be familiar with CIN as a potential complication and understand evidence-based strategies for prevention. Opportunities for improving CIN prevention definitely exist, but proven prophylactic interventions are not universally applied (Moos et al., 2014). In fact, volume expansion is used in less than 60% of at-risk patients undergoing IV- contrasted image studies despite it being relatively inexpensive, low risk and considered the minimum standard of care for patients at high risk for developing post contrast AKI (Davenport, Cohan, & Ellis, 2015; KDIGO, 2012; Ranji et al., 2015; Schilp et al., 2014). Continuing efforts to prevent CIN and interventions that attempt to reduce the risks are the main nursing challenges for delivering safe, efficient, quality care.

WORD COUNT: 4122
References


Deek, H., Newton, P., Sheerin, N., Noureddine, S., & Davidson, P. M. (2014). Contrast media induced nephropathy: A literature review of the available evidence and


APPENDIX J

AUTHOR GUIDELINES

Writing for the American Journal of Nursing: Author Guidelines
AJN is a peer-reviewed journal that follows publishing standards set by the International Committee of Medical Journal Editors (ICMJE; www.icmje.org), the World Association of Medical Editors (WAME; www.wame.org), and the Committee on Publication Ethics (COPE; www.publicationethics.org.uk) AJN’s mission is to promote excellence in nursing and health care through the dissemination of evidence-based, peer-reviewed clinical information and original research, discussion of relevant and controversial professional issues, adherence to the standards of journalistic integrity and excellence, and promotion of nursing perspectives to the health care community and the public.

AJN welcomes submissions of evidence-based clinical application and review papers, descriptions of best clinical practices, original research reports, case studies, narratives, commentaries, and other manuscripts on a variety of clinical and professional topics. The journal also welcomes submissions for its various departments and columns, including artwork and poetry that is relevant to nursing or health care. Guidelines on writing for specific departments—Art of Nursing, Viewpoint, Policy and Politics, and Reflections—are available below. Authors who wish to submit photo essays should send a query letter to the editor-in-chief before submission.

Manuscripts are subject to double-blind peer review. All accepted papers undergo intensive clinical and developmental editing that includes fact-checking, reference checking, determinations of balance and accuracy, and line editing to enhance the readability and accessibility of the paper. Submission of a manuscript implies the authors’ agreement to work on the manuscript with the editorial staff—on a continuing basis—during production. Poems and artwork are not edited. For more information on AJN’s editing process, go to http://edmgr.ovid.com/ajn/accounts/What_to_Expect-fr_AJNediting.doc.

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We encourage authors to familiarize themselves with the journal in print or online at www.AJNonline.com. Query letters should include a paragraph describing the proposed manuscript, its projected length, an abstract and outline, a short biographical sketch that includes the author’s qualifications for writing on the topic, and the author’s contact information (e-mail and street addresses and daytime and evening telephone numbers). Do NOT send the manuscript. Query letters should be sent to diane.szulecki@wolterskluwer.com. We do consider completed manuscripts without a prior query. Authors may send query letters to an unlimited number of journals simultaneously. However, it is not appropriate for authors to submit a manuscript to more than one journal at a time. We do not consider manuscripts that are being reviewed by another publication or previously published manuscripts. Authors who
violates this standard of biomedical publishing will not be welcome to submit other manuscripts to the journal.

SUBMISSION
Authors should carefully review these author guidelines. The journal will only review manuscripts formatted according to the style of the American Psychological Association (APA; www.apastyle.org).
Authors must submit all manuscripts online at http://ajn.edmgr.com. Log on to register and submit a manuscript. For questions about submitting a manuscript, contact Diane Szulecki, Associate Editor, at diane.szulecki@wolterskluwer.com
## APPENDIX K

### TABLE OF EVIDENCE

Evidence Table 1

*Implementation of Renal Protective Protocols to Prevent CIN in Patients with Vascular Disorders*

