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For Action by:
UHB/Trust CEOs,
UHB Directors of Therapies and Health Science,
UHB/Trust Medical Directors,
UHB/Trust Heads of Radiology and Physics,
UHB/Trust Quality and Safety Leads

Action required by:
See paragraph 7

Sender: Dr Rob Orford, Chief Scientific Adviser (health)

DHSS Welsh Government Contact(s) :
Rob Orford, Healthcare Technology, Innovation & Strategy Division, Health & Social Services Group,
Cardiff, CF10 3NQ, 03000 258315

Enclosure(s): None

Dr Rob Orford
Prif Ymgynghorydd Gwyddonol (Iechyd)/
Chief Scientific Advisor (Health)
Y Grŵp Iechyd a Gwasanaethau Cymdeithasol/
Health & Social Services Group



Llywodraeth Cymru
Welsh Government

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Dear Colleague

Guidance on Administration of Intravenous Contrast Medium to Patients with Renal Impairment

1. The Welsh Scientific Advisory Committee (WSAC) has issued guidance on administration of Intravenous Contrast Medium (CM) to patients with Renal Impairment. The guidance is attached and can be read below.
2. The guidance is designed to allow CT radiographers and radiologists to identify patients at risk of developing Contrast Induced Acute Kidney Injury (CI-AKI) and to advise the referring clinician if any action is needed to be taken prior to contrast injection.
3. The guidance provides information on the practical implications of administering intravenous CM to patients with renal impairment, either for a planned outpatient examination or in the emergency setting as an inpatient.
4. I would like to draw your attention to the guidance's six recommendations at paragraph 7 for improving the administration of CM and ensuring patient safety.

Yours sincerely

A handwritten signature in black ink, consisting of a series of loops and a long horizontal stroke extending to the right.

DR ROB ORFORD



GIG
CYMRU
NHS
WALES

Pwyllgor Ymgynghorol
Gwyddonol Cymru
Welsh Scientific
Advisory Committee

Guidance on Administration of Intravenous Contrast Medium to Patients with Renal Impairment

Produced on behalf of the Welsh Scientific Advisory Committee

Lead Author: Dr Jane Blethyn, MBChB FRCR
Medical Imaging Subcommittee 12/7/17

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1. Executive Summary

- 1.1. The possibility of causing contrast induced acute kidney injury (CI-AKI) is a significant factor in managing patients with both acute and chronic renal impairment. Contrast enhanced computed tomography (CT) is used for many indications; for diagnostic purposes, for staging and for surveillance of malignancy. The decision whether it is safe to administer intravenous contrast for CT affects the diagnostic information available for the report and therefore affects the patient's management.
- 1.2. Serum creatinine is a marker for renal function and is the basis for estimated Glomerular Filtration Rate (eGFR) calculation. eGFR is used to quantitate renal function across the age range and for both sexes. A range of values is proposed to define the risk of developing CI-AKI into 3 groups, based upon eGFR; no additional risk, low risk and high risk.
- 1.3. Contrast induced acute kidney injury is usually a transient asymptomatic condition not requiring treatment, which resolves in up to 5 days.
- 1.4. Early identification of contrast induced acute kidney injury after contrast administration in cases of renal insufficiency using serum creatinine, will allow patients to be followed up and managed appropriately if renal function does not recover in the usual time frame.
- 1.5. Patients at high risk of developing contrast induced acute kidney injury can be monitored closely after contrast medium (CM) injection or be directed towards other forms of imaging without contrast medium.
- 1.6. When the risk is small the patient with stable chronic impairment can have an examination booked without untoward delay.

1.1. Context – What has led to this Report?

- 1.1.1 Radiologists and radiographers have to decide whether it is safe to inject intravenous iodinated non-ionic contrast medium (CM) for a CT scan. Historically contrast medium administration to patients with renal impairment has been associated with a high incidence of acute kidney injury but recent publications have challenged the assumption that all of those cases of acute kidney injury were due to contrast medium and there is now recognition that many of the patients with co-morbidities, dehydration and/or sepsis have an increased chance of developing AKI irrespective of contrast medium administration. A meta-analysis in 2014 concluded that CI-AKI incidence was 6.4% compared with a control group of 6.5% (7).
- 1.1.2 There was no clear advice for the CT radiographers to use to decide which patients were at risk from CM administration. Serum biochemistry was not always available prior to booking an outpatient CT scan to allow the decision to be made safely. Guidance of what action was appropriate in the presence of renal impairment was not readily available for CT radiographers and radiologists. Many hospitals in Wales relied upon replacing high osmolar CM with iso-osmolar Iodixanol if there was renal impairment or unknown renal function.

