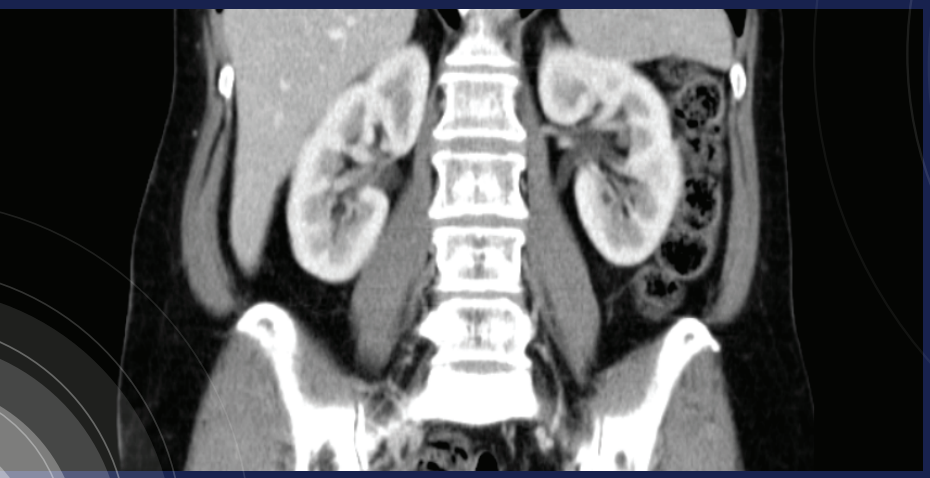
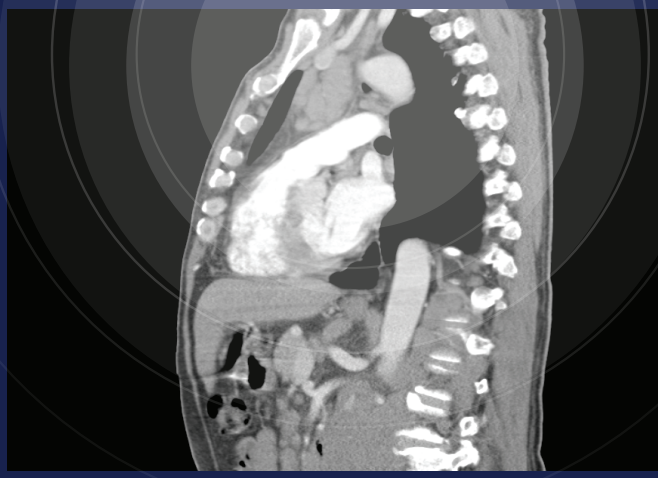
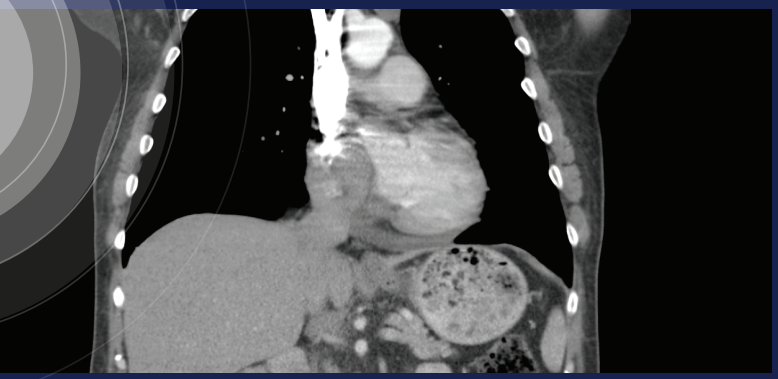
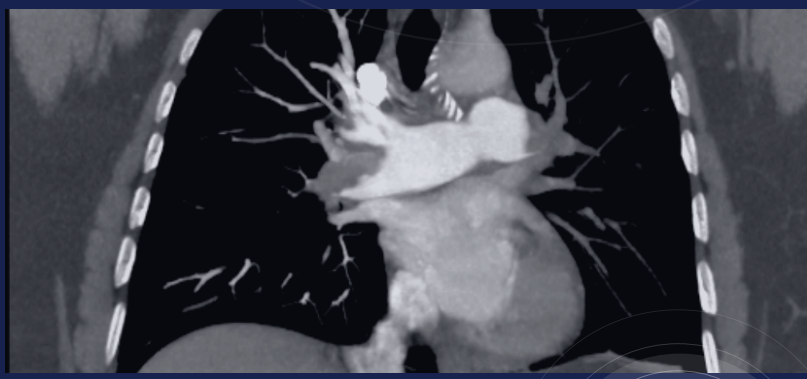

IODINATED CONTRAST MEDIA GUIDELINE

FACULTY OF **CLINICAL RADIOLOGY**

THE ROYAL AUSTRALIAN AND NEW ZEALAND COLLEGE OF RADIOLOGISTS®

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Document name	Iodinated Contrast Media Guideline	
Description	The Iodinated Contrast Media Guideline is intended to assist The Royal Australian and New Zealand College of Radiologists®, its staff, Fellows, members and other individuals involved in the administration of iodinated contrast media to patients undergoing medical imaging procedures.	
Created By	Standards of Practice and Accreditation Committee	
Date Created	2011	
Maintained By	Faculty of Clinical Radiology, Policy and Advocacy Unit	
Version Number	**Modifications Made**	**Date Modified**
2011	Document published	
2.0	Document updated and published	April 2016
2.1	Grammatical error corrected in R31	February 2017
2.2	Nitroglycerin dosages corrected in R39	June 2017
2.3	Adrenaline dosage corrected in R56	March 2018

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About the College

The Royal Australian and New Zealand College of Radiologists (RANZCR) is a not-for-profit association of members who deliver skills, knowledge, insight, time and commitments to promote the science and practice of the medical specialties of clinical radiology (diagnostic and interventional) and radiation oncology in Australia and New Zealand.

The Faculty of Clinical Radiology, RANZCR, is the peak bi-national body for setting, promoting and continuously improving the standards of training and practice in diagnostic and interventional radiology for the betterment of the people of Australia and New Zealand.

Our Vision

RANZCR as the peak group driving best practice in clinical radiology and radiation oncology for the benefit of our patients.

Our Mission

To drive the appropriate, proper and safe use of radiological and radiation oncological medical services for optimum health outcomes by leading, training and sustaining our professionals.

Our Values

Commitment to Best Practice

Exemplified through an evidence-based culture, a focus on patient outcomes and equity of access to high quality care; an attitude of compassion and empathy.

Acting with Integrity

Exemplified through an ethical approach: doing what is right, not what is expedient; a forward-thinking and collaborative attitude and patient-centric focus.

Accountability

Exemplified through strong leadership that is accountable to members; patient engagement at professional and organisational levels.

Code of Ethics

The Code defines the values and principles that underpin the best practice of clinical radiology and radiation oncology and makes explicit the standards of ethical conduct the College expects of its members

1. INTRODUCTION

1.1 Purpose and Scope

This Iodinated Contrast Media Guideline is intended to assist The Royal Australian and New Zealand College of Radiologists® (ABN 37 000 029 863) (RANZCR), its staff, Fellows, members and other individuals involved in the administration of iodinated contrast media to patients undergoing medical imaging procedures.

1.2 The Intent of this Document

(a) To inform the safe and appropriate use of iodinated contrast media.

(b) To provide health professionals in Australia and New Zealand with contemporary practice guidance for administration of iodinated contrast media.

(c) To help to prevent adverse patient outcomes in relation to contrast media administration.

(d) To provide point of care tools for use by patients and practitioners to facilitate implementation of the guideline recommendations.

1.3 Guideline Methodology – Agree II Tool

The AGREE II Tool was used to guide the methodology of development of this guideline. The AGREE II Tool resulted from a 2013 revision of the 2009 publication of the original AGREE tool by the AGREE Trust. The tool is designed both for critical appraisal of clinical practice guidelines and to inform quality guideline development methods. The AGREE II tool sets out 21 separate aspects of five domains that should be addressed by contemporary clinical practice guidelines.

Reference:
AGREE Next Steps Consortium (2009). The AGREE II Instrument [Electronic version]. Retrieved June 18 2015, from http://www.agreetrust.org/

1.4 Iodinated Contrast Media Guideline Working Group membership and method of recruitment

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Presenter/Organiser of AIR, IV cannulation and IVCM for Radiographers workshops
Guest Lecturer in CT, RMIT, Melbourne, VIC
Member, Victorian CT Technologist Group
Member, Deakin University Course Radiography Course Advisory Board

Robert Walker
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Merle Wigeson
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Member, RANZCR CT Reference Group
Member, RANZCR MRI Reference Group
Member, RANZCR BMD Reference Group

Melissa Doyle
Manager, Standards of Practice, RANZCR

Sharon Connolly
Senior Administrator, RANZCR

Katie Sherman
Medical Intern, Arcadia University Study Abroad Plan

Working group members were recruited via an advertisement on the RANZCR website in October 2014. The working group was chaired by Dr Ronny Low, Chair of the RANZCR CT Reference Group. The Australian and New Zealand Society of Nephrology recommended Prof Robert Walker to provide expert advice on renal issues. Prof Stacy Goergen provided expert advice on guideline development principles and metformin. Dr Jules Comin provided expert advice on the renal effects of contrast media. Ms Christine Vanderley-Reichner provided the radiographer / medical imaging technologist perspective on contrast media administration.

Drafting of individual sections of the guideline document was delegated to subgroups of the Contrast Guideline Working Group (CGWG) and these drafts were then edited and agreed upon by the group via teleconferences and email communication.

