Kliiniline küsimus nr 15

Kas kõikidel kroonilise neeruhaigusega patsientidel on kontrastainega teostatavate uuringute planeerimisel/teostamisel kaasnevate riskide vähendamiseks vajalik arvestada neerufunktsiooni (kreatiniin, eGFR) väärtusi vs mitte?

Kriitilised tulemusnäitajad: kroonilise neeruhaiguse ravi tulemuslikkus, komplikatsioonide teke, kroonilise neeruhaiguse progresseerumine, neeruasendusravi, hospitaliseerimine, patsiendi elukvaliteet, ravikulu, elulemus, üldsuremuse vähenemine

Otsiti andmebaasidest PubMed ja MedLine. Filtriteks kasutati süstemaatilised ülevaated, meta-analüüsid ja randomiseeritud-kontrollitud uuringud, viimased 5 aastat, inimesed, tasuta täistekst

Otsingud 02.-23. oktoober 2015

Otsingusõnad: krooniline neeruhaigus, eGFR, kontrastaine, kontrastainest tingitud nefropaatia

"chronic kidney disase"AND/"contrast" 144 artiklti, sobivad 3
"chronic kidney disase"AND"eGFR" 110 artiklit, sobivad 2
"chronic kidney disase"AND"nephropathy" 211 artiklit
"contrast inducted and nefropatynephropathy?" *125 artiklit (kahes otsingus paljud artiklid korduvad, sobivad 3)*

Lisaks andmebaasidest leitud uuringutele kasutati eelnevalt sekretariaadi poolt Agree II meetodil hinnatud ravijuhendeid.

Kokkuvõte leitud uuringutest

Antud kliinilise küsimuse kohta leiti üheksa teemakohast allikat, neist üks süstemaatiline ülevaade ja metaanalüüs, üks metaanalüüs, kaks retrospektiivset vaatlusuuringut, üks kohortuuring ja viis ülevaateartiklit.

Joodi sisaldavat kontrastainet kasutatakse paljudes röntgenuuringutes ja enamike nende puhul ei ole tüsistusi. Kõrge riskiga KNH patsientide KA nefropaatia tekke risk on suur, ulatudes 14,8-55%ni.

Kontrastaine põhjustatud äge neerukahjustus (KA ÄNK) on üks juhtivaid põhjuseid haiglasisese neerutalitushäire tekkeks. KA ÄNK seostatakse märkimisväärselt suurema haigestumusese ja suremusega. Samuti suurenenud haiglas viibimise aja ja ravikuluga. Uuringutes on KA nefropaatia ja KA ÄNK defineeritud kreatiniini absoluutse tõusuga minimaalselt 44 mcmol/L või suhteline kreatiniini tõus 25% ja eGFR langus 25%.

Retrospektiivne uuring (Kroneberger et al 2015), kuhu kaasati 128 statsionaarsel ravil olevat patsienti, kellele teostati joodi sisaldava madala osmolaarsusega kontrastainega perifeersete arterite angiograafia. Kõigil patsientidel esines glomerulaarfiltratsiooni kiiruse langus (eGFR <60 ml/min/1,73m2 mõõdetuna kas vahetult enne uuringut või kuni 2 päeva enne uuringut). Kontrastnefropaatia hindamiseks määrati seerumi kreatiniin ja eGFR 2-4 päeva pärast uuringut. Kõigile patsientidele teostati vähemalt 6 tunni jooksul protseduuri eelselt infusiooni NaCl 0,9% lahusega 1 ml/kg/h. Patsiendid jagati eGFRi järgi kahte gruppi 45-60 ml/min/1,73m2 (N=73) ja <45 ml/min/1,73m2 (N=55). Hindamiseks defineeriti nefropaatia kreatiniini absoluutse tõusuga minimaalselt 44 mcmol/L või suhteline kreatiniini tõus 25% ja eGFR langus 25%.
Lisaks võeti arvesse kaasuvate riskifaktorite (vanus, kontrastaine hulk ja manustamise kordade arv, kehakaal, KMI, hüpertensioon, diabeet, südame isheemiatõbi,

südamepuudulikkus, aju vereringehaigus, nefrotoksiliste ainete kasutamine, RAS-blokaatorite ja kaltsiumkanalite antagonistide kasutamine. **Tulemused:** Grupis, kelle esialgne eGFR oli 45-60 ml/min/1,73m2 nefropaatiale viitavaid muutuseid eGFRi põhjal ei olnud (0% 0/73). Grupis, kelle esialgne eGFR oli <45 ml/min/1,73m2 langes eGFR >25% 10.9% (6/55) patsientidest.
Kontrastaine nefropaatia ja teiste kaasuvate riskitegurite vahel statistiliselt olulist seost ei leitud.
Seega, tagades patsiendile kontrastaine manustamise eelselt piisava vedeliku manustamise, on raske neerufunktsiooni langusega patsientidel siiski risk kontrastainest tingitud nefropaatia tekkeks.

Ülevaateartikli (Susantitaphong & Eiam-Ong 2014) eesmärgiks oli teha lühikokkuvõte uuringutest (süstemaatilised ülevaated, metaanalüüsid ja randomiseeritud kontrollitud uuringud), mis keskenduvad mittefarmakoloogilistele kontrastainest põhjustatud ägeda neerukahjustuse (K/A ÄNK) ennetusmeetoditele. Sealhulgas rutiinne riskiga patsientide identifitseerimine, piisava vedeliku kasutamise raviskeem, neerutoksiliste ravimite ära jätmine enne kontrastainega uuringut, kontrastaine valik madala osmolaarsusega või isoosmolaarsed kontrastained ja kasutades minimaalset kontrastaine hulka, kui see on võimalik. Kontrastainest põhjustatud ÄNK defineeriti ≥0.5mg/dl kasvuga või 25% tõusuga kreatiniin seerumis, hinnatakse 48-72 tundi pärast kontrastaine manustamist. K/A ÄNK on elanike hulgas vähem kui 2%, kuid kaugele arenenud KNHga patsientidel üle 50%. Uuringus käsitletud meta-analüüs näitas, et peale kompuutertomograafia (CT) uuringut oli K/A ÄNK esinemissagedus 6,4% (95% CI 5,0-8,1). KNHga patsientidel oli riskisuhe 2,26 (*P* <0,001) või diabeediga patsientide riskisuhe oli 3,10 (*P* <0,001).
Kontrastnefropaatia riskidena tuuakse artiklis välja neerufunktsiooni langus alla 60 ml/min 1,73m2, eriti kombinatsioonis diabeerilise nefropaatia, dehüdratatsiooni, kroonilise südamepuudulikkuse (NYHA 3 – 4), äsjase (alla 24h) ägeda müokardiinfarkti, intraaortaalse kontrapulsatsiooni, periprotseduraalse hüpotensiooni, madala hematokriti, vanusega > 70 a või samaaegse nefrotoksiliste ravimite tarvitamisega. Samuti on risk suurem juba diagnoositud ägeda neerukahjustuse korral.
Protseduurist sõltuvateks riskifaktoriteks on kontrastaine intraarteriaalne manustamine, kõrge osmolaarsusega ained, suur kontrastaine annus ja korduv kontrastaine manustamine lühikese aja (mõned päevad) jooksul.
Soovitused
Esiteks selgitada välja kõrge riskiga patsiendid, eriti need, kellel on eGFR <60 ml/min/1,73m2, diabeet, nefrotoksiliste ravimitega kokkupuude, kontrastaine intraarteriaalne manustamine.
Riskirühma patsientidel kaaluda alternatiivina kontrastainevaba uuringumeetodit ja kasutada väiksemaid kontrastaine koguseid. Protseduuri eeslselt on vaja piisav vedelikupakkumine isotoonilise infusioonlahusega (NaCl või $NaHCO_3$).
Seerum kreatiniini määrata enne sekkumist ja peale sekkumist 12 ja 48 - 72 tunni pärast.