1.2 Purpose of this report

- 1.2.1 The guidance in this report is designed to allow CT radiographers and radiologists to identify patients at risk of developing CI-AKI and to advise the referring clinician if any action is needed to be taken prior to contrast injection. The CT scan may have to be done without CM if the risk is deemed to be too high. Routine checks of post CM serum urea and electrolytes (U&E) are required.
- 1.2.2 The calculated eGFR which must be derived from a serum creatinine value which is within 3 months of the examination. (NICE 2014) Although eGFR is accurate only for chronic stable renal impairment and should be recognised as a variable estimate in patients who are acutely sick, eGFR forms the basis of risk assessment in most published pathways because it allows for an estimation of renal function for men and women and across the age range.
- 1.2.3 Using eGFR based risk groups allows the CT radiographer to book scans for patients with minimal renal impairment and to identify patients with more severe renal impairment who require further consideration from the referring clinician. The classical scenario of CI-AKI is a self limiting transient increase in serum creatinine, manifest between 3-5 days after CM injection and subsequently returning to a normal value. The patients at risk need to have serum creatinine re-checked within the 3-5 day period and to receive ongoing follow up if they develop CI-AKI.

1.3 Developing this report

- 1.3.1 National and individual publications have been used to research reported rates of CI-AKI and risk factors. There is now a recognition both in Europe and in the USA that the assumption that AKI following CM administration was always due to CM is misplaced and that this is true in only a small percentage of cases. The incidence of permanent harm following CI-AKI is now widely reported to be low compared with historical figures which give outcomes of significant dialysis dependence and death following AKI. (13)
- 1.3.2 A significant publication in 2003 (12) comparing outcomes in patients having coronary angiography and percutaneous lumbar aortography with high (some were ionic CM) or iso-osmolar CM agents reported an improved outcome in the latter group which led to the practice of using iso-osmolar iodixanol (Visipaque GE) for CM administration in patients with renal insufficiency to attempt to protect against CI-AKI. Although subsequent publications challenged this assumption from 2006 onwards it continued to be the practice in many radiology departments in Wales, that patients with renal impairment were given iodixanol in the belief that the additional cost was justified by a better outcome.

2. Introduction

- 2.1** The report gives CT radiographers and radiologists guidance on the practical implications of administering intravenous CM to patients with renal impairment, either for a planned outpatient examination or in the emergency setting as an inpatient.
- 2.2** Reference ranges of eGFR values allow the patient to be put into a;- no additional risk, low risk or high risk group which then prescribes the appropriate pathway of actions that need to be taken prior to administering CM.

eGFR ml/min/1.73m²	Action required
>45	Book examination
30-45	Clinician reviews clinical risk, rehydrate if necessary, recheck Creatinine
<30	Significant risk. Proceed if emergency. Otherwise d/w renal physician if renal function can be improved. Consider non contrast imaging, US or MR.
dialysis	Proceed with contrast. Check next dialysis date.

3. Background

Acute Kidney Disease		Chronic Kidney Disease			
stage	Serum creatinine umol/L	stage	eGFR	description	qualifier
1	↑≥26 in 48hrs or ≥1.5-1.9 x baseline	1	≥90	Kidney damage, normal or ↑GFR	Kidney damage (structural abnormalities and/or persistent haematuria, proteinuria or microalbuminuria) for ≥ 6 months GFR ≤ 60ml/min/1.73m ² for ≥ 3 months ± kidney damage
2	2-2.9 x baseline	2	60-89	Kidney damage, mildly ↓ GFR	
3	X3 baseline Or ↑serum creatinine to ≥ 359umol/L	3A	45-59	Moderately ↓GFR ± other evidence of kidney damage	
		3B	30-44		
		4	15-29	Severely ↓ GFR ± other evidence of kidney damage	
		5	≤15	Established kidney failure	

Adapted from National Institute for Health and Care Excellence (NICE) 2013 and Kidney Disease: Improving Global Outcomes (KDIGO) 2012