<table>
<thead>
<tr>
<th>Purpose (Author, Year)</th>
<th>Design/Key Variables</th>
<th>Sample/Setting</th>
<th>Measures</th>
<th>Key Findings</th>
<th>Author Conclusion</th>
<th>Limitations/Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthesized evidence for prevention therapies CIN</td>
<td>Summary review Variables: CIN, prevention therapies</td>
<td>N = 172 RTC Medline (May 2004 to May 2014) Abstracts English language Clinical trials investigating therapies for prevention CIN</td>
<td>Characteristics, medications, &amp; CM procedures grouped; quantified with risk screening tool for CIN Prevention therapies compared to current published guidelines</td>
<td>Pre-contrast sCr &amp; CKD stage risk marker for CIN Isotonic saline most effective pre-procedural prevent CIN Age &gt;65 ↑risk factor CIN Nephrotoxic &amp; metformin caution with CM</td>
<td>No standardized definition CIN across studies Inconsistent CIN prevention therapies across studies Need for standardized methods to evaluate hydration type timing, volume, route for CIN prevention</td>
<td>Synthesis included both IA and IV prevention therapies No stratification for best practice recommendations</td>
</tr>
<tr>
<td>Summarize incidence &amp; risk factors associated with CIN in</td>
<td>Meta-analysis DV: CIN, RI, risk factors</td>
<td>N = 42 RCTs Outpts</td>
<td>Stratified analysis risk factors &amp; CIN</td>
<td>Overall pooled CIN incidence 4.96% (95% CI: 3.79-6.47). Mean incidence CIN overall ↓in stable, outpts; incidence ↑with</td>
<td></td>
<td>Only 65% of all studies described hydration plan</td>
</tr>
<tr>
<td>Purpose (Author, Year)</td>
<td>Design/Key Variables</td>
<td>Sample/Setting</td>
<td>Measures</td>
<td>Key Findings</td>
<td>Author Conclusion</td>
<td>Limitations/Notes</td>
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<tr>
<td>outpts undergoing IV-CEPT and low or iso-osmolar contrast studies</td>
<td>IDV: IV, CECT</td>
<td>International &amp; US publications (Jan 2002 to Nov 2012)</td>
<td>CIN definition: Rel increase sCr ≥25% or absolute increase sCr &gt; 0.5mg/dL.</td>
<td>Significant association between CIN &amp; RI, DM, age &gt; 65, NSAIDs, malignancy</td>
<td>associated risk factors: pre-existing RI, DM, old age, malignancy, use of NSAIDs</td>
<td>Definitions of CIN varies across studies, impacts incidence as absolute &amp; relative sCr not interchangeable</td>
</tr>
<tr>
<td>Moos et al., 2013</td>
<td></td>
<td></td>
<td>RI: sCr&gt; 1.5 mg/min &amp;/or eGFR &lt;60 mL/min</td>
<td>No association between gender, HTN, anemia, CHF, contrast medium &amp; volume</td>
<td>CIN associated with PAD</td>
<td></td>
</tr>
<tr>
<td>Risk factors evaluated: Time between IV-CEPT &amp; CIN, RI, DM, HTN, CHF, age, NSAIDs, anemia</td>
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<tr>
<td>Analysis summarizing effects of cumulative intravascular contrast exposure (CIVCE) on renal function &amp; survival post initial contrast procedure for elective arterial occlusive or aneurysmal disease</td>
<td>Retrospective longitudinal cohort chart review</td>
<td>Pts observed subsequent CIVCE over 14 year period</td>
<td>N = 1274 consecutive pts who underwent subsequent CIVCE after initial contrast procedure for elective arterial occlusive or aneurysmal disease</td>
<td>Pts followed for mean 5.8 yrs, had median 3 CIVCE post initial PAD elective procedure</td>
<td>PAD population least studied in terms of identifying effective hydration regimes</td>
<td>Included both IV and IA procedures in definition of CIVCE</td>
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<tr>
<td></td>
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<td></td>
<td>CIVCE = subsequent repeat contrast exposure for diagnostic, surveillance or therapeutic purposes post initial PAD procedure</td>
<td>33% cohort developed transient RF, 9% permanent renal failure</td>