1.5 Acknowledgments

RANZCR would like to thank the following individuals for providing ad hoc expert advice as required to the CGWG on various aspects of the guideline:

Peter Davoren
Director Diabetes and Endocrinology, Gold Coast University Hospital, QLD
Associate Professor, Griffith University School of Medicine, Southport, QLD

Tony Eliseo
Emergency Physician, Royal Adelaide Hospital, SA

Peter Kerr
Professor / Director, Nephrology Unit, Monash Health, Clayton, VIC

Adam Stormont
Senior Pharmacist - New Technology and Systems Development, Monash Health, Clayton VIC

Helena Teede
Executive Director Monash Partners
Director Monash Centre for Health Research and Implementation, SPHPM,
Monash University Diabetes and Endocrine Unit, Monash Health
President, Endocrine Society of Australia

Sophia Zoungas
Professor Sophia Zoungas
Chair of Diabetes, Vascular Health and Ageing
Deputy Director, Monash Centre for Health Research and Implementation, SPHPM, Monash University
Chair, Steering Committee, National Association of Diabetes Centres
Vice President & President Elect, Australian Diabetes Society

1.6 Consultation

A consultation draft was published on the RANZCR website, circulated to all RANZCR members and to the following organisations:

- Australasian College for Emergency Medicine
- Australia and New Zealand Society of Vascular Surgeons
- Australian Diabetes Society
- Australian and New Zealand College of Anaesthetists
- Australian and New Zealand Society of Nephrology

- Australian Diagnostic Imaging Association
- Australian Institute of Radiography
- Australasian Society of Clinical Immunology and Allergy
- Consumer Health Forum
- Commonwealth Department of Health
- Endocrine Society of Australia
- Kidney Health Australia
- Medical Imaging Nurses' Association of Australia
- Royal Australian College of General Practitioners
- The Cardiac Society of Australia and New Zealand
- The Royal Australasian College of Physicians
- The Royal Australian and New Zealand College of Obstetricians and Gynaecologists

Feedback received was considered in finalising this guideline.

1.7 Determination of Scope

(a) To consider key information covered by international peak professional body guidelines on this topic in formulating this guideline.

(b) To provide the results of literature searches on specific questions in regard to new or controversial issues relating to iodinated contrast media administration as part of medical imaging procedures.

(c) To provide references for guideline recommendations where these were derived directly from published scientific evidence.

(d) To clearly distinguish expert consensus recommendations from those supported by such scientific evidence.

(e) To develop point of care tools for patients and practitioners to support guideline recommendation implementation.

(f) To consider the health economic consequences of guideline recommendations.

(g) To make the draft guideline available for public consultation for a six-week period at the end of the development process and consider the results of this feedback in producing the final guideline.

(h) To survey the RANZCR membership regarding the recommendations.

1.8 Format

The CGWG agreed that the final guideline document should be delivered in multiple formats to enhance implementation including:

(a) An electronic document

(b) Printable point of care tools

(c) Patient Risk Factor checklist regarding

  (i) Renal risk factors

  (ii) Risk factors for anaphylactic reaction

  (iii) Other risk factor information that should be collected prior to contrast media administration

(d) Wall chart for clinical areas – treatment of atopic and anaphylactic reactions

(e) Equipment box checklist – treatment of atopic and anaphylactic reactions

(f) Patient information about the immediate and delayed risks of contrast media administration

1.9 Funding

No funding of the CGWG was sought from or provided by any external source. Librarian services were provided in kind by Ms Marie Garubba, medical librarian / information specialist, Monash Centre for Health Research and Innovation, Monash University Department of Preventive Medicine, Monash Health, Clayton, Victoria. Secretariat support to the working group, copyediting of the drafts of this document, and production of point of care tools was provided by RANZCR. CGWG members were not remunerated for their contributions to this project.

1.10 Conflicts of Interest

Dr Ronny Low notified the working group of a potential conflict of interest, having accepted an educational trip to Korea sponsored by Bayer Healthcare. Dr Low uses a variety of products, including Bayer, in public hospital work but does not use Bayer products in private practice.

1.11 Review Process

(a) If, in the view of the CGWG, new scientific evidence emerges that changes any of the key recommendations in this document, revision of the appropriate section of this document will occur accompanied by date of the revision.

(b) Notification to the membership via email or via regular RANZCR communications will occur when such revisions take place, depending upon the nature and medical urgency of the revision.

(c) Review of the entire guideline document three years from the date of final publication will occur regardless of interim revisions to one or more sections of this document.

(d) This document supersedes the *RANZCR Guidelines for Iodinated Contrast Administration – 2009 Edition*.

1.12 Definitions and Abbreviations

AED means Automated External Defibrillator

AKI mean Acute Kidney Injury

CI – AKI means Contrast Induced Acute Kidney Injury

CKD-EPI means Chronic Kidney Disease Epidemiology Collaboration

College means The Royal Australian and New Zealand College of Radiologists

CGWG means Contrast Guideline Working Group

eGFR means Estimated Glomerular Filtration Rate

FDA US Food and Drug Administration

IA means intra-arterial

IV means intravenous

Medsafe means New Zealand Medicines and Medical Devices Safety Authority

Member means a member of the College

RANZCR means The Royal Australian and New Zealand College of Radiologists

TGA means Therapeutic Goods Administration

2. RISK ASSESSMENT AND MANAGEMENT OF PATIENTS PRIOR TO IODINATED CONTRAST MEDIA ADMINISTRATION

2.1 Hypersensitivity Reaction to Iodinated Contrast Media

2.1.1 Background

Hypersensitivity reactions to iodinated contrast media can be classified into immediate anaphylactic reactions and delayed reactions. Histamine release, along with other active biological mediators such as serotonin, prostaglandins, bradykinin, leukotrienes, adenosine and endothelin have been implicated. Reactions may be classified as mild, moderate or severe.

Mild contrast media reactions include flushing, nausea, pruritus, vomiting, headache and mild urticaria. They are usually self-limited and resolve without specific treatment. Such may be seen in up to 1% of patients after non-ionic low-osmolality contrast media administration.

Reference
Wang CL, Cohan R, Ellis JH et al. Frequency, outcome, and appropriateness of treatment of nonionic iodinated contrast media reaction. Am J Roentgenol 2008, 191: 409-15.

Moderate contrast media reactions include severe vomiting, marked urticaria, bronchospasm or other respiratory symptoms, facial/laryngeal oedema and vasovagal attacks.

Severe contrast media reactions include hypovolaemic shock, respiratory arrest, cardiac arrest and convulsions. Severe anaphylactic reactions are uncommon, occurring in less than 1 in 100,000 patients.

The current non-ionic, low osmolar iodinated contrast media are in the order of 5 to 10 times safer, in terms of mild to moderate reactions, than the older, high osmolar ionic media.

(a) There is an approximate tenfold increase in reactions to both ionic and non-ionic contrast media following a previous hypersensitivity reaction. The likelihood of a recurrent reaction has been reported to be in the order of 8% to 60%.

(b) Patients with a history of asthma experience an approximate six-fold increased risk of a hypersensitivity contrast media reaction. The risk of a reaction appears related to the degree of control of a patient's asthmatic symptoms with the risk highest in patients with unstable disease.

(c) A history of multiple allergies requiring medical treatment is associated with a 3 to 5 fold increase in the risk of an acute reaction to iodinated contrast media. Most such reactions are mild.

(d) Shellfish allergy is not associated with an increased risk of adverse reaction to intravenous iodinated contrast media, over and above the approximate 3-fold increased risk associated with other food allergies.

(e) Skin irritation or “allergy” to topical iodine antiseptic solutions is not associated with an increased risk of adverse reaction to intravenous iodinated contrast media.

2.2 Delayed Hypersensitivity Reactions

Delayed contrast media reactions occur between one hour and one week after intravascular iodinated contrast media administration. These are typically skin reactions with a maculopapular rash being most common. Less frequent skin reactions include angioedema, urticaria and erythema. Delayed hypersensitivity reactions are not typically associated with bronchospasm or laryngeal oedema.

The incidence of reported delayed sensitivity reactions varies in the literature but is likely to be 4% or less. There may be an increased incidence of late reactions to iodinated contrast media in patients who have received interleukin-2 (IL-2). The effectiveness of premedication with corticosteroids in reducing the incidence of recurrent delayed hypersensitivity contrast media reaction is unknown.

Recommendations

R1. In order to minimise the risk of iodinated contrast media administration, the medical imaging department should have systems in place to identify individuals at increased risk of adverse reactions to iodinated contrast media. A point of care tool to facilitate this is provided at the end of this document.

a) Although beta adrenergic blocking medications do not appear to significantly increase the incidence of an anaphylactic contrast media reaction, any such reaction is more likely to be moderate or severe. In addition, the effects of intramuscular adrenaline in patients taking beta blockers may be reduced and intravenous glucagon may be required in addition to adrenaline in this situation.

b) Information which should be obtained from the patient, carer and/or referring clinician before iodinated contrast media administration include:

i. History and nature of a previous reaction to iodinated contrast media or history of reaction requiring medical treatment

ii. History of asthma

iii. Previous significant allergic reactions to other substances or history of eczema

iv. Current use of beta adrenergic blockers

R2. In patients who are at increased risk of an anaphylactic reaction to iodinated contrast media:

a) Consider performing a non-contrast media study or use of alternative imaging modalities which do not require administration of iodinated contrast media (e.g. Ultrasound, MRI).

b) If, after considering the risks of a contrast media reaction and the potential benefits of the procedure, it is decided to proceed with the contrast media enhanced study:

i. Use a different non-ionic low or iso-osmolar contrast media to the one used previously in the setting of a prior reaction if possible

ii. Maintain close medical supervision

iii. Leave the cannula in place and keep the patient under observation for 30 minutes after contrast media administration

iv. Ensure emergency drugs and equipment for resuscitation are readily available

v. Be prepared to treat any adverse reaction promptly. Consider use of premedication (see below)

2.3 Premedication of Patients with Prior Anaphylactic Reactions to Iodinated Contrast Media

While safe for the majority of patients, the medical literature supporting the routine use of premedication in patients with a prior contrast media reaction is limited.

Several older studies have shown premedication with steroids or antihistamines reduce the risk of anaphylactic reactions to ionic contrast media.

There is as yet no convincing evidence that premedication with corticosteroids and/or antihistamines reduces the incidence of severe acute reactions, including death, to non-ionic contrast media.

R3. Premedication with corticosteroids, with or without antihistamines has been shown to reduce the likelihood and severity of anaphylactic reactions but there is no evidence that it reduces the likelihood of death resulting from a breakthrough anaphylactic reaction.

a) If oral corticosteroid premedication is used, it must be commenced at least 6 hours prior to the contrast media study.

b) A typical premedication regimen for adults is:

i. Prednisolone 50mg orally, given at 13 hours and 1 hour before contrast media administration.

ii. Oral non-sedating antihistamines may be added to the above premedication regimen.