- 3.1** Contrast induced Acute Kidney Injury (CI-AKI) formerly called Contrast Induced Nephropathy (CIN) is a condition whereby administration of contrast medium (CM) either by intravenous or intra-arterial route causes acute impairment of renal function. It is usually a transient, asymptomatic condition diagnosed by raised creatinine at 3-5 days after injection.
- 3.2** Acute kidney injury was identified by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) as a major problem in hospitals in the UK and Northern Ireland in terms of failure to recognise the condition, identify an underlying cause and to treat it appropriately and in a timely manner, resulting in progression of disease and avoidable deaths from AKI. The report said that up to 30% of cases of AKI in inpatients may be preventable.
- 3.3** The publication of this report in 2009 led to NICE guidance Acute Kidney Injury CG169 published 2013, followed by a quality standard QS76 in 2014 aimed at improving the detection and management of AKI in inpatients and thereby improving the outcome of patients either with pre-existing or post-admission renal impairment.

- 3.4** Acute kidney injury is seen in 13-18% of all hospital admissions, is probably under-recorded and in England is estimated to cost £1.01 billion, more than the cost of breast, lung and bowel cancer combined.
- 3.5** The quality standard set by NICE (5) expects to produce improvements in avoidable death, deterioration in stage, requirement for renal replacement therapy, prevalence of chronic kidney disease, patient experience of hospital care, number of patient safety incidents, and admissions to critical care, length of stay, incidence of AKI and complications of AKI.
- 3.6 Patients with an acute illness** - The recommendations for defining risk factors in patients with an acute illness have been described in the NCEPOD report and centre around recognising the known major causes of acute renal impairment such as **dehydration/ hypovolaemia/ volume depletion with or without additional causes of morbidity such as sepsis.**
- 3.7** Known **chronic renal impairment with eGFR <60ml/min/1.73m²** is probably the single most important risk factor for developing AKI during a hospital admission.
- 3.8** NICE recommendations of additional risk factors are as following:-
- medication with nephrotoxic potential (the usual drugs are ACE inhibitors, ARBs, NSAIDs, amino-glycosides and loop diuretics).
 - diabetes (only when there is also chronic kidney injury)
 - Heart failure
 - Obstructive symptoms
 - History of AKI
 - Liver disease
 - Neurological impairment leading to difficulty in maintaining hydration
 - use of contrast medium within 1 week
 - deteriorating NEWS (national early warning scores)
 - age 65 or over.
- However the quality of evidence for these conditions being significant risk factors for developing AKI is low to very low and it is only when **multiple conditions co-exist** that they are likely to become risk factors.
- 3.9** NICE was unable to recommend a scoring system to identify patients at risk of developing AKI.
- 3.10** The advice for identifying risk factors in children and young people is similar with the inclusion of severe diarrhoea, nephritis and haematological malignancy.

4. Evidence/Findings

- 4.1** Contrast Induced AKI has been assumed to be a major cause of nephropathy in patients with renal impairment since 1960s (16,17) and has been the subject of many publications over past decades but until

recently all of the papers referred to intra-arterial CM administration for invasive coronary or femoral angiography. More recently several reviews and publications have described a low incidence of CI-AKI following intravenous contrast medium for CT and identified factors relating to fluctuations in serum creatinine in inpatients with co-morbidity unrelated to the administration of contrast medium and describing an unchanged incidence of acute nephropathy; nephropathy related dialysis and death, in patients having CT with and without intravenous CM (6,7,8,9).

- 4.2** The true risk of giving contrast medium to an inpatient population with renal impairment is difficult to define but some authors (6) have speculated that CI-AKI occurs rarely.
- 4.3** McDonald's meta-analysis of studies using a control group concluded that the rate of CI-AKI was 6.4% in the CM group compared with 6.5% in the non CM group (7). Previous studies from percutaneous coronary intervention (PCI) gave figures of over 20% (12,13).
- 4.4** Patients with stable moderate CKD do not appear to be at increased risk. Patients with severe renal impairment are at risk of irreversible deterioration and they should be discussed on an individual basis with the clinician and where possible, with the advice of a renal physician.
- 4.5** None of the national guidelines have defined a level of serum creatinine which can be used to assess the risk of giving intravenous contrast to patients with renal impairment. Therefore the radiologist and the clinician must consider the risks and benefits of giving a CM agent for CT in light of the trend of blood levels, the calculated eGFR, the response to rehydration and the urgency of the condition requiring imaging.