<td>Significant association between CIVCE &amp; development (transient or permanent) renal</td>
<td>Author bias, chart review</td>
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<tr>
<td></td>
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<td></td>
<td>Renal labs obtained at baseline, entry to</td>
<td></td>
<td>No stratification other associated risk factors</td>
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<tr>
<td>Analysis summarizing effects of cumulative intravascular contrast exposure (CIVCE) on renal function &amp; survival post initial contrast procedure for elective arterial occlusive or aneurysmal disease</td>
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<td>Renal labs obtained at baseline, entry to</td>
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<td>No stratification other associated risk factors</td>
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<td>Purpose (Author, Year)</td>
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<td>Measures</td>
<td>Key Findings</td>
<td>Author Conclusion</td>
<td>Limitations/Notes</td>
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<tr>
<td>aneurysmal disease survival</td>
<td>IDV: CIVCE</td>
<td>(VHA) Houston, TX</td>
<td>&amp; exit cohort, before and after CIVCE &amp; at every admission, discharge or change in renal status</td>
<td>CIVCE independent predictor for development stage 4 or 5 CKD and death</td>
<td>failure &amp; CIVCE &amp; death</td>
<td>Dehydration w/damage renal parenchyma most likely cause renal decline post subsequent CIVCE</td>
</tr>
<tr>
<td>Kougias et al., 2014</td>
<td>Diagnosed w/stage 1-2 CKD, GFR &gt; 60 at baseline</td>
<td>(Jan 1999-Dec 2012)</td>
<td>Renal failure = CKD to stage 4 (eGFR 15-29mL/min) or stage 5 (eGFR &lt;15mL/min)</td>
<td>Vascular reconstruction independent predictor renal decline</td>
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<td>Analyze prevalence of CIN risk factors (RF) &amp; their relationship with actual incidents of CIN in a Korean population</td>
<td>16 tertiary hospitals retrospective observational study all participants Korean National Health Insurance, conducted by radiology departments</td>
<td>N = 101,487 pts underwent IV-CECT</td>
<td>CIN: Difference pre and post sCr by ↑ 0.5 mg/dL or 25% increase from baseline</td>
<td>Prevalence of RF increase with age</td>
<td>Despite CIN rare, efforts are worthwhile to prevent</td>
<td>Pooled sample, no control group</td>
</tr>
<tr>
<td>Joongyub et al., 2014</td>
<td>EMR and CPOE</td>
<td>Age &gt;15, sCr (14 days prior) IV-CECT, and sCr (within 3 days post), and baseline eGFR ≥15mL/min</td>
<td>RF after preventive measures stratified, 2 sided statistical test p &lt; 0.05</td>
<td>Large sample 3,103 cases of CIN post IV-CECT (2.2%)</td>
<td>Gap exists between EBPG and practice of radiologist; most likely logistics for radiology department as unequipped to follow serial sCr measurements &amp; carry out IV</td>
<td>Excluded those with eGFR &lt;15mL/min, may alter incidence of CIN</td>
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<td></td>
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<td>Did not stratify for care setting (sample included inpts and outpts)</td>
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<td>Purpose (Author, Year)</td>
<td>Design/Key Variables</td>
<td>Sample/Setting</td>
<td>Measures</td>
<td>Key Findings</td>
<td>Author Conclusion</td>
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<td></td>
<td>NS hydration used only 26.6% of sample</td>
<td></td>
<td></td>
<td>Incidence CIN less when RFs stratified by use of prevention intervention</td>
<td>Preventive measures underutilized; system needed to improve preventive care.</td>
<td></td>
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</tbody>
</table>