Teises leitud **ülevaates (Andreucci, Solomon, Tasanarung 2014**) käsitletakse mitut prospektiivset ja retrospektiivset uuringut, kus kasutatakse KA uuringut ja on erinevate riskiteguritega patsiendid alates ambulatoorsetest kuni intensiivravi vajavate patsientideni.
Kontrastnefropaatia riskifaktoritena tuuakse välja eelnev neerufunktsiooni langus, vanus > 65a, südamepuudulikkus, diabeet, müeloomtõbi, sepsis, neerusiirik. Samuti suurte ja korduvate kontrastaine dooside manustamine, intraarteriaalne manustamistee, kõrgema osmolaalsusega kontrastaine, dehüdratatsioon, pikaaegne hüpotensioon, aneemia, samaaegne nefrotoksiliste ravimite tarvitamine, samaaegne ravi AKEI/ARB-ga.

Uuringute tulemuste analüüsi põhjal on antud järgnevad soovitused:
Esimene reegel on järgida riskiga patsientidel KA nefropaatia võimalikku teket jälgides neerufunktsiooni, mõõtes seerumi kreatiniini ja eGFRi enne ja üks kord päevas 5 päeva jooksul pärast protseduuri. Soovitav on ajutiselt katkestada potentsiaalselt nefrotoksiliste ravimite kasutamine, valida madalam KA annus ja manustada suukaudset või veenisisest vedeliku. Kõrge riskiga patsientidel võib kasutada ka N-atsetüültsüsteiini.

Ülevaade (Keaney et al 2014) keskendub küsimusele, kas kontrastaine annuse vähendamine vähendab riski haigestuda KA ÄNKi kõrge riskiga patsientidel.
Suurimaks riskiteguriks on eelnev KNH, diabeet, kardiogeenne šokk ja vasaku vatsakese düsfunktsioon. Isegi väike annus kontrastainet võib põhjustada KA ÄNKi šokis ja süstoolse südamepuudulikkusega patsientidel.
Kokkuvõtteks soovitatakse vähendada kontrastaine kogust vähendamaks KA ÄNKi, kuid see siiski ainult vähendab KA ÄNKi riski mitte ei kaota seda. Eelkõige peaks keskenduma kõrge riskiga patsientidele. Kontrastaine annust tuleks vähendada vastavalt neerufunktsioonile.

Multitsentrilise retrospektiivses uuringus (Lee et al 2014) analüüsiti KA nefropaatia riskitegurite levimuset ja nende tegelikku olemasolu KA nefrpaatiaga. Kokku 101487 patsienti, kesmine vanus oli 57,9 ja 25,1% olid üle 70 aastased. 40238 patsiendil oli kasutatud ennetavaid meetmeid.
Leiti, et riskitegurite arv oli seda suurem, mida väiksem oli eGFR.
Kontrastnefropaatia tuvastati 3103 patsiendil (2,2% kõigist KA-ga tehtud uuringutest). Analüüsist selgus, et statistiliselt oluliselt tekkis kontrastnefropaatia sagedamini patsientidel, kellel esines enne uuringut eGFR-i langus, diabeet või südamepuudulikkus.

Kohortuuringu eesmärgiks (Andò et al 2014) oli uurida neerufunktsioonile kohandatud kontrastaine koguse seost kontrastnefropaatia tekkel.
Uuringusse kaasati 470 STEMI patsienti, kellel teostati PKI. Nendest 25 patsiendil tekkis KA ÄNK, neil oli Killip klassi järgi raskem seisund, nad olid vanemad ja nende eGFR oli madalam. Samuti esines neil sagedamini hüpertensiooni ja diabeeti.
Leiti, et neerufunktsioonile kohandatud kontrastaine kogus on ägeda neerupuudulikkuse tekke riskifaktor.

Ülevaade (Andreucci et al 2014)
<u>Peamised soovitused ÄNK ennetamiseks, eriti kõrge riskiga patsientidel.</u>
Neerufunktsiooni jälgimine enne ja peale kontrastainega uuringut. Kõrge riskiga patsientidel peale KA uuringut 5 päeva 1x päevas.
Nefrotoksiliste ravimite ära jätmine enne KA uuringut.
Valida vähem nefrotoksiline kontrastaine. Kasutada madalamat KA annust uuringul.
Suukaudne rohke vedeliku tarbimine päev enne protseduuri. Madala ja mõõduka riskiga patsientidel: 500 ml vett või karastusjooke (nt tee) suukaudselt ja 2500 ml 24 tundi pärast kontrastaine manustamise või veenisiseselt süstimist 100 ml / h 0,9% soolalahust alustati 4 tundi enne kontrastaine manustamise ja jätkates 24 tundi hiljem.
Kõrge riskiga patsientidel peab jälgima ka piisavat diureesi, et määrata vedeliku koguseid, muidu võib tekkida kopsuturse. Nendel patsientidel on soovitav Infusioon kiirusel 1 ml/kg/h ja kasutatakse kliinilises praktikas seda 6-12 tundi enne protseduuri ja jätkatakse kuni 12-24 tundi pärast KA uuringut. Seda võib teha ainult siis, kui uriini kogus on piisav ja südame-veresoonkonna seisund võimaldab seda.

Süstemaatilises ülevaates ja metaanalüüsis (James, M.T. et al.2013) uuriti perkutaanse koronaarangioplastika järgse kotrastnefropaatiaga patsientide suremust, kardiovaskulaarsete sündmuste esinemist, lõppstaadiumi neerupuudulikkuse kujunemist ja haiglaravi kestust. Kaasati 39 vaatlusuuringut (n= 152 459). Kaasatud oli nii varasemalt normaalse neerufunktsiooniga patsiente kui ka teadaoleva KNH-ga patsiente. Negatiivse aspektina toovad autorid välja uuringute suure heterogeensuse, võimalik on publikatsiooninihe.
Uuringu tulemuste alusel seostub kontrastnefropaatia suurema suremusega (RR, 1.79; 95% CI, 1.47–2.18), seost mõjutab omakorda patsiendi eelnev seisund ja kaasuvad haigused (eelnevat seisundit arvestamata on risk ligi 8x kõrgem). Samuti esines seos kontrastnefropaatia ja kardiovaskulaarsete sündmuste tekke (RR 2.42; 95% CI 1.62–3.64), lõppstaadiumi neerupuudulikkuse (RR, 6.95; 95% CI, 2.51–19.26) ja pikenenud haiglaraviga (erinevate uuringute alusel 0,5 – 8,3 lisapäeva).

Kokkuvõte
Peamisteks soovitusteks analüüsitud tõendusmaterjali põhjal on välja selgitada kõrge riskiga patsiendid, eriti need, kellel on eGFR <60 ml/min/1,73m2, diabeet, nefrotoksiliste ravimitega kokkupuude ja varasem nefropaatia anamneesis. Suurem risk KA ÄNKile on ka raskemas seisundis (südamepuudulikkus, infarkt, madal südame väljutusfraktsioon ja kõrgem vanus) patsientidel. Risk tõuseb patsientidel, kelle eGFR on <45 ml/min/1,73 m2, ka siis kui on ennetusstrateegiat kasutatud.
Kõrge riskiga patsientidel kaaluda alternatiivina kontrastainevaba uuringumeetodi kasutamist.

Neerufunktsiooni jälgimine enne ja peale kontrastainega uuringut (48-72 tunni jooksul). Kõrge riskiga patsientidel peale KA uuringut 5 päeva 1x päevas.
Suukaudne rohke vedeliku tarbimine päev enne protseduuri.
Vähemalt 6-12 tundi enne sekkumist alustada intravenooset infusiooni NaCl 0,9% 1 ml/kg/h ja jätkata peale protseduuri 12-24 tundi.
Nefrotoksiliste ravimite ära jätmine enne KA uuringut.
Valida vähem nefrotoksiline kontrastaine (madalama osmolaarsusega või isoosmolaarne).
Kasutada madalamat KA annust uuringul.