4.6 Contrast medium agents

Evidence that high osmolar CM agents used in coronary angiography had a nephrotoxic effect in patients with renal impairment led to the development of an iso-osmolar compound, iodixanol (marketed as Visipaque GE). Early studies showed that iodixanol had a protective effect for high risk patients having coronary and translumbar femoral angiography compared with other CM agents in use at the time (12). Subsequent analysis of the papers concluded that the benefit related to comparison with the ionic and high osmolar compounds and that there was no advantage when compared with low osmolar non-ionic compounds and this view has been sustained with later publications and meta-analyses (14,15).

National guidelines from NICE, ESUR and the Renal Association agree that there is no evidence that iodixanol has a reduced rate of CI-AKI compared with low osmolar non-ionic CM agents for intravenous use although it may have an improved safety profile compared with iohexol (Omnipaque GE) for intra-arterial use (1,2,4).

4.7 KDIGO also states that there is no benefit from the use of iso-osmolar CM compared with low osmolar non-ionic CM. Further research on direct comparison between different CM agents was recommended.

4.8 Adults having iodinated contrast medium

It is necessary to distinguish between emergency and non-urgent imaging as the balance between harm and benefit will depend upon the degree of pre-existing renal impairment and the urgency of the condition requiring imaging with contrast medium.

It is important that patients with an urgent condition are not denied the use of contrast medium simply because of renal impairment if the diagnosis and management depends upon this imaging.

This balance must be considered on an individual basis by the clinician and the radiologist.

4.9 The evidence underlying NICE's recommendations for risk factors related to CM administration derives to a large extent from publications describing the incidence of CI-AKI in patients having percutaneous coronary intervention. There is no compelling evidence for the prevalence of CI-AKI in patients having intravenous contrast medium for CT (ESUR).

4.10 Nice identifies the following risk factors:-

- eGFR <40ml/min/1.73m²
- diabetes with CKD
- heart failure
- having a renal transplant
- age 75 or over
- hypovolaemia
- large volume injection and intra-arterial administration of contrast medium although the quality of evidence for these recommendations is also rated low.