Notes: CHF = congestive heart failure, CIN = contrast induced nephropathy, CIVCE = cumulative intravascular contrast exposure, CKD = chronic kidney disease, CM = contrast medium, CPOE = computerized provider order entry, DM = diabetes mellitus, DV = dependent variable, eGFR = estimated glomerular filtration rate, EMR = electronic medical record, EBPG = evidence based practice guideline, GFR = glomerular filtration rate, HTN = hypertension, DV = independent variable, IA = intra-arterial, IV = intravenous, IV-CECT = intravenous contrast enhanced computed tomography, NSAID = nonsteroidal anti-inflammatory drug, Outpts = outpatients, PAD = peripheral arterial disease, Pts = patients, RCT = random controlled trials, Rel = relative, RF = risk factors, RI = renal insufficiency, sCr = serum creatinine, yrs = years.
## Clinical Practice Guideline Adherence and Changing Physician Behaviors

<table>
<thead>
<tr>
<th>Purpose (Author, Year)</th>
<th>Design/Key Variable</th>
<th>Sample Setting</th>
<th>Measures</th>
<th>Key Findings</th>
<th>Author Conclusion</th>
<th>Limitations/Notes</th>
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</thead>
<tbody>
<tr>
<td>Review of barriers to MD adherence to clinical practice guidelines</td>
<td>Systemic review</td>
<td>N=76 studies on barriers to CPG adherence</td>
<td>Barriers defined factors limiting complete MD adoption to a guideline</td>
<td>CPG have limited effect on changing MD behavior</td>
<td>CPG assist providers to deliver appropriate care under specific circumstances</td>
<td>Did not explore barriers why MDs do not take ownership of or start process for CPG evaluation</td>
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<td></td>
<td></td>
<td>MEDLINE, ERIC, HealthSTAR databases; bibliographies, textbooks</td>
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<td>Mean 56.5% MDs identified lack of familiarity as a barrier</td>
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<td></td>
<td></td>
<td>Search terms: CPG, barriers to adherence</td>
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<td>85% high identified lack of agreement as barrier to adherence (lack of credibility), low of 7% perceived as taking away from autonomy</td>
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<td></td>
<td></td>
<td>(Jan 1966 to Jan 1998)</td>
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<td>Mean 69.5% identified lack of outcome expectancy as barrier to adherence</td>
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<td>MD adherence critical in translating recommendations into improved outcomes</td>
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<td>Purpose (Author, Year)</td>
<td>Design/Key Variable</td>
<td>Sample Setting</td>
<td>Measures</td>
<td>Key Findings</td>
<td>Author Conclusion</td>
<td>Limitations/Notes</td>
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<tr>
<td>Guideline adherence for identification and hydration of high-risk hospital pts for contrast induced nephropathy Schilp, J, de Blok, C., Langelaan, M., Spreeuwenberg, P., &amp; Wagner, C., 2014</td>
<td>Longitudinal retrospective Evaluation study of safety programs in Netherlands, between Nov 2011 and Dec 2012. 38 hospitals stratified by area and type of hospital drawn from total 92 Dutch hospitals  N = 20-25 random samples adult ≥ 18 years inpts medical</td>
<td>4297 pt records included in study. Mean age 65.4 years, 54% male. Mean length of hospital stay 3.6 days. Mean eGFR 66.6 mL/min. Significant difference in known eGFR (p&lt;0.001) found between hospitals types.</td>
<td>Extent high risk pts CIN identified and hydrated. High risk = eGFR &lt;4 eGFR &lt;45mL /min, eGFR &lt;60 mL /min and ≥2 RFs RF = peripheral vascular disease, heart failure, age &gt; 75 years old, anemia, symptomatic hypotension, contrast</td>
<td>627 of 4142 patients were assessed as high risk (mean eGFR 44), those at high risk older, acutely admitted, longer hospital stay, more RFs: age (mean 74.9), use of nephrotoxic drugs/diuretics, heart failure, diabetes and peripheral vascular disease 96.4% of patients had eGFR evaluated prior to IV contrast medium</td>
<td>Despite hospitals expected to comply as part of safety program and 97% patients had eGFR known prior to IV contrast medium, subsequent step in prevention of CIN was less performed</td>
<td>Strength: large representative sample of hospitals Many patients acutely admitted, treating MDs may not know all risk factors Sometimes hard to track IV hydration if not recorded systematically Only have information of identification and hydration, no</td>
</tr>
<tr>
<td>Purpose (Author, Year)</td>
<td>Design/Key Variable</td>
<td>Sample Setting</td>
<td>Measures</td>
<td>Key Findings</td>
<td>Author Conclusion</td>
<td>Limitations/Notes</td>
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<td>records from 19 area hospitals who had IV contrast administered in the month before the measurement. (2 academic, 6 tertiary teaching, and 11 general hospitals)</td>
<td></td>
<td></td>
<td>volume &gt; 150 ml, diuretic or use of nephrotoxic drug</td>
<td>68.5% patients who met criteria received hydration Those with higher eGFR were more often to not be hydrated</td>
<td>Explanations include lack of time and rapid admission events contributed to no hydration, although safety program module offered a shortened hydration scheme.</td>
<td>information if CIN actually prevented</td>
</tr>
<tr>
<td></td>
<td>Chart reviewed for IV hydration and pt advising on nephrotoxic medication</td>
<td></td>
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<td></td>
<td></td>
<td>Article presented good ideas for future: literature unclear if IV hydration for eGFR &gt; 30 required as guideline only, ↑cost, time, patient burden</td>
</tr>
</tbody>
</table>