Viited

Kokkuvõtte (abstract või kokkuvõtlikum info)	Viide kirjandusallikale
Abstract **Background:** The risk for contrast-induced nephropathy (CIN) after intra-arterial application of an iodine-based contrast material is unknown for patients with chronic kidney disease (CKD) and peripheral arterial disease (PAD). **Purpose:** To investigate the incidence of CIN in patients with CKD and PAD. **Material and Methods:** This retrospective study was approved by the local ethics committee. One hundred and twenty patients with 128 procedures (73 with baseline eGFR in the range of 45–60 mL/min/1.73m2, 55 with eGFR<45 mL/min/1.73m2) were evaluated. All patients received intra-arterially an iodine-based low-osmolar contrast material (CM) after adequate intravenous hydration with isotonic NaCl 0.9% solution. CIN was defined as an increase in serum creatinine of more than 44 lmol/L within 4 days. The influence of patient-related risk factors (age, weight, body mass index, eGFR, serum creatinine, hypertension, diabetes mellitus, coronary heart disease, heart failure) and therapy-related risk factors (amount of CM, nephrotoxic drugs, number of CM applications) on CIN were examined. **Results:** CIN developed in 0% (0/73) of procedures in patients with PAD and an eGFR in the range of 45–60 mL/min/1.73m2 and in 10.9% (6/55) of procedures in patients with an eGFR <45mL/min/1.73m2. No risk factor significantly influenced the development of CIN, although baseline serum creatinine (P<0.06) and baseline eGFR (P<0.10) showed a considerable dependency. **Conclusion:** Patients with an eGFR in the range of 45–60 mL/min/1.73m2 and PAD seem not at risk for CIN after intra-arterial CM application and adequate hydration. Whereas, an eGFR<45 mL/min/1.73m2 correlated with a risk of 10.9% for a CIN. **Table 1.** Incidence of CIN, according to baseline eGFR. | eGFR group (mL/min/1.73m^2) | Portion of all procedures (%) | Incidence of CIN (%, 95% confidence level) [95% CI] | |---|---|---| | 45 ≤ eGFR < 60 | 57% (73/128) | 0% (0/73) | | eGFR < 45 | 43% (55/128) | 10.9% (6/55) [2.4–19.4%] | **Table 2.** Incidence of CIN according to various definitions. | eGFR group (mL/min/1.73m^2) | SCr increase > 44 µmol/L (range) | SCr increase > 25% (range) | eGFR decrease > 25% (range) | |---|---|---|---| | 45 ≤ eGFR < 60 | 0/73 | 0/73 | 0/73 | | eGFR < 45 | 6/55 (46.9–116.7 µmol/L) | 6/55 (31.9–68.1%) | 6/55 (26.2–45.0%) |	**Contrast-induced nephropathy in patients with chronic kidney disease and peripheral arterial disease.** **2015** **Kroneberger, C; Enzweiler2,C. N; Schmidt-Lucke3, A et al.** http://www.ncbi.nlm.nih.gov/pubmed/26346218

Abstract Contrast-induced AKI (CI-AKI) has been one of the leading causes for hospital-acquired AKI and is associated with independent risk for adverse clinical outcomes including morbidity and mortality. The aim of this review is to provide a brief summary of the studies that focus on nonpharmacological strategies to prevent CI-AKI, including routine identification of at-risk patients, use of appropriate hydration regimens, withdrawal of nephrotoxic drugs, selection of low-osmolar contrast media or isoosmolar contrast media, and using the minimum volume of contrast media as possible. There is no need to schedule dialysis in relation to injection of contrast media or injection of contrast agent in relation to dialysis program. Hemodialysis cannot protect the poorly functioning kidney against CI-AKI. **Conclusion** The Contrast Media Safety Committee of ESUR [18] has updated its guidelines on CI-AKI (Table 5). First, identify high-risk patients, especially those with eGFR <60 mL/min/1.73m2, diabetes mellitus, recent nephrotoxic exposure, and intra-arterial route. In at-risk patients, consider an alternative imaging method, start volume expansion, and utilize the lowest dose of contrast media consistent with a diagnostic result. Finally, determining eGFR 48–72 hours after receiving contrast media should be performed for CIAKI detection. Similarly, the KDIGO Clinical Practice Guidelines on Acute Kidney Injury [60] recommend that balancing therisk for CI-AKI against the benefit of administering contrast media should be firstly considered. Alternative imaging methods not requiring contrast media administration in patients at increased risk for CI-AKI so long as these yield the same diagnostic accuracy might be required. Before an intervention which encompasses a risk for CI-AKI, a baseline serum creatinine should be determined. Volume expansion with either isotonic sodium chloride or sodium bicarbonate solutions, rather than no volume expansion in patients at increased risk for CI-AKI, should be considered during hospitalization. In high-risk patients, a repeated serum creatinine should be performed at 12 and 72 hours after administration of contrast media. Prophylactic intermittent hemodialysis or hemofiltration did not have strong evidence in updated data for the purpose of CI-AKI prevention only. In conclusion, contrast-induced AKI (CI-AKI) has been one of the leading causes for hospital-acquired AKI and is associated with independent risk for adverse clinical outcomes including morbidity and mortality. To prevent CI-AKI in patients who are receiving contrast media, every effort is required, including routine identification of at-risk patients, the use of appropriate hydration regimens, withdrawal of nephrotoxic drugs, selection of LOCM or IOCM, and using the minimum volume of contrast media as possible. There is no need to schedule the dialysis in relation to the injection of contrast media	**Nonpharmacological Strategies to Prevent Contrast-Induced Acute Kidney Injury.** **2014** **Paweena Susantitaphong, P and Eiam-Ong, S.** http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3984770/

or the injection of contrast agent in relation to the dialysis program. Hemodialysis does not protect the poorly functioning kidney against CI-AKI.

TABLE 1: Risk factors for contrast-induced acute kidney injury.

Patient-related	Procedure-related
(i) eGFR less than 60 mL/min/1.73 m^2 before intra-arterial administration	
(ii) eGFR less than 45 mL/min/1.73 m^2 before intravenous administration	
(iii) In particular, in combination with	
diabetic nephropathy	(i) Intra-arterial administration of contrast media
dehydration	(ii) High osmolality agents
congestive heart failure (NYHA grade 3-4) and low LVEF	(iii) Large doses of contrast media
recent myocardial infarction (<24 hours)	(iv) Multiple contrast media administrations within a few days
intra-aortic balloon pump	
periprocedural hypotension	
low hematocrit level	
age over 70 years	
concurrent administration of nephrotoxic drugs	
(iv) Known or suspected acute kidney injury	

Abstract

Radiocontrast media (RCM) are medical drugs used to improve the visibility of internal organs and structures in X-ray based imaging techniques. They may have side effects ranging from itching to a life-threatening emergency, known as contrast-induced nephropathy (CIN). We define CIN as acute renal failure occurring within 24–72 hrs of exposure to RCM that cannot be attributed to other causes. It usually occurs in patients with preexisting renal impairment and diabetes. The mechanisms underlying CIN include reduction in medullary blood flow leading to hypoxia and direct tubule cell damage and the formation of reactive oxygen species. Identification of patients at high risk for CIN is important. We have reviewed the risk factors and procedures for prevention, providing a long list of references enabling readers a deep evaluation of them both. The first rule to follow in patients at risk of CIN undergoing radiographic procedure is monitoring renal function by measuring serum creatinine and calculating the eGFR before and once daily for 5 days after the procedure. It is advised to discontinue potentially nephrotoxic medications, to choose radiocontrast media at lowest dosage, and to encourage oral or intravenous hydration. In high-risk patients N-acetylcysteine may also be given.

Side Effects of Radiographic Contrast Media: Pathogenesis, Risk Factors, and Prevention. 2014

Andreucci, M,[1] Solomon, R,[2] and Tasanarong, A.[3]

http://www.hindawi.com/journals/bmri/2014/741018/

TABLE 1: Risk factors for the development of contrast-induced nephropathy (CIN).

Nonmodifiable risk factors	Modifiable risk factors
Advanced age (>65 years)	Large doses and multiple injections of contrast media
Preexisting impairment of renal function	Route of administration
Advanced congestive heart failure	Osmolality of contrast media
Diabetes mellitus	Severe dehydration
Multiple myeloma	Prolonged hypotension
Sepsis	Anemia
Compromised left ventricle systolic performance	Reduction of effective intravascular volume
Renal transplant	Concomitant use of nephrotoxic drugs
	Concomitant use of ACEi and/or ARBs

Abbreviations: ACEi: angiotensin-converting enzyme inhibitors; ARBs: angiotensin II receptor blockers.