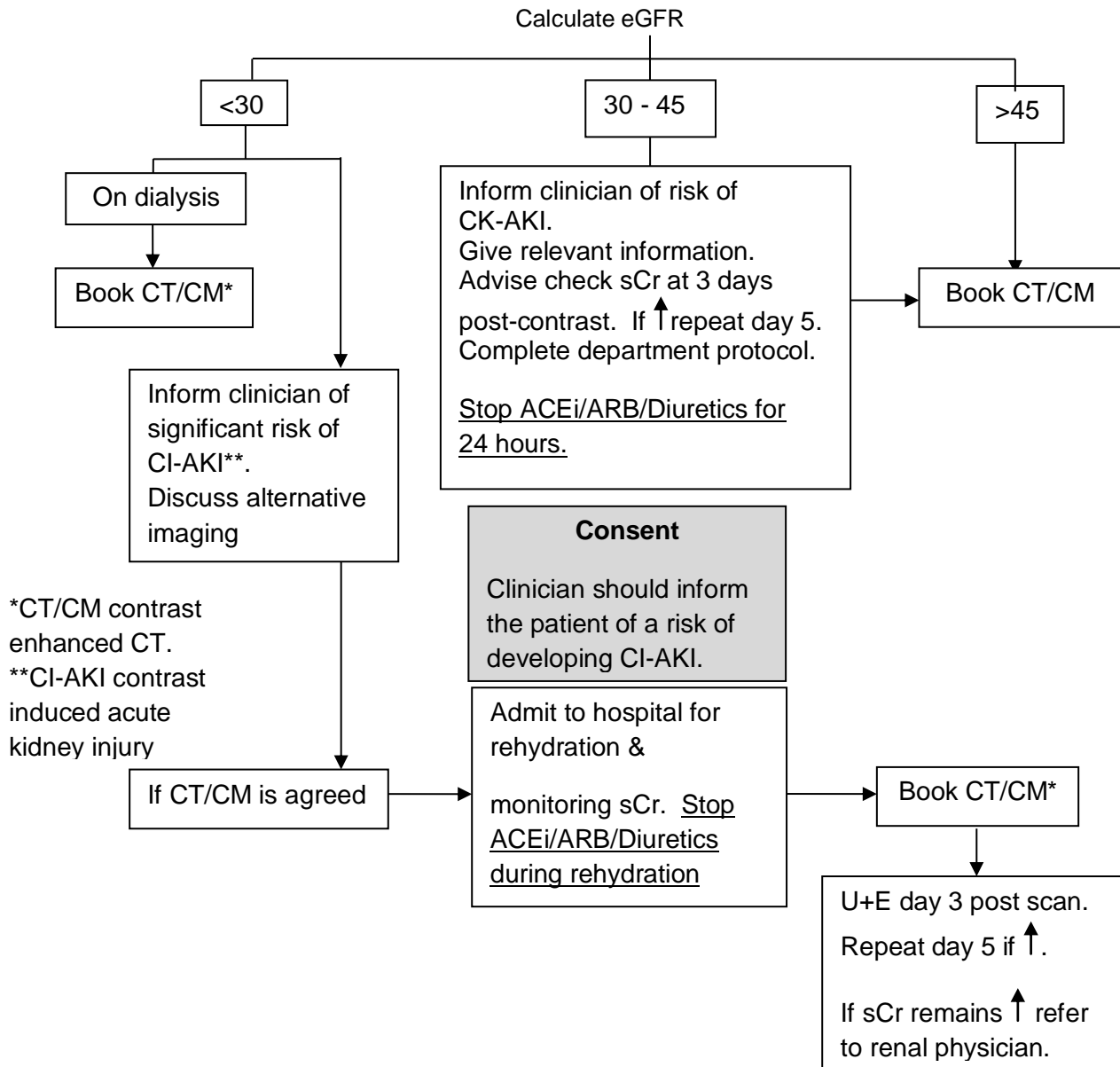
5. Options

5.1 Non-urgent patients with stable, moderate chronic renal impairment can receive intravenous contrast medium without coming to harm. Serum creatinine taken within 3 months must be available. (NICE)

5.2 Urgent cases with varying or increasing serum creatinine levels, sepsis and/or dehydration need to receive intravenous hydration to attempt to lower serum creatinine to a best achievable level and then the decision to scan with or without CM is made by the radiologist with the referring clinician based upon individual circumstances and the perceived risk of developing CI-AKI.