2.4 Contrast Media Induced Kidney Injury and Metformin Associated Lactic Acidosis

This section is divided into five interrelated parts that are of key relevance to practice. Each section begins with background information and ends with specific recommendations for practice.

(a) Intravascular iodinated contrast media and acute kidney injury – what do we know about the risks? Who is at risk?

(b) Renal function – recommended metrics, limitations to currently available renal function estimation methods.

(c) Screening patients for their need for renal function testing – who should have renal function testing prior to administration of iodinated media.

(d) Mitigating the potential risks of intravascular iodinated contrast media administration – summary of the evidence for various strategies.

(e) Precautions in patients taking metformin containing compounds.

2.4.2 Background

Since the previous version of the RANZCR Guidelines for Iodinated Contrast Administration (2009), a substantial amount of new evidence regarding the causal relationship, if any, between intravenously administered iodinated contrast media and acute kidney injury (CI – AKI) has accumulated. The American College of Radiology Manual on Contrast Media V10, 2015 and the current European Society of Uroradiology Guidelines have revised their previous advice about the severity of renal function impairment that is associated with an increase in the risk of CI – AKI.

The key studies that have influenced recent thinking on this issue are:

1. Rao QA, Newhouse JH. Risk of nephropathy after intravenous administration of contrast material: a critical literature analysis. Radiology 2006; 239:392-397

2. Newhouse JH, Kho D, Rao QA, Starren J. Frequency of serum creatinine changes in the absence of iodinated contrast medium: implications for studies of contrast nephrotoxicity. AJR 2008; 191:376-382

3. McDonald RJ, McDonald JS, Carter RE, et al. Intravenous contrast material exposure is not an independent risk factor for dialysis or mortality. Radiology 2014; 273:714-725

4. McDonald JS, McDonald RJ, Carter RE, et al. Risk of intravenous contrast material-mediated acute kidney injury: a propensity score-matched study stratified by baseline estimated glomerular filtration rate. Radiology 2014; 271:65-73

5. McDonald RJ, McDonald JS, Bida JP, et al. Intravenous contrast material-induced nephropathy: causal or coincident phenomenon? Radiology 2013; 267:106-118

6. McDonald JS, McDonald RJ, Comin J, et al. Frequency of acute kidney injury following intravenous contrast medium administration: a systematic review and meta-analysis. *Radiology* 2013; 267:119-128

7. Davenport MS, Cohan RH, Khalatbari S, et al. The challenges in assessing contrast-induced nephropathy: where are we now? AJR 2014; 202:784-789

8. Davenport MS, Khalatbari S, Cohan RH, et al. Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material: risk stratification by using estimated glomerular filtration rate. Radiology 2013; 268:719-728

9. Davenport MS, Khalatbari S, Dillman JR, et al. Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated iodinated contrast material. Radiology 2013; 267:94-105.

10. McCullough P, A, Brown J, R, Effects of Intra-Arterial and Intravenous Iso-Osmolar Contrast Medium (Iodixanol) on the Risk of Contrast-Induced Acute Kidney Injury: A Meta-Analysis. Cardiorenal Med 2011;1:220-234.

In addition, the Contrast Guideline Working Group commissioned a literature review to identify any systematic reviews since the McDonald et al review in 2013. The full references, methods and results are summarised here and in the detailed methods provided in Appendix 2.

In summary, these studies have raised questions about whether intravenous administration of iodinated contrast media results in a clinically significant rate of biochemical evidence of renal function impairment, increased risk of dialysis or death related to the development of AKI.

Based on detailed evaluation of the methodology and results of these studies, the following conclusions can be made:

(a) The risk of contrast-induced acute kidney injury (CI-AKI) remains uncertain for patients with an estimated glomerular filtration rate (GFR) less than 45 mL/min/1.73m^2, but if there is a risk, it is greatest in those with estimated GFR less than 30 mL/min/1.73m^2.

(b) There is greatest controversy about the risk of CI-AKI for patients with eGFR less than 30 mL/min/1.73m^2 with the odds of CI-AKI occurring in this group as a result of a single intravenous dose of iodinated contrast media being either the same as or up to 7 times greater than patients with normal renal function.

(c) Intra-arterial administration is associated with a higher risk for CI-AKI than is intravenous administration. This may relate both to the usually larger volume of contrast media administered and the potential for renal embolisation.

(d) No prospective randomised controlled trials have been conducted to test the hypothesis that there is a difference in the likelihood of AKI developing after iodinated contrast media administration in individuals with various levels of pre-existing renal function impairment at the time of contrast administration.

(e) The retrospective studies listed above that concluded that intravenous administration of iodinated contrast media does not cause AKI, or an increased risk of death or dialysis due to AKI, used propensity matching for a series of purported risk factors for CI-AKI, such as age, diabetes, and baseline renal function. In doing so, they retrospectively created a “control” population for the purpose of matching baseline risk of patients who did and did not receive intravenous contrast media.

(f) The studies disagreed with regard to the existence of and extent of risk of CI-AKI for patients with eGFR less than or equal to 45 mL/min/1.73m^2.

(g) Evidence of changing (actively increasing or decreasing) renal function immediately prior to contrast media administration was identified in one study as an independent risk factor for AKI following iodinated contrast media administration.

(h) Instability of kidney function in this context was strictly defined and can thus only be regarded as an independent risk factor, based on this study, if these strict conditions are met:

  (i) Two renal function measurements, one more than 5 days before CT (time unspecified) and the other within 5 days of the CT. Serum creatinine was used in this study as the metric.

  (ii) A serum creatinine 1.5 times higher just prior to CT compared with the earlier value (greater than 5 days before) OR serum creatinine just prior to CT that is 50% lower than the earlier value.

Reference

Davenport MS, Khalatbari S, Cohan RH, et al. Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material: risk stratification by using estimated glomerular filtration rate. Radiology 2013; 268:719-728.

(i) Methodological issues with the concept of using a retrospective study design and propensity matching include:

  (i) Failure to match for all potential confounders of the CI-AKI / contrast media administration relationship such as use of pre- and / or post procedural hydration and indication for the CT. This may be of particular relevance for emergency patients who more often have sepsis and haemodynamic instability as risk factors that could increase the risk of non-contrast media related AKI on blood testing within the days following CT.

(ii) Because these retrospective studies relied on performance of eGFR and / or serum creatinine measurement 24-72 hours post contrast media administration (otherwise the patients were excluded from the study), they have almost exclusively studied inpatients who did and did not receive iodinated contrast media as part of their CT examination. These patients are on average sicker than outpatients. Whether the lack of influence of iodinated contrast media administration on development of AKI can be extrapolated to healthier outpatients, who are the majority undergoing contrast media enhanced CT examinations in Australia and New Zealand, is unclear.

Recommendations

R4. Intravascular iodinated contrast media should be given to any patient regardless of renal function status if the perceived diagnostic benefit to the patient, in the opinion of the radiologist and the referrer, justifies this administration.

R5. Emergency imaging procedures requiring contrast media administration e.g. acute stroke, acute bleeding, trauma etc. should not be delayed in order to obtain renal function testing results prior to the procedure.

R6. The risk of intravenous contrast media related acute kidney injury (CI-AKI) is likely to be non-existent for patients with eGFR greater than 45 mL/min/1.73m^2.No special precautions are recommended in this group prior to or following intravenous administration of iodinated contrast media.

R7. The risk is of intravenous CI-AKI is also very likely to be low or non-existent for patients with eGFR 30 - 45 mL/min/1.73m^2. Universal use of periprocedural hydration in this group to prevent the theoretical risk of CI-AKI cannot be recommended but patients with impaired function in this range that is acutely deteriorating rather than stable may benefit from this intervention.

R8. In patients with severe renal function impairment (eGFR less than 30 ml/min/1.73m^2) or actively deteriorating renal function (acute kidney injury) careful weighing of the risk versus the benefit of iodinated contrast media administration needs to be undertaken. Consideration should be given to periprocedural renal protection using intravenous hydration with 0.9% saline (see relevant section). However, severe renal function impairment should not be regarded as an absolute contraindication to medically indicated iodinated contrast media administration.

2.5 Clinical Estimation of Renal Function

2.5.1 Background

(a) Estimation of the actual glomerular filtration rate (GFR) to assess kidney function facilitates the detection, evaluation, and management of kidney disease.

(b) Actual GFR is the best indicator of renal function, but there is no substance that can be administered in a routine clinical setting, that is purely excreted by the human kidney (without metabolism, reabsorption, or secretion) that would allow this measurement to be made in vivo in clinical practice. Therefore, GFR has to be estimated. This estimate is abbreviated as eGFR.

(c) Recent clinical studies indicates that eGFR may better identify patients at risk of AKI from any cause, including iodinated contrast media, than will serum creatinine.

(d) Manual estimation of GFR (eGFR) for clinical purposes using creatinine, age, gender and race should use the CKD-EPI creatinine equation which is in common use in Australia and New Zealand pathology laboratories. In most cases eGFR is provided routinely if a plasma creatinine has been requested.

(e) eGFR is less reliable in sick, hospitalised, frail, elderly, and cachectic or malnourished patients and will tend to overestimate renal function in these groups.

(f) eGFR using the below formula will automatically decrease with age even in healthy older individuals. The same serum creatinine in a 20 year old and a 75 year old can result in the former being classified as “low risk” for CI-AKI and the other as “higher risk” if a simple cut off value of eGFR is used.

2.5.2 CKD EPI Formula

$GFR = 141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018[\text{if female}] \times 1.159[\text{if black}]$

$\kappa = 0.7$ if female
$\kappa = 0.9$ if male

$\alpha = -0.329$ if female
$\alpha = -0.411$ if male

min = The minimum of Scr/κ or 1
max = The maximum of Scr/κ or 1

Scr = serum creatinine (mg/dL)

Reference

Levey AS, Stevens LA, et al. A New Equation to Estimate Glomerular Filtration Rate. Ann Intern Med. 2009; 150:604-612.

Recommendations

R9. eGFR using the CKD-EPI formula using serum creatinine, patient age, gender and race, should be used in preference to serum creatinine to identify patients with severely impaired renal function.