Conclusions

(i) The first rule to follow in patients at risk of CIN is monitoring renal function by measuring serum creatinine and calculating the eGFR before and once daily for 5 days after the radiographic procedure.
(ii) Potentially nephrotoxic medications, such as aminoglycosides, vancomycin, amphotericin B, metformin, and nonsteroidal anti-inflammatory drugs, should be discontinued before contrast media administration. If the use of aminoglycosides is absolutely necessary, avoid using more than one shot of aminoglycosides for the treatment of infections.
(iii) In the choice of the contrast agent, either IOCM or LOCM should be preferred.
(iv) Use the lowest dosage of contrast media.
(v) Fluid intake should be encouraged, for example, 500 mL of water or soft drinks (tea, mineral water) orally before and 2,500 mL for 24 hours after contrast administration. High-risk patients should be administered 0.9% saline by IV infusion at a rate of approximately 1 mL/kg per hour, beginning 6–12 hours before the procedure and continuing for up to 12–24 hours after the radiographic examination, if diuresis is appropriate and cardiovascular condition allows it.
(vi)In high-risk patients N-acetylcysteine may also be given with an oral dose of 600 mg twice daily on the day before and the day of procedure. For patients unable to take it orally, IV doses of 150 mg/kg over half an hour before the procedure or 50 mg/kg administered over 4 hours may be used.

ABSTRACT
Iodinated contrast media (CM) are used in many investigations that a patient may undergo during the course of an inpatient stay. For the vast majority of patients, exposure to CM has no sequelae; however, in a small percentage, it can result in a worsening in renal function termed contrast-induced acute kidney injury (CI-AKI). CI-AKI is one of the leading causes of in-hospital renal dysfunction. It is associated with a significant increase in morbidity and mortality as well as an increased length of hospital stay and costs. Unfortunately, the results of extensive research into pharmacological inventions to prevent CI-AKI remain disappointing. In this article, we briefly outline the

Contrast-induced acute kidney injury: how much contrast is safe?
2014

1. **Keaney, J.J.**1;
2. **Hannon, C.M.**2; **and**
3. **Murray, P.T.**2

http://ndt.oxfordjournals.org/content/28/6/1376.long

pathophysiological mechanisms by which iodinated CM may cause CI-AKI and discuss the evidence for reducing CI-AKI by limiting contrast volumes. In particular, we review the data surrounding the use of contrast volume to glomerular filtration rate ratios, which can be used by clinicians to effectively lower the incidence of CI-AKI in their patients.

Table 1. Comparison of studies to date investigating contrast to creatinine ratios, and their role in contrast-induced acute kidney injury

First author (reference)	Patient cohort	CI-AKI definition	Percentage cases of CI-AKI (%)	Contrast volume limit
Cigarroa [34]	115 patients with renal dysfunction (SCr >1.8 g/dL) undergoing diagnostic coronary angiography	Creatinine increase of 1 mg/dL over 5 days	6.9	5 mL/kg/creatinine
Marenzi [41]	561 patients with STEMI	>25% increase over 72 h	20.5	5 mL/kg/creatinine
Laskey [31]	3179 consecutive patients undergoing PG	Creatinine increase of 0.5 mg/dL or 25%	1.5	CV/CrCL <3.7
Gurm [43]	45 429 patients with PCI 16.1% emergency 20.2% acute MI (<24 h)	Creatinine increase of 0.5 mg/dL	3.2	CV/CCC ratio <2
Mager [43]	871 patients with STEMI	Creatinine increase of0.5 mg/dL or 25% in48 h	8.3	CV/GFR <3.7
Nyman [45]	391 with STEMI	>44.2 µmol/L rise in creatinine	16.6	g-I/GFR Ratio grades from 1:2 to 3:1 mainly advocated ratioof 1:1

STEMI: ST segment elevation MI; PCI: percutaneous coronary intervention; CV/CrCL: ratio of the volume of contrast (in millilitres) to creatinine clearance (in millilitres per minute); MI: myocardial infarction; GFR: glomerular filtration rate in millilitres per minute; g-I: grams of iodine.

CONCLUSION

CI-AKI can be reduced by reducing contrast volumes administered. Doctors should remain cognizant of the risk of AKI during procedures involving CM and restrict contrast doses accordingly. Evidence to date would suggest that contrast doses should be limited to the g-I/GFR ratio of 1, which will minimize, but not nullify the risk of CI-AKI. This should be even less in the presence of additional risk factors. Further improvement on the contrast ratios would be welcomed, but should concentrate on those most at risk of developing CIAKI, for example, those with baseline CKD.

Objective: To evaluate the prevalence of known risk factors for contrast-induced nephropathy (CIN) and their association with the actual occurrence of CIN in patients undergoing intravenous contrast-enhanced computed tomography (CECT) in Korea. **Materials and Methods:** Patients who underwent CECT in 2008 were identified in the electronic medical records of 16 tertiary hospitals of Korea. Data on demographics, comorbidities, prescriptions and laboratory test results of patients were collected following a standard data extraction protocol. The baseline renal function was assessed using the estimated glomerular filtration rate (eGFR). We identified the prevalence of risk factors along the eGFR strata and evaluated their influence on the incidence of CIN, defined as a 0.5 mg/dL or 25% increase in serum creatinine after CECT.

Contrast-Induced Nephropathy in Patients Undergoing Intravenous Contrast-Enhanced Computed Tomography in Korea: A Multi-Institutional Study in 101487 Patients
2014
Lee,J, MD,[1] Jeong Yeon Cho, J.Y. MD;[2,3,4] Hak Jong Lee,H.J. MDet al.[5]

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4105808

Results: Of 432425 CECT examinations in 272136 patients, 140838 examinations in 101487 patients met the eligibility criteria for analysis. The mean age of the participants was 57.9 } 15.5 years; 25.1% of the patients were older than 70 years. The prevalence of diabetes mellitus was 11.9%, of hypertension 13.7%, of gout 0.55% and of heart failure was 1.7%. Preventive measures were used in 40238 CECT examinations (28.6%). The prevalence of risk factors and use of preventive measures increased as the renal function became worse. A CIN was occurred after 3103 (2.2%) CECT examinations, revealing a significant association with decreased eGFR, diabetes mellitus, and congestive heart failure after adjustment.
Conclusion: Risk factors for CIN are prevalent among the patients undergoing CECT. Preventive measures were seemingly underutilized and a system is needed to improve preventive care. In conclusion, we found that DM, CHF and a decreased eGFR were significantly associated with the occurrence of CIN after CECT in Korea and preventive measures were underutilized. Further efforts are needed to develop a system for the identification of susceptible patients and for the facilitation of preventive measures are needed.

Table 3. Association of Risk Factors of CIN with Actual Occurrence of CIN

Risk Factors	Non-CIN		CIN		Univariable Analysis	Multivariable Analysis
	N = 137735	%	N = 3103	%	RR* (95% CI)	RR* (95% CI)
Diabetes mellitus	16238	11.8	507	16.3	1.50 (1.35–1.66)	1.13 (1.01–1.27)
Hypertension	18697	13.6	547	17.6	1.37 (1.24–1.51)	0.88 (0.79–0.99)
Congestive heart failure	2249	1.6	154	5.0	3.21 (2.69–3.84)	1.49 (1.22–1.82)
Gout	744	0.5	27	0.9	1.70 (1.16–2.50)	0.78 (0.52–1.18)
Advanced age (≥ 70)	34428	25.0	940	30.3	1.36 (1.25–1.47)	0.84 (0.76–0.92)
Decreased eGFR (< 45)	4813	3.5	971	31.3	12.99 (11.92–14.17)	11.52 (10.43–12.73)
NSAIDs	34694	25.2	816	26.3	1.07 (0.98–1.16)	0.92 (0.83–1.02)
Diuretics	15917	11.6	368	11.9	1.03 (0.92–1.16)	0.93 (0.76–1.12)
ACEI or ARB	16177	11.8	395	12.7	1.10 (0.98–1.23)	1.07 (0.88–1.31)
Preventive measures	38474	27.9	1764	56.9	3.33 (3.08–3.60)	2.83 (2.62–3.07)