*Notes. CPG= clinical practice guideline, CIN = contrast induced nephropathy, CM = contrast media, eGFR = estimated glomerular filtration rate, IV = intravenous, MD = physician, pt = patient, RF = risk factors.*
### Evidence Table 3

**Evidence-Based Guidelines to Prevent Contrast-Induced Nephropathy**

<table>
<thead>
<tr>
<th>EBPG (Author, Year)</th>
<th>Definition/Diagnosis</th>
<th>Risk Factors</th>
<th>Screening Recommendations</th>
<th>Prevention Strategies</th>
<th>Prophylactic Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>American College of Radiology (ACR) Manual on Contrast Medium Consensus statements, opinions &amp; recommendations prevention CIN ACR, 2015</td>
<td>Sudden deterioration renal function following recent ioted CM in absence of other nephrotoxic event (causative diagnosis) Diagnosis no standard criteria; often used % change in baseline sCr (25-50%) and absolute elevation 0.5 to 2.0 mg/dL within 48 hours nephrotoxic event</td>
<td>Most important RF pre-existing RI. Not rigorously confirmed: DM, dehydration, CVD, diuretic use, old age, multiple myeloma, HTN, hyperuricemia, &amp; multiple iodinated CM doses &lt;24 hours apart, proteinuria, prior kidney surgery, gout</td>
<td>Consensus- sCr pre CM considered at risk CIN: age &gt;65, hx renal disease (dialysis, kidney transplant, single kidney, renal CA, renal surgery), hx HTN, DM, metformin (or drug combination)</td>
<td>Adequate patient assessment, good communication provider &amp; radiologist</td>
<td>Isotonic fluids preferred (LR or 0.9 NS), possibly 100mL/hr 6-12 hr pre and 4-12 post (ideal unknown)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>sCr and CM 30 day interval acceptable, prudence is less than</td>
<td></td>
<td>Oral hydration not effective</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Recommend eGFR &amp; sCr as screen prior to CM, but defers post CM to referring provider</td>
<td></td>
<td>No NaHC03, mannitol, furosemide, or NAC hydration infusions</td>
</tr>
</tbody>
</table>