R10. eGFR should not be relied upon as an accurate indicator of renal function in patients who are known to have acute kidney injury for any reason.

2.6 Screening Patients with Regard to Their Need for Renal Function Testing

Not all patients undergoing procedures involving intravenous iodinated contrast media administration require formal testing of their renal function prior to contrast media administration. Severe renal function impairment that ideally should be identified prior to iodinated contrast media administration is rare in patients who are unaware that they have either diabetes or kidney disease. The AusDiab Study established that the frequency of undiagnosed severe (eGFR less than 30ml/min/1.73m^2) renal function impairment in Australian adults aged over 25 years was less than 1%.

Reference

Chadban SJ, Briganti EM, Kerr PG, Dunstan DW, Welborn TA, Zimmet PZ, Atkins RC. Prevalence of kidney damage in Australian adults: The AusDiab kidney study. J Am Soc Nephrol. 2003 Jul;14(7 Suppl 2):S131-8.

Many risk factors have been thought to be associated with subsequent CI-AKI but current guidelines do not agree on which ones should result in pre-contrast media renal function testing, with the exception of known kidney disease and diabetes. Furthermore, as the occurrence of severe renal impairment that the patient is unaware of is very uncommon, the usefulness of asking patients about large numbers of risk factors to identify a very small proportion of patients with clinically important renal impairment is not clear. The larger the number of screening questions, the more patients have renal function testing that does not contribute to decision making about contrast media administration or periprocedural hydration, and this adds to healthcare costs without patient benefit.

The following summary of current systematic reviews and international guideline recommendations is provided as background information.

- A recent systematic review by Moos et al (2013) "Contrast induced nephropathy in patients undergoing intravenous (IV) contrast enhanced computed tomography (CECT) and the relationship with risk factors: a meta-analysis." European Journal of Radiology 82(9): e387-399 found that only:
  - Known renal insufficiency
  - diabetes
  - malignancy
  - age over 65 years
  - use of non-steroidal anti-inflammatory drugs

  were positively associated with the development of CI-AKI but that hypertension, anaemia, and congestive heart failure were not.

  Mc Donald et al. found that the following were independent risk factors for the outcomes of death or dialysis following iodinated contrast media administration:

  - acute or chronic kidney disease
  - congestive heart failure and
  - diabetes mellitus

  The European Society of Uroradiology Guidelines on Contrast Media Version 8.1 lists the following as patient related risk factors for CI-AKI:

  - Diabetic nephropathy
  - Dehydration
  - Congestive heart failure (NYHA grade 3-4) and low LVEF
  - Recent acute myocardial infarction (less than 24 hours)
  - Intra-aortic balloon pump
  - Peri-procedural hypotension
  - Low haematocrit
  - Age over 70 years
  - Concurrent nephrotoxic drugs

  Procedurally related risks are:

  - High contrast media volumes
  - Multiple administrations of contrast media within a few days

- The ACR Manual on Contrast Media, Version 10, provides a list of suggested indications for renal function assessment before the intravascular administration of iodinated contrast media (p37). If none of these risk factors are present, no renal function testing is required before intravascular iodinated contrast media administration. These risk factors are:

- Age greater than 60
- History of kidney disease including
  - Dialysis
  - Kidney transplant
  - Single kidney
  - Renal cancer
  - Renal surgery
- History of hypertension requiring medical therapy
- History of diabetes mellitus
- Metformin or metformin containing drug combinations (due to the risk of lactic acidosis, not CI-AKI, if the patient has impaired renal function while taking metformin).

However, it is stated in the ACR manual that this list is based on consensus and a "blend" of published risk factors.

The maximum safe interval between an eGFR result and contrast media administration is unknown, with various guidelines recommending intervals of 7 days (ACR), 30 days (ESUR), 3 months (RCR and RANZCR 2009) and 6 months (CAR) as "consensus" rather than evidence based recommendations.

References

Moos et al. Contrast induced nephropathy in patients undergoing intravenous (IV) contrast enhanced computed tomography (CECT) and the relationship with risk factors: a meta-analysis. European Journal of Radiology 82(9): e387-399

McDonald et al Risk of intravenous contrast material-mediated acute kidney injury: a propensity score-matched study stratified by baseline estimated glomerular filtration rate. Radiology 2014; 271:65-73"

American College of Radiology. ACR Manual on Contrast Media, V10.1. 2015.

Thomsen HS, Webb JAW (eds.) Contrast Media. Safety Issues and ESUR Guidelines 3rd ed. Heidelberg, Springer 2013.

Recommendations

R11. Prior to intravascular administration of iodinated contrast media patients should be asked the following. If present, an eGFR should be obtained prior to iodinated contrast media administration in non-emergency patients.

a) known kidney disease (including kidney transplant)

b) presence of diabetes

c) whether they are currently taking a drug containing metformin. (see Point of Care Risk Assessment of Patients Who Are To Receive Intravascular (Arterial Or Venous) Iodinated Contrast Media)

R12. Non-anuric patients currently on short or long term dialysis may require consultation with a renal physician prior to iodinated contrast media administration.

R13. Age should not be considered as an independent risk factor that should mandate testing as eGFR declines with age even in healthy individuals, due to the way it is calculated.

R14. The time elapsed between renal function testing and contrast media administration should be governed by clinical judgment based upon the likelihood that renal function has deteriorated to a clinically significant degree since the renal function was assessed.

2.7 Periprocedural Strategies to Mitigate the Risk of CI – AKI in Higher Risk Individuals

The National Institute for Clinical Excellence (NICE) in the United Kingdom has published an evidence-based guideline regarding renal protective strategies for patients undergoing procedures involving intravascular iodinated contrast media administration. The systematic review conducted for this guideline included almost exclusively studies of intra-arterial, higher dose contrast media administration e.g. catheter coronary angiography and interventional angiography. Therefore, the recommendations regarding periprocedural hydration are not readily applicable to patients receiving lower contrast media doses via the intravenous route.

The full guideline can be found here: http://www.nice.org.uk/guidance/cg169/evidence

RANZCR commissioned a literature review to answer the following question (see Appendix 2 for detailed methodology and results)

“In patients with impaired renal function who are to receive intravenous iodinated contrast medium how does oral administration of fluids/NAC (for the purpose of hydration) compare with intravenous administration of fluids/NAC in preventing contrast induced acute kidney injury?”

Based on the NICE review and the review commissioned for this guideline, the following recommendations are made and apply to intra-arterial administration.

The equivalence of oral periprocedural hydration to intravenous delivery of the same fluids is not supported by current evidence. Oral periprocedural hydration cannot be recommended as a substitute for the intravenous administration route based on lack of demonstrated efficacy. This may relate to variable absorption / administration of oral fluids and lack of standardisation of an administration regimen.

There is no evidence to support a specific volume or duration of pre and post procedural hydration due to heterogeneity of the published studies. A practical protocol suggested in the Guidelines of the ESUR on Contrast Media v8.1 is 0.9% intravenous saline, 1.0-1.5 ml/kg/h, for at least 6 hours before and after contrast media injection.

Exact administration protocols depend on, amongst other things, the patient’s pre-test risk of cardiac failure / pulmonary oedema as a result of intravenous administration of normal saline.

Recommendations

R15. For patients who are at higher risk of CI- AKI, pre and post procedural 0.9% IV saline is recommended as the first line preventive strategy to mitigate the risk of CI-AKI.

R16. The evidence in support of the additional benefit of N – acetyl cysteine and/or sodium bicarbonate alone or in combination with intravenous 0.9% saline is mixed and currently these additional measures are not recommended due to additional expense and complexity without clear evidence of incremental risk reduction.

2.8 Metformin and Contrast Media

2.8.1 Background

The theoretical risk of lactic acidosis being precipitated by iodinated contrast media administration is entirely the same as the risk of CI-AKI. Iodinated contrast media administration does not precipitate lactic acidosis by another independent mechanism.

Therefore, patients with stable renal function and eGFR greater than 30mL/min/1.76m^2 are at low to no risk of developing lactic acidosis as a direct consequence of iodinated contrast media administration alone.

References

Goergen SK, Rumbold G, Compton G, Harris C. Systematic review of current guidelines, and their evidence base, on risk of lactic acidosis after administration of contrast medium for patients receiving metformin. Radiology.2010 Jan;254(1):261-9.

ESUR Guidelines on Contrast Media v8.1 http://www.esur.org/guidelines/

Recommendations

R17. Intravenous administration of iodinated contrast media: Patients receiving intravenous iodinated contrast media with an eGFR above 30 ml/min/1.73 m^2 should continue taking metformin. Patients with an unknown recent eGFR or an eGFR less than 30 ml/ min/1.73 m^2, or who are unwell or have deteriorating renal function should cease metformin for at least 48hrs from the time of the examination and an eGFR performed prior to restarting metformin.

R18. Intra-arterial administration of iodinated contrast media: Patients undergoing an intra-arterial procedure requiring iodinated contrast media with an eGFR above 45 ml/min/1.73 m^2 should continue taking metformin. Patients undergoing an intra-arterial procedure involving larger volumes of contrast media and/or a procedure involving a risk of renal embolisation with an unknown recent eGFR or an eGFR less than 45 ml/ min/1.73 m^2, or who are unwell or have deteriorating renal function should cease metformin for at least 48hrs following intra-arterial administration of contrast media and have eGFR estimated prior to restarting metformin.

2.9 Other Medical Conditions That Need to Be Considered Before the Administration of Iodinated Contrast Media

2.9.1 Thyroid Disease

Patients with clinical or biochemical evidence of hyperthyroidism prior to iodinated contrast media administration are at risk of developing clinical hyperthyroidism and / or acute thyrotoxicosis.

Patients with:

- normal thyroid function OR
- treated hyperthyroidism that is medically controlled

are at low risk of developing clinically important or sustained hyperthyroidism following iodinated contrast media administration.

Patients with:

- Untreated hyperthyroidism OR

- A hyperfunctioning thyroid nodule with or without a multinodular goitre, especially if they reside in an iodine deficient environment

are at increased risk of developing clinically important thyrotoxicosis following iodinated contrast media administration.

A recent study has suggested that iodinated contrast media are associated with biochemical evidence of both hyper and hypothyroidism but that this is most often temporary and subclinical.