Note.— Estimated glomerular filtration rate (eGFR) was calculated using MDRD formula whose unit was mL/min/1.73 m^2. *Estimates were calculated using generalized estimating equations. ACEI = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker, CI = confidence interval, CIN = contrast-induced nephropathy, MDRD = Modification of Diet in Renal Diseases, NSAID = non-steroidal anti-inflammatory drugs, RR = relative risk

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Background—Age, estimated glomerular renal function (eGFR), and ejection fraction are preprocedural predictors of contrast-induced acute kidney injury (CI-AKI) after primary percutaneous coronary intervention. The effect of renal function–adjusted contrast volume (CV) remains not totally explored, and a threshold has not yet been established.
Methods and Results—Logistic regression and receiver-operating characteristic curve analyses were used to assess whether CV/eGFR was an independent predictor of CI-AKI. The increased discriminative value of CV/eGFR over the preprocedural model based on age, eGFR, and ejection fraction was examined using the net reclassification improvement analysis. Of 470 patients enrolled, we observed 25 (5.3%) cases of CI-AKI. Patients with CI-AKI had received a higher renal function–adjusted CV (CV/eGFR 3.62 versus 1.96; P<0.001),

Renal Function–Adjusted Contrast Volume Redefines the Baseline Estimation of Contrast-Induced Acute Kidney Injury Risk in Patients Undergoing Primary Percutaneous Coronary Intervention. 2014

1. **Andò, G MD,PhD;**
2. **Gregorio,de C, MD;**
3. **Morabito, G, MD et al.**

http://circinterventions.ahajournals.org/content/7/4/465.

and CI-AKI incidence was higher (15%; *P*<0.001) in patients in the highest quartile of CV/eGFR, corresponding to the cutoff indicated by the receiver-operating characteristic curve (>2.5; area under the curve, 0.77). At multivariable analysis, CV/eGFR above the cutoff (odds ratio, 5.57; *P*=0.002) remained an independent predictor of CI-AKI. The model with CV/eGFR demonstrated a statistically significantly net reclassification improvement of 0.23 (*P*=0.021) over the baseline preprocedural model, largely driven by a correct decrease in risk estimates for patients not experiencing CI-AKI, with a likelihood ratio $\chi 2$ of 5.973 (*P*=0.029). ***Conclusions***—CV remains a key risk factor for CI-AKI after primary percutaneous coronary intervention and our study supports the need for minimizing CV, independently from baseline preprocedural risk. A CV restricted to no more than twice and a half the baseline eGFR might be valuable in reducing the risk of CI-AKI. During the study period, 535 patients with STEMI underwent primary PCI. Of these, 65 were excluded from the study: 4 patients on chronic hemodialysis, 17 patients who died within 2 days after the procedure, 8 patients who were transferred soon after the procedure to undergo emergency cardiac surgery, and 36 patients were also excluded because their data set was incomplete to assess the occurrence of CI-AKI. The final study population consisted of 470 patients. Demographic characteristics and procedural data are summarized in Table 1. Briefly, mean age was 62±12 years. Seventy-three percent were men, 43% were current smokers, 30% were diabetic, 60% had a history of hypertension, and 58% of dyslipidemia. Mean eGFR was 91±32 mL/min per 1.73 m2. We observed 25 (5.3%) cases of CI-AKI. These patients (Table 1) were older, had a more severe impairment of global hemodynamic status, as expressed by the Killip class (Killip>1 in 32% versus 12%; *P*<0.001), and worse basal renal	**long**

Table 1. Clinical and Procedural Variables in Patients With and Without CI-AKI in the Development Series

	CI-AKI	No CI-AKI	*P* Value
Patients (%)	25 (5.3)	445 (94.7)	
Age, y	73±10	61±12	<0.001
Men (%)	18 (72)	327 (73)	0.51
Familiar history of coronary artery disease (%)	13 (52)	244 (55)	0.47
Cigarette smoking (%)	5 (20)	199 (45)	0.02
Hypertension (%)	21 (84)	259 (58)	0.01
Diabetes mellitus (%)	13 (52)	129 (29)	0.02
Dyslipidemia (%)	14 (56)	260 (58)	0.48
Obesity (%)	9 (36)	116 (26)	0.19
Previous acute myocardial infarction (%)	5 (20)	74 (17)	0.43
LVEF (%)	39±14	48±11	<0.001
sCr, mg/dL	1.49±0.62	0.91±0.31	<0.001
eGFR, mL/min per 1.73 m²	52±19	94±32	<0.001
eGFR<60 mL/min per 1.73 m² (n=70)	17 (68%)	53 (12%)	<0.001
LDL cholesterol, mg/dL	95±35	111±45	0.08
Hemoglobin, g/dL	12.9±2.1	13.9±1.8	0.003
Troponin, ng/mL	22±68	8±22	0.01
Heart rate, bpm	86±23	79±18	0.07
Preprocedural Killip class	1.4±0.7	1.1±0.4	0.002
AGEF score	2.85±1.15	1.49±0.65	<0.001
Mehran risk score	9.4±5.7	4.5±3.3	<0.001
Use of IABP (%)	3 (12)	7 (1.5)	0.01
Postprocedural TIMI flow	2.6±0.9	2.9±0.4	<0.001
Grade 0 (%)	2 (8)	3 (0.7)	<0.001
Grade 1 (%)	3 (12)	9 (2)	
Grade 2 (%)	1 (4)	28 (6)	
Grade 3 (%)	19 (76)	406 (91)	
Total CV, mL	165±79	164±62	0.94
Total CV>200 mL	3 (12%)	80 (18%)	0.33
Total CV>300 mL	1 (4%)	13 (3%)	0.54
MACD (Cigarroa formula)	0.51±0.25	0.40±0.22	0.07
CV/eGFR	3.62±2.6	1.96±1.05	<0.001
In-hospital stay, d	9±5	7±3	<0.001
In-hospital mortality (%)	4 (16)	6 (1.3)	0.001

AGEF indicates age, estimated glomerular filtration rate and ejection fraction; CI-AKI, contrast-induced acute kidney injury; CV, contrast volume; eGFR, estimated glomerular renal function; IABP, intra-aortic balloon pump; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; MACD, maximum accepted contrast dose; sCr, serum creatinine concentration; and TIMI, thrombolysis in myocardial infarction.

Table 3. Reclassification Table for the Addition of CV/eGFR (Model 2) to the Baseline Risk Model Based on the AGEF Score (Model 1): Patients With CI-AKI

Model 2 (AGEF+CV/eGFR)	≤2% (CI-AKI)	3%–5% (CI-AKI)	5%–25% (CI-AKI)	≥26% (CI-AKI)	Upward	Downward
Model 1 (AGEF)						
≤2% (CI-AKI)	1	0*	1*	0*	1*	...
3%–5% (CI-AKI)	0†	2	1*	0*	1*	...
5%–25% (CI-AKI)	0†	0†	9	3*	3*	...
≥26% (CI-AKI)	0†	0†	1†	7	...	1†
					5*	1†

* and † Cases correctly and incorrectly, respectively, reclassified with model 2. Model 2 allowed 5 patients having CI-AKI to be correctly reclassified in the higher risk category and only 1 patient to be incorrectly reclassified in the lower risk category. AGEF indicates age, estimated glomerular filtration rate and ejection fraction; CI-AKI, contrast-induced acute kidney injury; CV, contrast volume; and eGFR, estimated glomerular renal function.

Table 4. Reclassification Table for the Addition of CV/eGFR (Model 2) to the Baseline Risk Model Based on the AGEF Score (Model 1): Patients Without CI-AKI

Model 2 (AGEF+CV/eGFR)	≤2% (No CI-AKI)	3%–5% (No CI-AKI)	5%–25% (No CI-AKI)	≥26% (No CI-AKI)	Upward	Downward
Model 1 (AGEF)						
≤2% (no CI-AKI)	285	8*	0*	0*	8*	...
3%–5% (no CI-AKI)	28†	28	3*	0*	3*	28†
5%–25% (no CI-AKI)	0†	17†	62	3*	3*	17†
≥26% (no CI-AKI)	0†	0†	2†	9	...	2†
					14*	45†

* and † Cases incorrectly and correctly, respectively, reclassified with model 2. Forty-five patients not having CI-AKI were correctly reclassified downward and 14 patients not having CI-AKI were incorrectly reclassified upward. AGEF indicates age, estimated glomerular filtration rate and ejection fraction; CI-AKI, contrast-induced acute kidney injury; CV, contrast volume; and eGFR, estimated glomerular renal function.