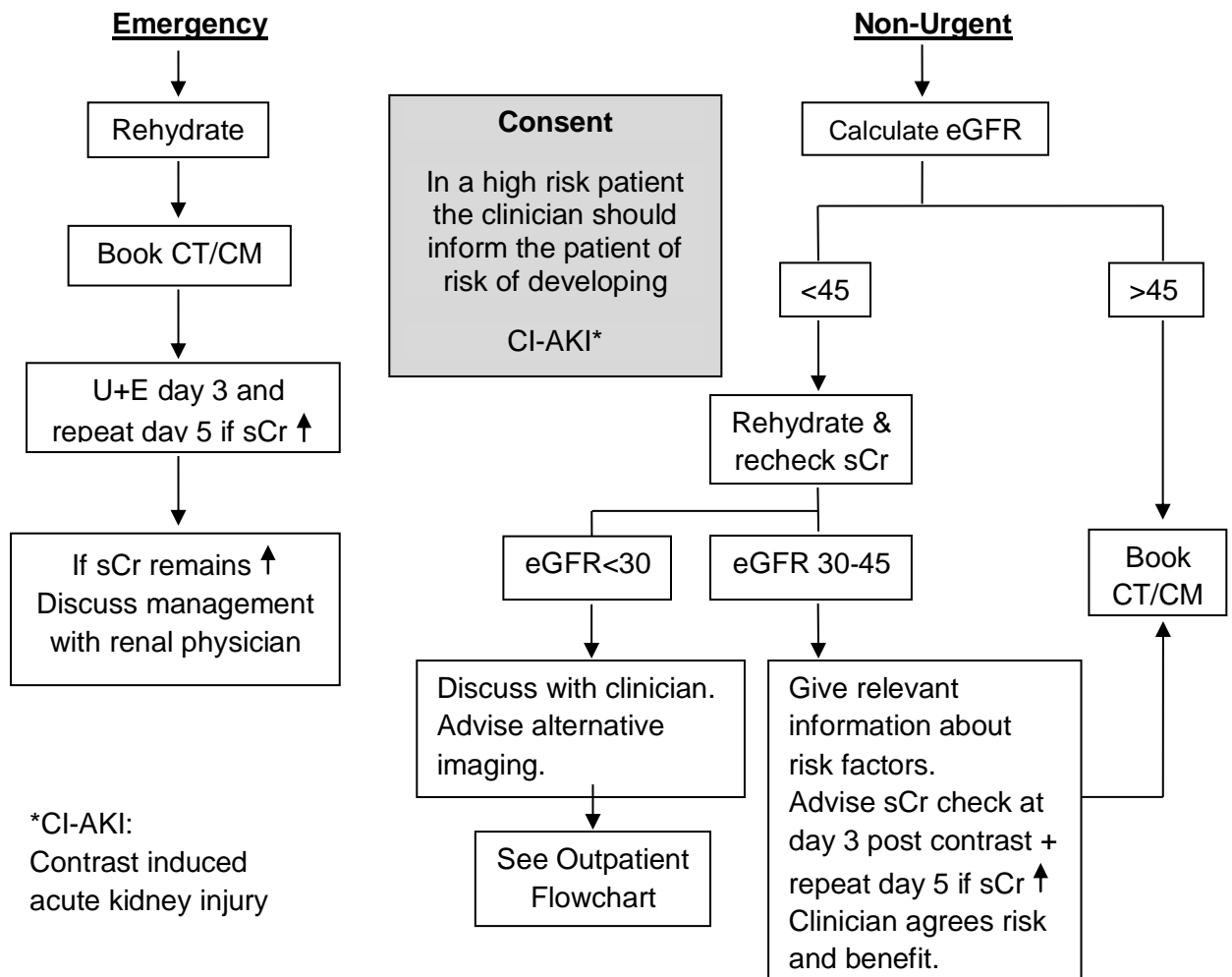
- 5.3 Surgery** - Patients requiring urgent surgery are at particular risk of developing AKI and many will also require contrast enhanced CT for a timely and effective diagnosis. Risk factors are similar to those above and the presence of hypovolaemia and sepsis in a high risk patient should prompt the clinician to take prophylactic measures to avoid CI-AKI by appropriate rehydration, reviewing medication for nephrotoxic potential and in severe renal failure, taking advice from a renal physician regarding management before and after surgery.
- 5.4 Nephrotoxic drugs** - Stopping nephrotoxic drugs for 24 hours prior to contrast administration in patients at high risk of CI-AKI should be considered by the clinician, bearing in mind that stopping drug treatment may cause more harm than benefit. (ESUR).
In acutely ill patients with diarrhoea, vomiting or sepsis, consider stopping ACE inhibitor or ARB until the clinical condition has stabilised. (NICE 2013).
- 5.5** The use of n-acetyl cysteine with a sodium bicarbonate or sodium chloride infusion relates entirely to coronary angiography and the evidence supporting its use is limited and contradictory and therefore has not been recommended by NICE or KDIGO for use in non-coronary contrast imaging.
- 5.6** Based upon advice in NICE 2013 the following algorithms have been constructed to allow the CT radiographer and the radiologist to define groups of patients with differing values of eGFR who can then be managed safely, in terms of receiving intravenous CM.

Guideline for Management of OUTPATIENTS >65 years with renal impairment who require intravenous contrast medium administration



Adapted from NICE. Acute kidney injury - prevention, detection and management up to the point of renal replacement therapy CG169 August 2013.
 Contrast induced nephropathy: updated ESUR contrast media safety committee guidelines - Eur. Radiol (August 2011) 21:2527-2541.
 Iodinated Contrast Media Guideline; Faculty of Radiology Royal Australian & New Zealand College of Radiologists 2016 Edition.
 Replaces RCR Guidance "Standards for intra-vascular contrast administration to adult patients"

Guideline for Management of INPATIENTS with renal impairment who require intravenous contrast medium administration



Adapted from NICE. Acute kidney injury - prevention, detection and management up to the point of renal replacement therapy CG169 August 2013.
 Contrast induced nephropathy: updated ESUR contrast media safety committee guidelines - Eur. Radiol (August 2011) 21:2527-2541.
 Iodinated Contrast Media Guideline; Faculty of Radiology Royal Australian & New Zealand College of Radiologists 2016 Edition.
 Replaces RCR Guidance "Standards for intra-vascular contrast administration to adult patients"

6. Conclusions

- 6.1 The risk of developing CI-AKI following intravenous injection of low osmolar non-ionic CM appears to be much lower than in previous publications relating to intra-arterial CM used for percutaneous coronary intervention (PCI), or from ionic CM no longer in use. Patients with chronic stable renal impairment are not at additional risk and can be given CM injection without causing harm. Performing CT without CM is the last resort as the diagnostic information obtained is low.
- 6.2 A department protocol which requires the referring clinician to check serum creatinine before the CT is booked allows the decision for CM administration to be made safely. Subsequent checks of serum creatinine are also recommended if the initial level is high.
- 6.3 **Intravenous rehydration is the key to managing renal impairment in inpatients requiring urgent CM enhanced CT scans.**