Suggest CIN definition based on AKIN criteria (modified version RIFLE) system, but still calculations use sCr which lag behind renal changes, need to look at other non renal markers (cystatin)
<table>
<thead>
<tr>
<th>EBPG (Author, Year)</th>
<th>Definition/Diagnosis CIN</th>
<th>Risk Factors</th>
<th>Screening Recommendations</th>
<th>Prevention Strategies</th>
<th>Prophylactic Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canadian Association of Radiologist Consensus Guidelines for the Prevention of Contrast-Induced Nephropathy: Update 2012</td>
<td>AKI (24-72 hrs) after CM, absence other causes</td>
<td>CKD single most significant RF</td>
<td>Scr and eGFR obtained 6 months before CM in stable outpt w/one or more risk factor and no RI</td>
<td>Pts carefully assessed, cautions taken with RI</td>
<td>eGFR &lt;45 mL/min: IV hydration 0.9% NS at 3mL/kg/hr for 1-3 hr pre and 6 hr post CM (oral fluids if impractical)</td>
</tr>
<tr>
<td>Owen et al., 2014</td>
<td>Peak sCr &gt;25% baseline or absolute sCr by at least 44µmol/L post CM, then returns to baseline within 14 days</td>
<td>Comorbidities: combined RI &amp; DM (CIN ↑ by 50%)</td>
<td>sCr &amp; eGFR up to 1 week for inpts and pts with unstable or acute renal disease</td>
<td>All pts eGFR&lt;60 mL/min recommended alternative imaging considered first</td>
<td>Depending on weight, at least 300-500mL of IV hydration prior to CM</td>
</tr>
<tr>
<td></td>
<td>eGFR &amp; CrCl more accurate measure renal function than sCr level</td>
<td>DM, RD, solidary kidney, sepsis, age &gt; 70, acute hypotension, dehydration, HIV, previous chemotx, organ transplant, vascular disease (HTN, CHF, cardiac or PVD), nephrotoxic drugs</td>
<td>eGFR recommended as screen for risk assessment</td>
<td>Minimize CM volume</td>
<td>No NaHCO3, no advantage over NS</td>
</tr>
<tr>
<td></td>
<td>IA still recommended at ≤ 60mL/min</td>
<td>Efforts should be targeted at eGFR &lt;45mL/min &amp; severe eGFR &lt;30 mL/min with risk factors for IV</td>
<td>Follow up sCr &amp; eGFR level 48-72 hrs</td>
<td>Avoid repeat iodinated CM studies with 48 hr</td>
<td>Avoid fluid restriction, encourage all to drink fluids and salt (e.g., salty soup). If NPO keep to minimum ≤ 4 hours</td>
</tr>
<tr>
<td>EBPG (Author, Year)</td>
<td>Definition/Diagnosis</td>
<td>Risk Factors</td>
<td>Screening Recommendations</td>
<td>Prevention Strategies</td>
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<td>A European Renal Best Practice (ERBP) Clinical Practice Guidelines on Acute Kidney Injury: Definitions, conservative management and contrast induced nephropathy</td>
<td>Recommends uniform definition CIN using same definition and grading for AKI</td>
<td>CIN $\uparrow$ pre-existing decreased GFR $\leq 60$ mL/min</td>
<td>Before any intervention encompasses risk CIN baseline sCr obtained &amp; repeated 12 and 72 hours after CM administrated</td>
<td>Balance risk for CIN against benefit; consider alternatives non contrast imaging</td>
<td>Volume expansion isotonic NS or NaHCO3 for patient at risk CIN</td>
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<td>Fliser et al., 2012</td>
<td>(sCr $\geq 1.3$ mg/dL in men and $\geq 1.0$ mg/dL in women; both equivalent eGFR) Use of concurrent NSAIDs, loop diuretics $\uparrow$ risk but need to be stopped weeks in advance vs. days</td>
<td>CIN risk $\uparrow$ diabetes &amp; dehydration</td>
<td>Screening threshold could drop to eGFR $\leq 45$ mL/min before instituting risk prevention strategies</td>
<td>Most ambulatory pts at low risk CIN, could consider oral</td>
<td>IV route leads to substantial $\uparrow$ cost</td>
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<td>Insufficient evidence support universal use of NAC, oral or IV hydration</td>
<td>No hospitalization just for hydration</td>
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<td>Consider all causes AKI, not only CIN</td>
<td>Oral route fluid and salt load on premise intake assured, does not confer same degree of protection as IV</td>
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<td>Kidney Diseases: Improving Global Outcomes Chronic Kidney Disease (KDIGO) Guideline. Section IV: Contrast Induced Acute Kidney Injury KDIGO</td>
<td>RIFLE/AKIN criteria however, CIN widely used in literature as $\uparrow$sCr of $\geq 0.5$ mg/dl or a 25% $\uparrow$ from baseline value assessed at 48 hrs after radiologic procedure</td>
<td>Pre-existing RD alone or in presence of RF or in combination RF: diabetes, CHF, advanced age, concurrent use of NSAIDs drugs</td>
<td>Screening for both acute and CKD highly recommended</td>
<td>Lowest does CM possible in pts at risk for CI-AKI</td>
<td>IV volume expansion with either NS or NaHCO3 rather than no IV volume expansion in pts at risk CIN</td>
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<td></td>
<td>Recognizes HTN, volume depletion,</td>
<td>Screening threshold could drop to eGFR $\leq 45$ mL/min before instituting risk prevention strategies</td>
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<td>Iso-osmolar or low osmolar iodinated contrast medium in pts at $\uparrow$CIN risk</td>
<td>Suggest NAC together with IV NS</td>