Abstract

It is well known that iodinated radiographic contrast media may cause kidney dysfunction, particularly in patients with preexisting renal impairment associated with diabetes. This dysfunction, when severe, will cause acute renal failure (ARF). We may define contrast-induced Acute Kidney Injury (AKI) as ARF occurring within 24–72 hrs after the intravascular injection of iodinated radiographic contrast media that cannot be attributed to other causes. The mechanisms underlying contrast media nephrotoxicity have not been fully elucidated and may be due to several factors, including renal ischaemia, particularly in the renal medulla, the formation of reactive oxygen species (ROS), reduction of nitric oxide (NO) production, and tubular epithelial and vascular endothelial injury. However, contrast-induced AKI can be prevented, but in order to do so, we need to know the risk factors. We have reviewed the risk factors for contrast-induced AKI and measures for its prevention, providing a long list of references enabling readers to deeply evaluate them both.

5. Prevention of AKI

It is absolutely necessary to try to prevent contrast-induced AKI. This is even more necessary in high risk patients. The following are useful suggestions for its prevention.

5.1. Monitoring Renal Function

Renal function should be monitored in any patient before any radiographic procedure that requires the use of radiographic iodinated contrast agents. SCr should be checked before and after the use of contrast medium. In patients at high risk of AKI, SCr should be checked before and once daily for 5 days after the radiographic procedure [1]. The increase in SCr after the contrast agent administration will indicate nephrotoxicity.

5.2. Removal of Nephrotoxic Drugs

Potentially nephrotoxic drugs should be discontinued, whenever possible, before the contrast procedure. This is the case with aminoglycosides, whose direct nephrotoxic effect would potentiate the contrast nephrotoxicity, vancomycin, amphotericin B, cisplatin, and nonsteroidal anti-inflammatory drugs.

In those cases in which aminoglycosides cannot be removed, its dosage should be reduced. Thus, the European Renal Best Practice (ERBP) [115] suggests, for the treatment of infections in patients with normal kidney function in steady state, to

Acute Kidney Injury by Radiographic Contrast Media: Pathogenesis and Prevention.
2014

Andreucci, M; Faga, T; Pisani, A et al.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4150431/

administer aminoglycosides as a single dose daily rather than multiple doses, but with monitoring of aminoglycoside blood levels. For amphotericin B, the ERBP recommends that saline loading be implemented in all patients receiving any formulation of amphotericin B [115].

Metformin is a biguanide (dimethylbiguanide) that is used in patients with non-insulin-dependent diabetes mellitus (type II diabetes) as an oral antihyperglycemic medication. Since it stimulates intestinal production of lactic acid, potential harm may happen when renal failure occurs. Approximately 90% of metformin is eliminated via the kidneys in 24 hrs. Thus, renal insufficiency (GFR < 70 mL/min) will lead to its retention in the tissues and to lactic acidosis that can be fatal, since the onset of renal injury after the administration of contrast medium is quite rapid. Thus, the drug has to be discontinued at least 12 hours before the contrast and not be resumed for a minimum of 36 hours after the procedure, or longer if the SCr has not returned to baseline [116].

We have already discussed the controversial opinions on the role of ACEIs and ARBs as potential risk factors for contrast-induced AKI. According to KDIGO guidelines for Acute Kidney Injury Work Group, there is insufficient evidence to recommend discontinuation of these medications prior to contrast administration [117].

5.3. The Choice of the Radiographic Contrast Agent

It is very important to choose the least nephrotoxic radiocontrast agent. The LOCM (e.g., iohexol) are less nephrotoxic than HOCM (e.g., diatrizoate). Furthermore, the IOCM (e.g., iodixanol) seem to be less nephrotoxic than the LOCM [1, 10]. A multicenter, randomized, double-blind comparison of iopamidol (LOCM) and iodixanol (IOCM) has been performed by Solomon et al. [91] in patients with chronic kidney disease. The incidence of contrast-induced AKI was not statistically different after the intra-arterial administration of iopamidol or iodixanol to high-risk patients, with or without diabetes mellitus. The authors conclude that iodixanol (IOCM) and iopamidol (LOCM) are iodinated contrast agents of choice to reduce risk of AKI.

5.4. The Dosage of the Radiographic Contrast Agent

The lowest dosage possible of the radiographic contrast agent should be used.

High doses of contrast agents are required in PCI. For this procedure, some formulas have been suggested to calculate the dosage that is least dangerous for renal function [1].

1. Cigarroa's formula: 5 mL of contrast per kg b.w./SCr (mg/dL) with maximum acceptable dose of 300 mL for diagnostic coronary arteriography [118].
2. Laskey's formula: volume of contrast to calculated creatinine clearance ratio with a cut-off point of the ratio at 3.7 for PCI; a ratio >3.7 would be associated, following contrast use, with a decrease in CrCl [119]. Recently

Gurm et al. [120] have suggested a cut-off point at 2.0: below a ratio of 2.0 AKI would be a rare complication of PCI, but it would increase dramatically at a ratio of 3.0. 3. A new formula seems to be superior and consists of a ratio of grams of iodine to the eGFR; a ratio of 1.42, or even better a ratio of 1.0, would prevent contrast-induced AKI [121].	
A Systematic Review and Meta-Analysis ***Background***—Contrast-induced acute kidney injury (CI-AKI) has been associated with mortality, although it has been suggested this association may be attributable to confounding. We performed a systematic review and meta-analysis to characterize the associations between CI-AKI and subsequent clinical outcomes. ***Methods and Results***—We identified studies using MEDLINE (1950 to June 2011) and Embase (1980 to June 2011), manual bibliographic searches, and contact with experts. We included observational studies that characterized outcomes among patients with and without AKI (based on changes in serum creatinine) after coronary angiography. Eligible studies reported at least 1 of mortality, cardiovascular events, end-stage renal disease, or length of hospital stay. Thirtynine observational studies met inclusion criteria. Of 34 studies reporting mortality (including 139 603 participants), 33 reported an increased risk of death in those with CI-AKI, although the effect size varied between studies ($I2$=93.5%). Between-study heterogeneity was partially explained by whether adjustment for confounding features was performed (11 studies without adjustment; pooled crude risk ratio, 8.19; 95% confidence interval, 4.30–15.60; $I2$=77.3% versus 23 studies with adjustment; pooled adjusted risk ratio, 2.39; 95% confidence interval, 1.98–2.90; $I2$=88.3%). CI-AKI was consistently associated with an increased risk of cardiovascular events in 14 studies, end-stage renal disease in 3 studies, and prolonged hospitalization in 11 studies. ***Conclusions***—CI-AKI is associated with an increased risk of mortality, cardiovascular events, renal failure, and prolonged hospitalization. However, the association between CI-AKI and mortality is strongly confounded by baseline clinical characteristics that simultaneously predispose to both kidney injury and mortality, and the risk attributable to CI-AKI is much lower than that reported from unadjusted studies.	**Contrast-Induced Acute Kidney Injury and Risk of Adverse Clinical Outcomes After Coronary Angiography.** **2013** 1. **James, M.T,MD, PhD,** 2. **Samuel, S.M, MD, MSc,** **3. Manning, M.A, BSc. et al.** http://circinterventions.ahajournals.org/content/6/1/37.long

Lisamaterjal:

Meta-analysis: Serum creatinine changes following kontrast enhanced CT imaging
Judith Kooiman , Sharif M. Pasha, Wendy Zondag, Yvo W.J. Sijpkens, Aart J. van der Molen, Menno V. Huisman a, Olaf M. Dekkers
European Journal of Radiology 81 (2012) 2554–2561