7. Recommendations

- 7.1 Serum creatinine must be available within 3 months of a planned CT scan requiring intravenous CM. The CT radiographer informs the referring clinician by email if it is not available. The CT scan is not booked until a value is available.
- 7.2 eGFR is calculated. A value >45 allows the scan to be booked. A result for an outpatient in the low risk or high risk range requires an email to be sent to the referring clinician requesting confirmation that the administration of CM is appropriate. The serum creatinine must be checked afterwards and acted upon. Alternatively discussion with a radiologist may lead to a different form of imaging if the perceived risk of renal deterioration outweighs the benefits of the CT scan.
- 7.3 The medical team are contacted to start i.v. hydration when inpatients have renal impairment.
- 7.4 In cases when the risk of subsequent renal deterioration is high, the clinician should inform the patient of the risk and discuss alternative methods of imaging.
- 7.5 Follow up of patients with renal impairment (eGFR <45) who have received CM injection is required with repeat U&E between 3-5 days and until baseline levels of serum creatinine have been achieved. Patients with a high risk of developing AKI should be closely monitored and may need the input of a renal physician.
- 7.6 A department protocol should be available for radiographers and radiologists which reflects local practice.

8. References

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Annexes

ABMU OUTPATIENT REFERRAL FOR CT SCAN WITH IV CONTRAST FOR PATIENTS WITH RENAL IMPAIRMENT AND A LOW RISK OF AKI

Dear

Patient ID Label

The above patient has been referred for an outpatient CT scan which will require intravenous contrast injection. The creatinine level taken on.....ismicromol/L giving eGFR of.....

This gives him/her an additional risk of developing contrast induced acute kidney injury (CI-AKI) after the scan.

You can look on the Radiology home page under Medical Info on the tool bar of ABMU intranet for advice on managing chronic renal impairment or on COIN under Clinical systems/ COIN/ Medicine/ Renal Medicine/Acute Kidney Injury.

You can download the app <http://app.rx-guidelines.com/view/ABMU-Renal/Neph> and select **Recognising and Managing AKI/Special circumstances/CIN** for risk factors and also **Medication review/potential to impair renal function** to see which drugs affect renal function adversely.

Take advice from a physician before stopping medication.

You will need to check if renal function is stable. If yes, email me to acknowledge this and arrange for the patient to have **U&E checked 3 days after the contrast has been given.**

If no, optimise renal function as above, consider whether a non-contrast scan or alternative imaging is possible. If contrast is needed consider admitting the patient for medical workup.

You can find out when the CT has been booked by checking on ABMU clinical portal/radis appointments. The scan will be booked when you acknowledge to me by email that you have received this letter.

It is important to make sure that the appropriate steps have been taken to minimise harm to the kidneys following injection of contrast medium.

Yours sincerely,

Superintendent CT Radiographer

**ABMU OUTPATIENT REFERRAL FOR CT SCAN WITH IV CONTRAST
FOR PATIENTS WITH RENAL IMPAIRMENT AND A HIGH RISK OF AKI**

Dear.....

Patient ID Label

The above patient has been referred for a CT scan which requires intravenous contrast injection. The serum creatinine was..... micromol/L on..... giving an eGFR of

This is in the range where giving contrast medium carries a significant risk of permanent renal damage.

You can download the app <http://app.rx-guidelines.com/view/ABMU-Renal/Neph> and select **Recognising and Managing AKI/Special circumstances/CIN** for risk factors and also **Medication review/potential to impair renal function** to see which drugs affect renal function adversely.

A non contrast scan or alternative imaging should be discussed with a radiologist. There is advice on managing patients with renal impairment requiring iv contrast on the Radiology home page under Medical Info on the ABMU intranet toolbar or Clinical Systems/COIN/Medicine/Renal Medicine/Acute Kidney Injury. If intravenous contrast is given, arrangements need to be made for renal replacement therapy to be given if renal function deteriorates. The patient should be admitted for iv hydration and monitoring of renal function.

The scan has not been booked.

Please inform me by email how you want to manage the patient.

Yours sincerely,

Superintendent CT Radiographer