The large amount of iodine within contrast media can prevent uptake of thyroid-specific radioisotopes into the thyroid for up to 8 weeks after contrast media administration.

Reference

Satoh M, Aso K, Katagiri Y. Thyroid Dysfunction in Neonates Born to Mothers Who Have Undergone Hysterosalpingography Involving an Oil-Soluble Iodinated Contrast Medium. Horm Res Paediatr. 2015 Sep 25.

Recommendations

R19. Patients with known or suspected hyperthyroidism (clinical or biochemical) should be tested and treated for this in consultation with the referrer or an endocrinologist prior to contrast media administration. Treatment typically consists of beta blockade and carbimazole.

R20. If contrast media administration is urgently required for a patient with known untreated hyperthyroidism, the advice of an endocrinologist should be sought whenever possible prior to or following contrast media administration in patients with biochemical or clinical hyperthyroidism. Thyrotoxicosis generally occurs three to six weeks following iodinated contrast media administration. Emergency procedures can be performed if benefit outweighs risk and the patient can be appropriately monitored during this period.

R21. Patients who are known to have a hyperfunctioning thyroid nodule, with or without associated multinodular goitre, are at increased risk of thyrotoxicosis following intravenous iodinated contrast media administration, even if they have no clinical / biochemical evidence of hyperthyroidism. Patients in this situation should be advised about this risk and monitored for the development of this complication in the weeks following the injection.

R22. Routine thyroid function testing of all patients with multinodular goitre prior to contrast media administration is not recommended.

R23. Patients who are to undergo diagnostic or therapeutic procedures involving radioisotope scanning of the thyroid (including thyroid cancer treatment) will have radioisotope uptake prevented for 8 weeks following iodinated contrast medai administration. This risk should be considered and weighed against the benefits of iodinated contrast media administration.

Reference

Kornelius E, Chiou JY, Yang YS, Peng CH, Lai YR, Huang CN. Iodinated Contrast Media Increased the Risk of Thyroid Dysfunction: A 6-year retrospective cohort study. J Clin Endocrinol Metab. 2015 Sep;100(9):3372-9. doi: 10.1210/JC.2015-2329. Epub 2015 Jul 13.

2.9.2 Myasthenia Gravis

It remains controversial whether iodinated contrast media are contraindicated in this group of patients. A recent study found a 6.7% incidence of symptom exacerbation in patients with myasthenia gravis following intravenous administration of low osmolar contrast media compared with 0.6% of patients who did not receive it.

Recommendation

R24. Symptoms of myasthenia gravis, including breathing difficulties, may be worsened by iodinated contrast media although the risk is thought to be low. Patients should be advised of the possibility of worsened symptoms prior to contrast media administration.

Reference

Somashekar DK, Davenport MS, Cohan RH, Dillman JR, Ellis JH. Effect of Intravenous Low-Osmolality Iodinated Contrast Media on Patients with Myasthenia Gravis. *Radiology* 2013.

2.9.3 Phaeochromocytoma

Phaeochromocytomas and paragangliomas may secrete catecholamines and can induce life threatening episodes of hypertension.

Intravenous non-ionic iodinated contrast media has not been demonstrated to produce a statistically significant elevation in catecholamine levels in comparison to injection of normal saline.

Recommendations

R25. Direct intravascular injections of iodinated contrast media into adrenal or renal arteries or veins may precipitate a hypertensive crisis and should therefore be avoided in patients with known phaeochromocytoma, unless the patient is appropriately treated with alpha plus or minus beta blockers.

R26. No specific preparation is required prior to intravenous administration of iodinated contrast media in patients with a suspected phaeochromocytoma

Reference

Blake MA, Kalra MK, Maher MM et-al. Pheochromocytoma: an imaging chameleon. Radiographics. 2004;24 Suppl 1

Leung K, Stamm M, Raja A et-al. Pheochromocytoma: the range of appearances on ultrasound, CT, MRI, and functional imaging. AJR Am J Roentgenol. 2013;200 (2): 370-8.

Bessell-Browne R; O'Malley ME, CT of pheochromocytoma and paraganglioma: Risk of adverse events with IV administration of nonionic contrast material. By AJR. American Journal Of Roentgenology [AJR Am J Roentgenol], 2007 Apr; Vol. 188 (4), pp. 970-4;

Smita K. Baid, MD; Edwin W. Lai, BS; Robert A. Wesley, PhD; Alex Ling, MD; Henri J.L.M. Timmers, MD, PhD; Karen T. Adams, MSN, CRNP; Anna Kozupa, MD; and Karel Pacak, MD, PhD, DSc. Brief Communication: Radiographic Contrast Infusion and Catecholamine Release in Patients with Pheochromocytoma . Ann Intern Med. 2009;150(1):27-32

2.9.4 Sickle Cell Disease

Recommendation

R27. There is no known serious medical risk associated with iodinated contrast media administration to patients with sickle cell disease. However, patients with sickle cell disease (homozygous HbS) should be advised that a small proportion of patients experience temporary worsening of pain following intravenous iodinated contrast media administration.

Reference

Safety of iodinated intravenous contrast medium administration in sickle cell disease.Campbell KL, Hud LM, Adams S, Andrel J, Ballas SK, Feldman AM, Axelrod D.Am J Med. 2012 Jan;125(1):100.

2.9.5 Interleukin-2 (IL-2) Therapy

Interleukin-2 therapy is rarely used in Australia or New Zealand at present. Limited older studies suggested an increased risk of delayed anaphylactic reaction in patients receiving iodinated contrast media who were on IL-2 therapy. Patients currently taking IL-2 or who have finished IL-2 therapy in the past 6 months should be cautioned about the risk of a delayed contrast media reaction although no specific precautions are required. Corticosteroid pre-medication is not recommended as it may counteract the effects of IL-2.

Recommendation

R28. Patients currently taking or who have finished IL-2 therapy in the past 6 months should be cautioned regarding a possible mild increase in the risk of a delayed anaphylactic contrast media reaction. No further precautions are required.

Reference

ESUR Guidelines on Contrast Media v8.1 http://www.esur.org/guidelines/

Boehm I. Is interleukin-2 therapy still a risk factor for adverse reactions in concert with iodinated contrast medium injection? Act Radiol 2009, 50: 752-3.

2.10 Breast Feeding

Recommendations

R29. Cessation of breast feeding or expression and discarding of breast milk after iodinated contrast media administration are not required.

Reference

Bettmann MA. Frequently asked questions: iodinated contrast agents. Radiographics. 2004;24 Suppl 1 (suppl_1): S3-10.

Tremblay E, Thérasse E, Thomassin-Naggara I et-al. Quality initiatives: guidelines for use of medical imaging during pregnancy and lactation. Radiographics. 2012;32 (3): 897-911.

Wang PI, Chong ST, Kielar AZ et-al. Imaging of pregnant and lactating patients: part 1, evidence-based review and recommendations. AJR Am J Roentgenol. 2012;198 (4): 778-84.

Kubik-Huch RA, Gottstein-Aalame NM, Frenzel T et-al. Gadopentetate dimeglumine excretion into human breast milk during lactation. Radiology. 2000;216 (2): 555-8.

2.11 Pregnancy

The Therapeutic Goods Administration (TGA) currently categorises the safety of iodinated contrast media during pregnancy as B1 or B2. Animal studies have not shown evidence of an increased occurrence of fetal injury. Limited cases of pregnant women receiving intravenous iodinated contrast media during pregnancy have shown no significant increase in the frequency of malformations or adverse effects.

Reference

Atwell TD, Lteif AN, Brown DL et al. Neonatal thyroid function after administration of IV iodinated contrast agent to 21 pregnant patients. Am J Roentgenol 2008, 191: 268-71.

Rajaram S, Exley CE, Fairlie F et al. Effect of antenatal iodinated contrast agent on neonatal thyroid function. Br J Radiol 2012, 85: e238-42.

Kochi MH, Kaloudis EV, Ahmed W et al. Effect of in utero exposure of iodinated intravenous contrast on neonatal thyroid function. J Comput Assist Tomogr 2012, 36: 165-9.

Bourjeily G, Chalhoub M, Phornphutkul C et al. Neonatal thyroid function: effect of a single exposure to iodinated contrast medium in utero. Radiol 2010, 256: 744-50.

A recent Japanese study has suggested that the risk of neonatal biochemical hypothyroidism increased from 0.7% to 2.4% in infants born to women who had iodinated oil contrast media used for hysterosalpingography immediately prior to conception. The risk was higher in women receiving higher volumes of contrast media. It is unclear whether this increased risk would also apply to water soluble media, which are more commonly used for this procedure in Australia and New Zealand.

Recommendation

R30. Infants born to women who received iodinated contrast media while pregnant should have testing for hypothyroidism in the neonatal period. In Australia and New Zealand, this is routinely performed in every neonate via a heel prick test as part of formal newborn screening programs.

Reference

Satoh M, Aso K, Katagiri Y. Thyroid Dysfunction in Neonates Born to Mothers Who Have Undergone Hysterosalpingography Involving an Oil-Soluble Iodinated Contrast Medium. Horm Res Paediatr. 2015 Sep 25.

3. GENERAL SAFETY ISSUES

Any radiological examination requiring administration of iodinated contrast media involves the risk of an adverse contrast media reaction. While most reactions are minor, life-threatening and fatal reactions may occur without warning. It is essential to minimise the risk of contrast media reactions and to be prepared to appropriately treat any reactions that may occur. The risk of a contrast media reaction should always be carefully weighed against the expected benefit from a contrast media enhanced imaging examination.

3.1 Intravenous Access and Contrast Media Extravasation

Recommendations

R31. A medical practitioner (ideally a radiologist) must be immediately available to attend to the patient in the event of an emergency or complication of iodinated contrast media administration and must be trained in recognising and treating severe contrast media reactions, including anaphylaxis.

R32. The task of obtaining intravenous access for administering intravenous contrast media can be performed by a medical practitioner (ideally a radiologist) or delegated to a suitably qualified healthcare professional trained and certified in cannulation for contrast media administration as per Appendix A of the RANZCR Standards of Practice for Diagnostic and Interventional Radiology. This training and certification may be performed by the radiology practice.