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<td>No prophylactic intermittent</td>
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<tr>
<td>EBPG (Author, Year)</td>
<td>Definition/Diagnosis CIN</td>
<td>Risk Factors</td>
<td>Screening Recommendations</td>
<td>Prevention Strategies</td>
<td>Prophylactic Recommendations</td>
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<td>workgroup, 2012</td>
<td>substantial variation in sCr depending on threshold criterion for CI-AKI</td>
<td>hemodynamic instability, large volume or high osmolality contrast agent</td>
<td>Outpatient radiology centers where renal function data unavailable, simple survey or questionnaire</td>
<td>hemodialysis or hemofiltration for CM removal in pts with CIN risks</td>
<td>Against using oral fluids alone in pts at risk CIN, insufficient evidence for effectiveness</td>
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<td>Stacul, et al., 2011</td>
<td>↑in sCr by more than 25% within 3 days following intravascular administration CM in absence of alternative etiology</td>
<td>CKD is most significant RF for CIN, CKD as classified by K/DOQI criteria</td>
<td>sCr not ideal marker of renal function, better to estimate using predictive equation, eGFR</td>
<td>Low or iso-osmolarity in pts with risk factors for CIN</td>
<td>Insufficient research IV hydration over oral</td>
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<td>Definition CIN same as 1999, will keep as topic complex and understanding of CIN continues to evolve</td>
<td>CKD stage 3-5, does not require evidence renal damage. eGFR &lt; 60 mL/min threshold for diagnosis. eGFR &gt; 60 mL/min regarded as normal</td>
<td>Consensus: genuinely at risk CIN, CKD stage 3b, 4, 5 and eGFR &lt;45mL/min before IV &lt;60 mL/min for IA particularly in combination with risk factors</td>
<td>Minimum amount CM volume necessary to answer clinical question</td>
<td>Recommend either NS at 1.0 to 1.5ml/kg/h at least 6 hours before and after CM, NaHC03 at 3 ml/kg/h for 1 hour before and 1ml/kg/h for 6 hours after CM</td>
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<td>Higher risk CIN with IA</td>
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<td>Obtain eGFR 48-72 hours after CM</td>
<td>Pts at risk CIN, need to establish clinical need vs. alternative</td>
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<td>Does not recommend routine withdrawal of nephrotoxic drugs, lack of evidence to support makes difference in terms</td>
<td>No NAC or any other drug in reducing incidence CIN</td>
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<td>VA/DoD Practice Guideline for the management of chronic kidney disease in primary care</td>
<td>Acute kidney dysfunction following exposure to intravascular contrast medium.</td>
<td>Preexisting CKD, Diabetes, heart failure, age &gt; 75, volume of contrast &gt;100ml, use of high-osmolar contrast</td>
<td>No need to screen if known CKD</td>
<td>No study has clearly demonstrated an effect on patient outcomes with preventive strategies, such as prevention of acute or chronic dialysis</td>
<td>Low risk or when not feasible patients should be offered oral hydration 1000ml over prior 12 hours contrast exposure</td>
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<tr>
<td>VA/DoD, 2014</td>
<td>sCr &gt;1.5mg/dL or eGFR &lt; 60mL/min</td>
<td>Diabetes independent RF, advanced age &gt; 70, Dehydration</td>
<td>No need to screen if known CKD</td>
<td>No study has clearly demonstrated an effect on patient outcomes with preventive strategies, such as prevention of acute or chronic dialysis</td>
<td>Low risk or when not feasible patients should be offered oral hydration 1000ml over prior 12 hours contrast exposure</td>
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<td>Nephrotoxic drugs and multiple myeloma not well supported as RF</td>
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<td>Diabetics with normal renal function, risk for CIN low</td>
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<td>Low incidence lactic acidosis associated with metformin, recommend stop 48 hrs before only if eGFR 30-44 mL/min, reassess 48 hrs after CM and restarted only if no evidence renal deterioration</td>
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<td>No prophylactic hemodialysis or hemofiltration immediately after CM</td>
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<td></td>
<td>CIN</td>
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<td>Inform patient of risk for CIN prior to IV-CECT</td>
<td>No NAC</td>
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</tbody>
</table>

*Notes.* AKI = acute kidney injury, CHF = congestive heart failure, AKIN = (Acute Kidney Injury Network (AKIN), chemotx = chemotherapy, CKD = chronic kidney disease, CM = contrast medium, CI-AKI = contrast induced acute kidney injury, CIN = contrast induced nephropathy, CrCl = creatinine clearance, CVD = cardiovascular disease, DM = diabetes mellitus, eGFR = estimated glomerular filtration rate, HD = hemodialysis, HIV = human immunodeficiency virus, HTN = hypertension, hx = history, IA = intra-arterial, IV-CECT = intravenous contrast enhanced computed tomography.