Purpose: Contrast induced nephropathy (CIN) is defined as a decrease in renal function following administration of contrast media. The aim of this meta-analysis was to asses the overall risk of CIN, chronic loss of kidney function and the need for renal replacement therapy (RRT) after intravenous contrast enhanced CT-scan. Secondly, we aimed to identify subgroups at increased risk for CIN.
Materials and methods: A literature search in Pubmed, Medline, Embase and Cochrane databases was performed. Data extraction was carried out independently by two reviewers. Meta-analysis and metaregression were performed using an exact likelihood approach.
Results: Forty studies evaluating the incidence of CIN after CT were included. **The pooled incidence of CIN was 6.4% (95% CI 5.0–8.1). The risk of RRT after CIN was low, 0.06% (95% CI 0.01–0.4).** The decline in renal function persisted in 1.1% of patients (95% CI 0.6–2.1%). **Patients with chronic kidney disease (odds ratio 2.26, $p < 0.001$) or diabetes mellitus (odds ratio 3.10, $p < 0.001$) were at increased risk for the development of CIN.**
Conclusion: **CIN occurred in 6% of patients after contrast enhanced CT. In 1% of all patients undergoing contrast enhanced CT the decline in renal function persisted.**

Ravijuhendid
Sekretariaadi poolt AGREEga hinnatud ja kasutusele võetud ravijuhenditest oli kahes ravijuhendis käsitletud kontrastaine kasutamist KNHga patsientidel.

KDIGO ravijuhend

Risk ägeda neerupuudulikkuse (AKI) tekkeks kasutades jodeeritud kontrastainega uuringut tuleb eelnevalt hinnata kontrastainega radioloogilise diagnostika kasu ja kontrastaine kahju riski suhet (Not GRADE).
Kõik inimesed kellel on GFR väiksem kui <60 ml / min / 1,73m2 (GFR kategooriad G3A-G5) ja kellel teostati plaaniline intravaskulaaruuring koos joodi sisaldava kontrastainega peaks järgima vastavat KDIGO Clinical Practice ravijuhendit ennetamaks ÄNK.

- Kõik kellel on GFR <60 tuleks vältida kõrge osmolaarsusega aineid (1B)
- Kasutada võimalikult väikest kontrastaine annust (Not GRADE)
- Enne ja peale protseduuri ära jätta kõik nefrotoksilised ravimid (1C)
- Piisav hüdratatsioon NaCl lahusega enne protseduuri, protseduuri ajal ja peale protseduuri (1A)
- Mõõta GFRi 48-96 tunni jooksul peale protseduuri (1C)

4.5.2: We recommend that all people with GFR <60 ml/min/1.73m2 (GFR categories G3a-G5) undergoing elective investigation involving the intravascular administration of iodinated radiocontrast media should be managed according to the KDIGO Clinical Practice Guideline for AKI including:
*** Avoidance of high osmolar agents (1B);**
*** Use of lowest possible radiocontrast dose (Not Graded);**
***Withdrawal of potentially nephrotoxic agents before and after the procedure (1C);**
***Adequate hydration with saline before, during, and after the procedure (1A);**
***Measurement of GFR 48–96 hours after the procedure (1C).**

Gadoliiniumi sisaldusega kontrastained
Gadoliiniumisisaldusega kontrastaine võib põhjustada nefrogeenset süsteemset fibroosi (NSF; Nephrogenic systemic fibrosis).

- Soovitame mitte kasutada gadoliniumi sisaldavaid kontrastaineid inimestel kelle GFR on <15 ml/min/1,73 m2 (GFR kategooria G5), va. Juhul kui ei ole alternatiivseid asjakohaseid teste. (1B)
- Soovitame inimestele, kellel on GFR <30 ml / min /1,73 m2 (GFR kategooriad G4-G5) ning kes vajavad gadoliniumi sisaldavat kontrastainet peaks kasutama eelistatult makrotsüklilist kelaatpreparaati. (2B)

Arstid peavad olema teadlikud riski-kasu suhtest enne gadoliniumisisaldusega kontrasaine kasutamist inimestel, kelle GFR on15-29 ml / min / 1,73 m2.
GFR <15 ml / min / 1,73 m2 patsientidele soovitavad juhendid kohe peale protseduuri dialüüsi ja dialüüsi kordamist 24 tunni pärast. GFR >15 ml / min / 1,73 m2 dialüüsi kasu on ebakindel.

***4.5.3: We recommend not using gadolinium-containing contrast media in people with GFR <15 ml/min/1.73 m2 (GFR category G5) unless there is no alternative appropriate test. (1B)**

***4.5.4: We suggest that people with a GFR <30 ml/min/1.73 m2 (GFR categories G4-G5) who require gadolinium-containing contrast media are preferen-tially offered a macrocyclic chelate preparation. (2B)**

Table 40 | GRADE system for grading quality of evidence

Step 1: Starting grade for quality of evidence based on study design	Step 2: Reduce grade	Step 3: Raise grade	Final grade for quality of evidence and definition
Randomized trials = High	*Study quality* -1 level if serious limitations -2 levels if very serious limitations *Consistency* -1 level if important inconsistency	*Strength of association* +1 level is strong[a], no plausible confounders +2 levels if very strong[b], no major threats to validity *Other* +1 level if evidence of a dose-response gradient +1 level if all residual plausible confounders would have reduced the observed effect	High = Further research is unlikely to change confidence in the estimate of the effect Moderate = Further research is likely to have an important impact on confidence in the estimate of effect, and may change the estimate
Observational study = Low	*Directness* -1 level if some uncertainty -2 levels if major uncertainty		Low = Further research is very likely to have an important impact on confidence in the estimate and may change the estimate
Any other evidence = Very low	*Other:* -1 level if sparse or imprecise data[c] -1 level if high probability of reporting bias		Very low = Any estimate of effect is very uncertain

Abbreviation: GRADE, Grading of Recommendations Assessment, Development, and Evaluation.
[a]Strong evidence of association is defined as 'significant relative risk of >2 (<0.5)' based on consistent evidence from two or more observational studies, with no plausible confounders.
[b]Very strong evidence of association is defined as 'significant relative risk of >5 (<0.2)' based on direct evidence with no major threats to validity.
[c]Sparse if there was only one study or if the results include just a few events or observations and were uninformative. Imprecise if the confidence interval spans a range greater than 1 or confidence limits are <0.5 to >2.0
Adapted by permission from Macmillan Publishers Ltd: *Kidney International*. Uhlig K, Macleod A, Craig J et al.[725] Grading evidence and recommendations for clinical practice guidelines in nephrology. A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2006; 70: 2058-2065; accessed http://www.nature.com/ki/journal/v70/n12/pdf/5001875a.pdf

Table 41 | Final grade for overall quality of evidence

Grade	Quality of evidence	Meaning
A	High	We are confident that the true effect lies close to that of the estimate of the effect.
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C	Low	The true effect may be substantially different from the estimate of the effect.
D	Very low	The estimate of effect is very uncertain, and often will be far from the truth.

Table 42 | Balance of benefits and harm

When there was evidence to determine the balance of medical benefits and harm of an intervention to a patient, conclusions were categorized as follows:

- For statistically significant benefit/harm, report as 'benefit [or harm] of drug X'.
- For non-statistically significant benefit/harm, report as 'possible benefit [or harm] of drug X'.
- In instances where studies are inconsistent, report as 'possible benefit [or harm] of drug X'.
- 'No difference' can only be reported if a study is not imprecise.
- 'Insufficient evidence' is reported if imprecision is a factor.

Malaysia ravijuhend

Võimalusel vältida kontrastaineid:

- Kõrge riskiga patsientidel, kellel on varem esinenud nefropaatia, (seerumi kreatiniinisisaldus ≥132 mcmol/L või eGFR <60 ml/min/1,73 m2), DM, vedelikupuudus, kongestiivne kardiaalnepuudulikkus, nefrootiline sündroom, dekompenseeritud maksatsirroos või samaaegne NSAIDide/diureetikumide kasutamine.
- Kaaluda alternatiivina uuringuid nagu ultraheli, ilma kontrastaineta kompuutertomograafia (CT) skaneerimist või magnettomograafiat (MRI).
- Gadoliiniumoksiidi sisaldusega kontrastainet tuleks vältida patsientidel, kellel neerupuudulikkuse tõttu on suurenenud risk nefrogeensele süsteemsele fibroosile.
- Kasutada madala osmolaarsusega mitteioonseid või iso-osmolaarsusega kontrastaineid. Kasutada väikseimaid kontrastaine annuseid ja vältida korduvaid kontrastainega uuringud 48 tunni jooksul.