R33. The intravenous cannula should be left in place and the patient instructed to remain under supervision at the facility where contrast media has been administered for at least 15 minutes following contrast media injection. This period should be 30 minutes for patients at increased risk of an anaphylactic reaction.

R34. Extravasation of contrast media into the subcutaneous tissues is uncommon occurring in less than 1% of patients. Most injuries are minor and resolve without permanent injury with conservative treatment. Extravasation occurs more frequently with use of power injectors in comparison to hand injection of contrast media. Risk factors include use of small veins, fragile or previously damaged veins, obesity and large volume contrast

media injections. The risk of contrast media extravasation can be reduced by use of an appropriately sized vein in relation to the contrast media injection rate and testing of the cannula with saline prior to contrast media administration. Where possible, direct visual monitoring of the injection site during the injection is advised.

R35. If contrast media extravasation occurs, conservative treatment with limb elevation, cold or warm compresses and monitoring for compartment syndrome is recommended. Surgical referral is required if serious injury such as cutaneous ulceration, tissue necrosis or compartment syndrome develop.

3.2 Training

Recommendations

R36. Healthcare practitioners and medical practitioners who administer intravenous contrast media shall be trained in the recognition of contrast media reactions, the procedures for treating these reactions, and resuscitation procedures.

R37. Suitably trained people who administer intravenous contrast media shall also be trained in basic life support including CPR, and in advanced life support where possible.

3.3 Contrast Media Administration

Recommendations

R38. Iodinated contrast media should be administered in accordance with the manufacturers' product information and the TGA (in Australia) or Medsafe (in New Zealand) registration requirements. This applies to contrast media, contrast bottles/containers, syringes and all components of the delivery system. Radiologists and other health care practitioners who administer contrast media should be aware of relevant national guidelines for the safe administration of medication.

3.4 Emergency Equipment

Recommendations

R39. The following equipment must be readily available and within or nearby any room in which contrast media is to be injected (adult or paediatric sizes are optional for facilities that do not inject adult or paediatric patients, respectively):

a) Automated external defibrillator (AED)

b) Stethoscope, sphygmomanometer

c) Cardiac monitor

d) Pulse oximeter

e) Oxygen cylinders or wall-mounted oxygen source, flow valve, tubing, oxygen masks (adult and paediatric sizes if adult and paediatric patients are treated at the facility)

f) Suction: wall-mounted or portable; tubing and catheters

g) Oral and/or nasal airways: rubber/plastic

h) Bag and mask device; masks in adult and paediatric sizes; protective barriers for mouth-to-mouth respiration are optional if the bag-valve-mask device is stocked

i) Nebuliser equipment.

j) Intravenous solutions (0.9% [normal] saline and IV tubing. 500ml or 1litre bags and also 10ml ampoules for mixing of IV medication.

k) Syringes and IV cannulas: variety of sizes; tourniquets

l) Needles: Several sizes

m) Necessary medications:

i. Adrenaline 1:1000, 1mg/mL

ii. Atropine (eg. 1-mg in 10-ml preloaded syringe)

iii. Salbutamol inhaler with or without spacer

iv. Salbutamol for nebuliser

v. Hydrocortisone

vi. Nitroglycerin (GTN) – 0.6mg tabs, sublingual or 0.4mg/dose spray

vii. Glucagon 1-2mg IV

n) Optional medications:

i. Frusemide 20-40mg IV

ii. Labetalol 20mg

iii. Dextrose 50%

iv. Antiemetic drugs e.g. ondansetron

v. Aspirin (for chest pain where myocardial ischemia is a consideration)

3.5 Contrast Media Storage, Warming and Disposal

Recommendations

R40. Contrast media is to be stored in designated cupboards / shelving with clear separation of type, volume and density to prevent confusion.

R41. Contrast media is to be stored away from direct sunlight.

R42. Contrast media is to be stored away from radiation sources.

R43. Contrast media is to be rotated as new orders arrive with new stock placed at the rear of the storage.

R44. Contrast media is to remain stored in original packaging until being placed in a contrast media warmer or used.

3.5.1 Contrast media warmer

Intravenous contrast media viscosity is related to its ambient temperature. Warming the media from 20°C to 37°C decreases its viscosity (cP) resulting in lower injection pressures and may allow a reduction in cannula or catheter diameter. There is insufficient data to support the idea that warming the contrast media reduces the number of adverse reactions. It has been reported that warmed contrast media reduces the rate of contrast media extravasations.

Recommendations

R45. Contrast media warmers should not be used for long-term storage of contrast media. Follow the manufacturer's directions regarding storage.

R46. Contrast media warmers should not be used for storing other products.

R47. Contrast media warmers should be cleaned monthly.

R48. Maximum and minimum temperatures of the contrast media warmer should be monitored. Major temperature variations should be reported to the quality manager (however named) and should be recorded in a temperature log. This is best done at the beginning of the day prior to door opening. The ideal temperature is 37°C.

R49. Low turnover contrast media which risks being kept in the contrast media warmer for longer than 30 days should be clearly labelled with the date placed in the contrast media warmer.

3.5.2 Disposal

Recommendations

R50. Used plastic /vials/syringes/glass vials are to be disposed of safely and should comply with national or state/territory regulatory requirements.

R51. The unused portion of an opened contrast media syringe/vial is to be discarded according to national or state/territory regulatory requirements.

R52. Disposal of damaged or outdated contrast media comply with national or state/territory regulatory requirements which may include returning contrast media to the supplier or pharmacy.

References

American Society of Radiologic Technologists: Safety Considerations In Contrast Media Handling and Administration 2007.

Mayo Department of Diagnostic Radiology Policy: Iodinated Contrast Media, Administration and Storage 2007.

Visipaque Product Information MIMS Online last reviewed 01/04/2014

Material Safety Data Sheet for Iodixanol (Visipaque)

Brunette J, Mongrain R, Rodes-Cabau J, et al. Comparative rheology of low- and iso-osmolarity contrast agents at different temperatures. Cath and Cardiov Interv 2008; 71:78-83.

Hughes PM, Bisset R. Non-ionic contrast media: a comparison of iodine delivery rates during manual injection angiography. Brit J Radiol 1991; 64:417-419.

Roth R, Akin M, Deligonul U, Kern MJ. Influence of radiographic contrast media viscosity to flow through coronary angiographic catheters. Cathet Cardiovasc Diagn 1991; 22(4):290-294.

Busch HP, Stocker KP. Iodine delivery rate in catheter angiography under pressure conditions in manual injection. Aktuelle Radiol 1998; 8:232-235.

Pugh ND. Haemodynamic and rheological effects of contrast media: the role of viscosity and osmolality. Eur Radiol 1996;

Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology 2010;256:32-61.

Hazirolan T, Turkbey B, Akpinar E, et al. The impact of warmed intravenous contrast media on the bolus geometry of coronary CT angiography applications. Korean J Radiol 2009; 10:150-155.

Schwab SA, Kuefner MA, Anders K, et al. Peripheral intravenous power injection of iodinated contrast media: the impact of temperature on maximum injection pressures at different cannula sizes. Acad Radiol 2009; 16:1502-1508.

Turner E, Kentor P, Melamed JL, et al. Frequency of anaphylactoid reactions during intravenous urography with radiographic contrast media at two different temperatures. Radiology 1982; 143:327-329.

Vergara M, Seguel S. Adverse reactions to contrast media in CT: effects of temperature and ionic property. Radiology 1996;199:363-366.

Davenport MS, Wang CL, Bashir MR, et al. Rate of contrast media extravasations and allergic-like reactions: effect of extrinsic warming of low-osmolality iodinated CT contrast media to 37oC. Radiology 2012; 262:475-484.

3.6 Patient Information and Consent

Recommendation

R53. Fellows should be familiar with the RANZCR Medical Imaging Consent Guidelines.

4. MANAGEMENT OF ANAPHYLACTIC IODINATED CONTRAST MEDIA REACTION

Severity	Signs/Symptoms	Treatment
Mild	Mild Nausea / Vomiting	Supportive measures (antiemetics if prolonged vomiting)
	Urticaria	Supportive measures
	Urticaria (protracted)	Non-sedating antihistamine(s)
Moderate	Urticaria	Non-sedating antihistamine(s)
		Consider use of adrenaline 1:1000 • In adults: 0.1-0.25ml (0.1-0.25mg) intramuscularly into the anterolateral thigh – repeat as necessary • In children: 0.01mg/kg intramuscularly up to 0.3mg maximum dose

Severity	Signs/Symptoms	Treatment
Moderate	Bronchospasm or other respiratory symptoms	Keep supine; allow patient to sit if dyspnoeic
		Oxygen by mask (6-10 L/min).
		Salbutamol or Terbutaline metered dose inhaler (2-3 deep inhalations)
		In more severe cases give Salbutamol or adrenalin by nebuliser.
		Consider adrenaline • Normal blood pressure o In adults: 1:1,000, 0.1-0.5ml (0.1-0.5mg) intra-muscularly (use smaller dose in patients with coronary artery disease or elderly patients) o In paediatric patients: 0.01mg/kg up to 0.3mg intramuscularly • Decreased blood pressure o In adults: 1:1,000, 0.5ml (0.5mg) intramuscularly o In paediatric patients: 0.01mg/kg intramuscularly
	Hypotension	Isolated hypotension • Keep supine; elevate patient's legs • Oxygen by mask (6-10L/min) • Intravenous fluid: rapidly, normal saline or lactated Ringer's solution • If unresponsive: adrenaline: 1:1,000, 0.5ml (0.5mg) intramuscularly, repeat as needed
		Vaso-vagal reaction (hypotension and bradycardia) • Keep supine, elevate patient's legs • Oxygen by mask (6-10L/min) • Atropine o In adults 0.6-1.0mg intravenously, repeat if necessary after 3-5 min, to 3mg total (0.04mg/kg). o In paediatric patients give 0.02mg/kg intravenously (max. 0.6mg per dose) repeat if necessary to 2mg total. o Intravenous fluids: rapid infusion of normal saline or Hartmann's solution 20ml/kg, repeat as necessary.
Severe	Respiratory or circulatory collapse and/or seizures	Call for resuscitation team
		Keep supine. Allow patient to sit if dyspnoeic.
		Suction and maintain airway as needed
		Oxygen by mask (6-10L/min), ventilate patient if required

<table>
<tr><th>Severity</th><th>Signs/Symptoms</th><th>Treatment</th></tr>
<tr><td rowspan="3">Severe</td><td rowspan="3">Respiratory or circulatory collapse and/or seizures</td><td>Intramuscular adrenaline into the anterolateral thigh
• In adults (and in children greater than 25kgs), adrenaline 1:1000
less than 50 kg give 0.25 -0.5mL
greater than 50 kg give 0.5mL
• In children, Adrenaline 1:1,000
1 year 10kg give 0.1mL
3 years 15kg give 0.15mL
5 years 20kg give 0.2mL
8 years 25kg give 0.25mL
• If necessary, repeat intramuscular dose every 5 minutes.
• Large doses of adrenaline may be needed, up to a maximum of 5mL (5mg).
• In adrenaline resistant cases, especially if the patient has taken beta blocking drugs, consider glucagon 1-2mg intravenous over 5 minutes.
• If the patient remains shocked after two intramuscular doses, consider an adrenaline infusion to restore blood pressure.</td></tr>
<tr><td>Intravenous fluids (e.g. normal saline or Hartmann’s solution 20mL/kg); continue as necessary.</td></tr>
<tr><td>Additional measures
• Bronchodilators: for bronchospasm, give salbutamol or via nebuliser or aerosol with spacer device
• Corticosteroids: Hydrocortisone 2-6mg/kg or Dexamethasone 0.1-0.4mg/kg intravenously
• Nebulised adrenaline: May be tried for laryngeal oedema (5ml of 1:1000)</td></tr>
<tr><td></td><td></td><td>Supportive measures
• Observe vital signs frequently; monitor ECG and pulse oximetry
• Arrange for transfer to hospital if reaction occurs in an outpatient facility
• Keep under observation for at least 4-6 hours after complete resolution of signs and symptoms, as biphasic reactions may occur</td></tr>
</table>

Recommendations

R54. If a patient is suffering from a moderate or severe anaphylactic reaction additional extra care should be called for early.

R55. Adrenaline is potentially life-saving and must be used promptly. Withholding adrenaline due to misplaced concerns of possible adverse effects can result in deterioration and death of the patient.

R56. Adrenaline 1:1000 contains 1000 micrograms in 1mL (1mg/mL). The volumes of adrenaline recommended for adults and children approximate to 5 to 10 microgram/kg. Children's weights are approximate for age. Repeated doses may be necessary.

R57. Adrenaline should be administered intramuscularly into the anterolateral thigh (vastus lateralis muscle). Administration into the deltoid muscle has been shown to result in a lower and slower rise in peak plasma adrenaline.

R58. Some cases are resistant to multiple doses of adrenaline, especially if the patient is taking beta blocking drugs. If adequate doses of adrenaline are not effective give glucagon 1 to 2mg intravenously over 5 minutes.

R59. Intramuscular adrenaline auto-injectors may have needle lengths which are inadequate to reach the vastus lateralis in overweight or obese patients (especially females). A suitable length needle should be used to ensure intra muscular administration into the vastus lateralis.

R60. Patients with moderate or severe reactions should be managed in a supine position to maximise circulation. If breathing is difficult, allow the individual to sit, but not stand. If vomiting or unconscious, lay the individual on their side in the recovery position. If hypotension is the sole or predominant problem, leg elevation may be useful.

R61. Emergency intubation for impending airway obstruction is a very high-risk procedure and should only be attempted by an expert.

R62. Corticosteroids may modify the overall duration of a reaction and may prevent relapse. However, onset of action will be delayed. Never use these to the exclusion of adrenaline.

R63. Patients who have experienced a reaction to contrast media should be provided with the exact name of the contrast media used and prompted to consider providing this detail in a MedicAlert bracelet.

4.1 Confirmation of Anaphylactic Reaction

After a suspected anaphylactic reaction, timed blood samples for mast cell tryptase testing should be considered and performed as follows:

(a) The largest SST tube available should be used.

(b) A sample should be taken as soon as possible after emergency treatment has started.

(c) A second sample ideally within 1-2 hours (but no later than 4 hours) from the onset of symptoms should also be collected.

Reference
NICE Guidelines: Anaphylaxis: assessment to confirm an anaphylactic episode and the decision to refer after emergency treatment for a suspected anaphylactic episode

4.2 Delayed Contrast Media Reactions

Late adverse contrast media reactions occur between one hour and one week after intravascular iodinated contrast media administration. These are typically skin reactions with a maculopapular rash being most common. Less frequent skin reactions include angioedema, urticaria and erythema and painful salivary gland swelling. Delayed contrast media reactions are not typically associated with bronchospasm or laryngeal oedema.

The effectiveness of premedication with corticosteroids in reducing the incidence of recurrent delayed contrast media reaction is unknown.

The incidence of reported late adverse reactions varies in the literature but is likely to be 4% or less. There is a possible increased incidence of late reactions to iodinated contrast media in patients who have received interleukin-2 (IL-2).

5. PAEDIATRIC ADMINISTRATION OF IODINATED CONTRAST MEDIA – SPECIAL CONSIDERATIONS

The information contained in Section 4 *Anaphylactic Contrast Media Reactions* applies equally to children.

6. ORAL AND OTHER NON-INTRAVASCULAR CONTRAST MEDIA ADMINISTRATION

Small amounts of iodinated contrast media are absorbed from the gastrointestinal tract after oral administration. It is estimated that up to 1% of the administered dose is absorbed in healthy individuals, and potentially more in people with inflammation in the gastrointestinal tract. While anaphylactic reactions resulting from non-vascular administration of iodinated contrast media are rare, the same precautions should be taken as with intravascular administration. Side effects due to the physical properties of oral iodinated contrast media are common. Pulmonary oedema due to the aspiration of ionic contrast media into the lungs can be life threatening. Common gastrointestinal side effects include diarrhoea, nausea and vomiting. These are usually self-limiting, but can result in serious electrolyte disturbances in seriously ill or dehydrated patients.

Recommendations

R64. Anaphylactic reactions can occur with non-vascular administration of iodinated contrast media and the same precautions should be taken as with intravascular use.

R65. Severe electrolyte disturbances and or dehydration should be corrected where possible prior to the administration of oral iodinated contrast media and electrolytes should be monitored in severely ill patients or those with severe diarrhoea and/or vomiting.

R66. Ionic contrast media should not be given orally to patients at risk of aspiration. Non-ionic contrast media or barium sulfate can be used as safer alternatives.

Reference

MD-Gastroview (Diatrizoate Meglumine and Diatrizoate Sodium Solution USP) Product Information Leaflet. Mallinckrodt Pharmaceuticals, Sep 2014.

Gastrografin (Diatrizoate Meglumine and Diatrizoate Sodium Solution USP) Product Information Leaflet. Bracco Diagnostics, Dec 2013.

Omnipaque (Iohexol) 300 Solution. Product Information Leaflet. GE Healthcare, May 2007.

Davis PL. Anaphylactoid Reactions to the Nonvascular Administration of Water-Soluble Iodinated Contrast Media. AJR Am J Roentgenol 2015; 204: 1140-1145.

Ridley LJ. Allergic reactions to oral iodinated contrast agents: Reactions to oral contrast. Australasian Radiology 1998; 42: 114-117.

7. RELATED POLICY DOCUMENTS

- RANZCR Standards of Practice for Diagnostic and Interventional Procedures, V10
- Guidelines on the use of Gadolinium-containing MRI contrast agents in Patients with Renal Impairment
- Medical Imaging Consent Guidelines
- RANZCR Code of Ethics

8. APPENDICES

- Appendix 1. Agree II Tool
- Appendix 2. Search Strategies and Results – Metanalyses / Systematic Reviews Relating to the Risk of Contrast Induced Acute Kidney Injury and Intravenous Iodinated Contrast Administration

9. POINT OF CARE TOOLS

- Wall Chart - Recommended Treatment Regimen for Management of Anaphylaxis in a Radiology Suite
- Wall Chart - Treatment of Adverse Reactions to Iodinated Contrast Media – Drugs and Equipment
- Information for Patients
- Patient Questionnaire - For patients who are receiving iodinated contrast media. Including information for health care practitioners on how to assess the patient questionnaire.
- Sample letter to referrer for patients on metformin requiring cessation

APPENDIX 1. AGREE II TOOL

Scope and Purpose

1. The overall objective(s) of the guideline is (are) specifically described.
2. The health question(s) covered by the guideline is (are) specifically described.
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.

Stakeholder Involvement

4. The guideline development group includes individuals from all relevant professional groups.
5. The views and preferences of the target population (patients, public, etc.) have been sought.
6. The target users of the guideline are clearly defined.
7. The guideline has been piloted

Rigour of Development

8. Systematic methods were used to search for evidence.
9. The criteria for selecting the evidence are clearly described.
10. The strengths and limitations of the body of evidence are clearly described.
11. The methods for formulating the recommendations are clearly described.
12. The health benefits, side effects, and risks have been considered in formulating the recommendations.
13. There is an explicit link between the recommendations and the supporting evidence.
14. The guideline has been externally reviewed by experts prior to its publication.
15. A procedure for updating the guideline is provided.

Clarity of Presentation

16. The recommendations are specific and unambiguous.
17. The different options for management of the condition or health issue are clearly presented.
18. Key recommendations are easily identifiable.
19. The guideline is supported with tools for application.

Applicability

20. The guideline describes facilitators and barriers to its application.
21. The guideline provides advice and/or tools on how the recommendations can be put into practice.
22. The potential resource implications of applying the recommendations have been considered.
23. The guideline presents monitoring and/or auditing criteria.

Stakeholder Involvement

24. The guideline development group includes individuals from all relevant professional groups.
25. The views and preferences of the target population (patients, public, etc.) have been sought.
26. The target users of the guideline are clearly defined.

APPENDIX 2. SEARCH STRATEGIES AND RESULTS

Metanalyses / Systematic Reviews Relating to the Risk of Contrast Induced Acute Kidney Injury and Intravenous Iodinated Contrast Administration

Q1: In patients receiving intravenous contrast medium how does receiving intravenous iodinated contrast medium compare with no intravenous iodinated contrast medium effect the need for dialysis or death from acute kidney injury?

P: patients receiving intravenous contrast medium
I: intravenous iodinated contrast medium
C: patient who do not receive intravenous iodinated contrast medium
O: dialysis or death from acute kidney injury

Information for Requestors:

- The searches were conducted in Medline and the Cochrane Library.
- The following systematic review was identified *"McDonald et al. 2013. Frequency pf Acute Kidney Injury Following Intravenous Contrast Medium Administration: A Systematic Review and Meta-Analysis". Radiology: Vol 267:1."*
- This paper searched several databases through to September 2011
- The search conducted here was from 2010 to present to identify any new literature.
- The search identified the one new review: *"Moos, S. I., et al. (2013). "Contrast induced nephropathy in patients undergoing intravenous (IV) contrast enhanced computed tomography (CECT) and the relationship with risk factors: a meta-analysis." European Journal of Radiology **82**(9): e387-399."*
- *And one new protocol: Kayibanda, J. F., et al. (2014). "Does intravenous contrast-enhanced computed tomography cause acute kidney injury? Protocol of a systematic review of the evidence." Systems Review **3**: 94.*
- *The authors of the protocol were contacted and the systematic review is in the process of being prepared for publication, I will let you know when the expected publication date is.*

Medline Search Strategy Q1 – Search date 06/07/2015

(Ovid MEDLINE(R) 1946 to Present with Daily Update, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations July 02, 2015)

1	exp Contrast Media/ae, to [Adverse Effects, Toxicity]	11815	Contrast Terms
2	(contrast or radiocontrast or radiopaque).m_titl.	46043	
3	1 or 2	51884	
4	exp Administration, Intravenous/	126463	Method of contrast
5	3 and 4	2381	
6	contrast-induced nephropathy.mp.	1206	Outcome
7	exp Kidney Diseases/	429217	
8	(nephrotoxic* or nephropath* or ((kidney or renal) adj3 (disease* or failure or insufficiency))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	318652	
9	(((contrast or radiocontrast) adj induc* adj2 (nephropath* or nephrotoxi* or aki or arf or acute kidney injury or acute renal	8697	

	failure)) or cin or ciaki or ci-aki or ci-arf or ((contrast or radiocontrast) adj2 prophlya*)).ti,ab.		
10	6 or 7 or 8 or 9	513641	
11	meta-analysis/	57351	Systematic Review Filter
12	Meta-Analysis as Topic/	14355	
13	(meta analy* or metanaly* or metaanaly*).ti,ab.	79415	
14	((systematic or evidence) adj2 (review* or overview*)).ti,ab.	88289	
15	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.	28553	
16	(search strategy or search criteria or systematic search or study selection or data extraction).ab.	30633	
17	(search* adj4 literature).ab.	32987	
18	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.	104715	
19	((pool* or combined) adj2 (data or trials or studies or results)).ab.	36062	
20	cochrane.jw.	11651	
21	((indirect or mixed) adj2 comparison*).ti,ab.	1527	
22	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	258073	
23	5 and 10 and 22	24	
24	limit 23 to (english language and humans and yr="2010 - Current")	11	1 = Relevant SR 1 = Protocol awaiting SR publication

Cochrane Search Strategy Q1 – Search date 07/07/2015

Cochrane Library Search

1	MeSH descriptor: [Contrast Media] explode all trees and with qualifier(s): [Adverse effects - AE]	728	Intravenous contrast medium terms
2	(contrast or radiocontrast or radiopaque):ti	2978	
3	**(#1 or #2)**	3221	
4	MeSH descriptor: [Administration, Intravenous] explode all trees	15960	
5	(#3 and #4)	265	
6	contrast-induced nephropathy	405	AKI terms
7	MeSH descriptor: [Kidney Diseases] explode all trees	10205	
8	(nephrotoxic* or nephropath* or ((kidney or renal) near/3 (disease* or failure or insufficiency)))	21051	
9	(((contrast or radiocontrast) adj induc* near/2 (nephropath* or nephrotoxi* or aki or arf or acute kidney injury or acute renal failure)) or cin or ciaki or ci-aki or ci-arf or ((contrast or radiocontrast) near/2 prophlya*)):ti,ab	646	

10	(#6 or #7 or #8 or #9)	23819	
11	(#5 and #10) Publication Year from 2010 to 2015	20	0 = Cochrane Reviews 3 = Other Reviews (not relevant to the question) 17 = Trials (Not reviewed)

The Kayibanda et al study has not yet been published (as of August 2015) and the authors have agreed to notify the RANZCR Contrast Guideline Working Group when this occurs. The current recommendations will be updated, if necessary, when the study has been appraised with regard to its clinical implications.

The SR and meta-analysis by Moos et al, included patients with eGFR ranging from 4-256mL/min. It found the overall pooled CI-AKI incidence was low (3.79-6.47%) and that renal insufficiency, diabetes, malignancy, age over 65 years and use of non steroidal anti inflammatory drugs were positively associated with the development of CI – AKI but that hypertension, anaemia, and congestive heart failure were not. However, their meta-analysis did not require, that all included studies had a control group. Therefore, it is possible that the prevalence of AKI after iodinated contrast administration has been overestimated because of their inclusion criteria.

Q2: In patients with impaired renal function who are to receive intravenous iodinated contrast medium how does oral administration of fluids/NAC (for the purpose of hydration) compare with intravenous administration of fluids/NAC in preventing contrast induced acute kidney injury?

P: patients with impaired renal function who are to receive intravenous iodinated contrast medium
I: oral administration of fluids/NAC for the purpose of hydration
C: intravenous administration of fluids/NAC for the purpose of hydration
O: prevention of contrast induced acute kidney injury

Information for Requestors:

- The searches were conducted in Medline and the Cochrane Library using the search string outlined in the NICE Guideline for AKI.
- This Guideline covered the topic of preventing contrast induced acute kidney injury. http://www.nice.org.uk/guidance/cg169/evidence
- We searched forward from 2013 to identify any new reviews post publication of the guideline
- The following systematic review was identified *Hiremath, S., et al. (2013). "Prevention of contrast-induced acute kidney injury: is simple oral hydration similar to intravenous? A systematic review of the evidence." PLoS ONE [Electronic Resource]* ***8****(3): e60009.*
- *The new Systematic review reaches the same conclusion as the NICE guideline with regard to Oral Vs Intravenous administration of NAC/fluids for hydration and prevention of AKI*
- *Please refer to Pg 138 of the NICE guideline "Oral fluids as a possible regimen" where there is a discussion around the lack of evidence in this area.*

It is important to note that a minority of patients in only one study included in the NICE UK guideline received intravenous contrast media – all other patients had intra-arterial administration mainly for coronary or peripheral angiography and therefore received on average higher doses that would be administered for 1 CT examination, for example.

Therefore, there is no evidence to inform the administration of periprocedural hydration to patients receiving intravenous iodinated contrast media. The following recommendations apply to patients scheduled for intra-arterial administration.

Medline Search Strategy Q2 – Search date 07/07/2015

(Ovid MEDLINE(R) 1946 to Present with Daily Update, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations July 02, 2015)

1	exp Contrast Media/ae, to [Adverse Effects, Toxicity]	11815	Contrast Induced AKI
2	(((contrast or radiocontrast) adj induc* adj2 (nephropath* or nephrotoxi* or aki or arf or acute kidney injury or acute renal failure)) or cin or ciaki or ci-aki or ci-arf or ((contrast or radiocontrast) adj2 prophlya*)).ti,ab.	8697	
3	1 or 2	19286	
4	Acetylcysteine/	10726	Intervention
5	(acetylcysteine or n-acetylcysteine or n acetyl l cysteine or parvolex).ti,ab.	12298	
6	Saline Solution, Hypertonic/	4990	
7	Bicarbonates/	20692	
8	(saline or sodium chloride or bicarbonate or ((iv or intravenous*) adj2 fluid*)).ti,ab.	170398	
9	4 or 5 or 6 or 7 or 8	199769	
10	meta-analysis/	57351	Systematic Review Filter
11	Meta-Analysis as Topic/	14355	
12	(meta analy* or metanaly* or metaanaly*).ti,ab.	79415	
13	((systematic or evidence) adj2 (review* or overview*)).ti,ab.	88289	
14	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.	28553	
15	(search strategy or search criteria or systematic search or study selection or data extraction).ab.	30633	
16	(search* adj4 literature).ab.	32987	
17	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.	104715	
18	((pool* or combined) adj2 (data or trials or studies or results)).ab.	36062	
19	cochrane.jw.	11651	
20	((indirect or mixed) adj2 comparison*).ti,ab.	1527	
21	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	258073	
22	3 and 9 and 21	108	
23	limit 23 to (english language and humans and yr="2013 - Current")	17	Duplicates removed N=12 in Endnote library

Cochrane Search Strategy Q2 – Search date 07/07/2015

Cochrane Library Search

1	MeSH descriptor: [Contrast Media] explode all trees and with qualifier(s): [Adverse effects - AE]	728	Intravenous contrast medium terms
2	(((contrast or radiocontrast) near induc* near/2 (nephropath* or nephrotoxi* or aki or arf or acute kidney injury or acute renal failure)) or cin or ciaki or ciraf or ci-aki or ci-arf or ((contrast or radiocontrast) near/2 prophlya*)):ti,ab,kw	872	
3	**(#1 or #2)**	1371	
4	MeSH descriptor: [Acetylcysteine] this term only	611	Hydration methods
5	(acetylcysteine or n-acetylcysteune or n acetyl l cysteine or parvolex):ti,ab,kw	1184	
6	MeSH descriptor: [Saline Solution, Hypertonic] this term only	409	
7	MeSH descriptor: [Bicarbonates] this term only	697	
8	(saline or sodium chloride or bicarbonate or ((iv or intravenous*) near/2 fluid*)):ti,ab,kw	19659	
9	(#4 or #5 or #6 or #7 or #8)	20913	
10	(#3 and #9) Publication Year from 2013 to 2015	66	1 = Cochrane Protocol not relevant to question 4 = Other Reviews (not relevant to the question) 61 = Trials (Not reviewed)


LUMEN·AFFERIMUS·MORBIS