- Kasutada isotoonilise soolalahuse või naatriumvesinikkarbonaadi infusioone ilma või koos N-acetylcysteiiniga enne protseduuri.

Avoid radio-contrast agents if possible:
***Patients undergoing contrast procedure should be assessed for risk of contrast-induced nephropathy. High risk patients are those with pre-existing renal impairment (serum creatinine ≥132 µmol/L or an eGFR <60 ml/1.73 m2), DM, volume depletion, CCF, nephrotic syndrome, decompensated liver cirrhosis or concurrent NSAIDs/diuretic use.**
***Consider an alternative imaging study such as ultrasound, non-contrasted computerised tomography (CT) scan or magnetic resonance imaging (MRI). Gadolinium should be avoided in patients with advanced renal failure due to increased risk of nephrogenic systemic fibrosis.**
***Use non-ionic contrast media with low osmolarity (such asioversol and iopamidol) or iso-osmolarity (such as iodixanol).**
***Use the lowest dose of contrast possible and avoid repeated studies within 48 hours.**
***Use isotonic saline or sodium bicarbonate peri-procedure with or without N-acetylcysteine.**

Kokkuvõte

- **Riski ägeda neerupuudulikkuse (ÄNK) tekkeks kasutades jodeeritud kontrastainega uuringut tuleb eelnevalt hinnata kontrastainega radioloogilise diagnostika kasu ja kontrastaine kahju riski suhet (Not GRADE). KDIGO**
- **Kõik, kellel on GFR <60 tuleks vältida kõrge osmolaarsusega aineid (1B). KDIGO**
- **Kasutada võimalikult väikest kontrastaine annust (Not GRADE). KDIGO**
- **Enne ja peale protseduuri ära jätta kõik nefrotoksilised ravimid (1C). KDIGO**
- **Piisav hüdratatsioon NaCl lahusega enne protseduuri, protseduuri ajal ja peale protseduuri (1A). KDIGO**
- **Kasutada isotoonilise soolalahuse või naatriumvesinikkarbonaadi infusioone ilma või koos N- acetylcysteiiniga enne protseduuri. Malaysia**
- **Mõõta GFRi 48-96 tunni jooksul peale protseduuri (1C). KDIGO**
- **Kõrge riskiga patsientidel, kellel on varem esinenud nefropaatia, (seerumi kreatiniinisisaldus ≥132 pmol/L või eGFR <60 ml/1,73 m2), DM, vedelikupuudus, CCF, nefrootiline sündroom, dekompenseeritud maksatsirroos või samaaegne NSAIDide/ diureetikumide kasutamine. Malaysia**
- **Kaaluda alternatiivina uuringuid nagu ultraheli, ilma kontrastaineta kompuutertomograafia (KT) või magnetresonantstomograafiat (MRI). Malaysia**
- **Gadoliiniumoksiidi sisaldusega kontrastainet tuleks vältida patsientidel, kellel neerupuudulikkuse tõttu on suurenenud risk nefrogeensele süsteemsele fibroosile. Malaysia, KDIGO**

[Type text]

Lisamaterjal:

Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury.
Kidney inter., Suppl. 2012; 2: 1–138.

4.2.1: Assess the risk for CI-AKI and, in particular, screen for pre-existing impairment of kidney function in all patients who are considered for a procedure that requires intravascular (i.v. or i.a.) administration of iodinated contrast medium. (Not Graded)
Pre-existing renal functional impairment is the most important risk factor above all other risk factors for developing CI-AKI[408] and screening for both acute and chronic kidney disease is highly recommended. There is no sharp GFR threshold below which the risk for CI-AKI is clearly increasing.
A CI-AKI Consensus Working Panel[410] agreed that the risk of CI-AKI becomes clinically important when the baseline SCr concentration is >1.3 mg/dl (>115 mmol/l) in men and >1.0 mg/dl (>88.4 mmol/l) in women, equivalent to an eGFR ≤60 ml/min per 1.73 m^2. The CI-AKI Consensus Working Panel[410] recommended that precautions to reduce the risk should be implemented in patients with a baseline eGFR ≤60 ml/min per 1.73 m^2. In light of more recent information, this threshold could probably be lowered to 45 ml/min per 1.73 m^2.
The Work Group recommends that, when a recent SCr is not available, a simple questionnaire or a dipstick testing for urine protein may be useful for identifying pre-existing kidney disease. Risk stratification hinges on age, baseline kidney function, other comorbidities, and other risk factors.

Other risk factors for developing CI-AKI include diabetes, hypertension, CHF, advanced age, volume depletion, hemodynamic instability, use of concurrent nephrotoxic medications, and large volume or high osmolality of the contrast agent.[408,412] Metabolic syndrome, prediabetes, and hyperuricemia have been identified as new risk factors for CI-AKI, while the use of ACE-I and angiotensin-receptor blockers (ARB), renal transplantation, diabetes mellitus with normal renal function, low-osmolar contrast media, multiple myeloma, female gender, and cirrhosis have been classified as conflicting risk factors for CI-AKI.[413]

When possible, the administration of contrast media should be delayed in patients with circulatory collapse or CHF until their hemodynamic status is corrected.
Concurrent nephrotoxic medication—including, in particular, NSAIDs, aminoglycosides, amphotericin B, high doses of loop diuretics, and antiviral drugs like acyclovir and foscarnet—should preferably be stopped.

4.2.2: Consider alternative imaging methods in patients at increased risk for CI-AKI. (Not Graded)

Ravijuhendi töörühm manitseb ettevaatusele gadoliinumi sisaldavate kontrastainete kasutamisel. Mainitakse Gd nefrotoksilisuse riski, kuid uuringud selles osas on vasturääkivad.
Gd kasutamise hoiatus lähtub eelkõige nefrogeense süsteemse fibroosi tekkeriskist KNH-ga patsientidel:
It should be noted here that the European Medicines Agency stated a contraindication for use of gadodiamide in
patients with a GFR <30 ml/min per 1.73 m^2, and issued a warning for its use in patients who have a GFR between 30 and 60 ml/min per 1.73 m^2. The US FDA requested that vendors add warnings about the risk for developing NSF to the full prescribing information on the packaging for all Gd-containing contrast agents.[427] New labeling describes the risk for NSF following exposure to Gd in patients with a GFR o30 ml/min per 1.73 m^2 and in patients with AKI of any severity due to hepato-renal syndrome or in the perioperative liver transplantation period. Additional recommendations were recently proposed by Perazella[420] and were endorsed by the Work Group:
- Use of a macrocyclic chelate (gadoteridol in the USA), is preferred over linear chelates. The risk associated with the various Gd-containing agents is likely different. Gadoteridol, the only FDA-approved macrocyclic chelate, maintains less risk. Clearly, high dosages and large cumulative dosages of all these agents will increase risk for NSF.
- Use the lowest dosage of the agent possible to achieve the image.
- Avoid repeat exposures with Gd.
- Consider performing IHD after the exposure (and the next 2 days) in patients who are already maintained on IHD, recognizing that there are no data that support prevention of NSF with this modality. This recommendation is based on the pharmacokinetics of Gd and the theoretical benefit of removing it with IHD (>95% plasma clearance).

4.3.1: Use the lowest possible dose of contrast medium in patients at risk for CI-AKI. (Not Graded)

Table 16 | Additional radiological measures to reduce CI-AKI

Some CT strategies in patients at risk of CI-AKI

- Perform CT, when possible, without contrast media; scrutinize the examination and discuss with the referral physician-surgeon before deciding on the need for contrast media.
- Dosing per kilogram body weight to reduce the amount of contrast media is needed in thin patients.
- Adapt injection duration to scan duration when performing CT-angiography, so that the injection is not still running when the scan is finished.
- Use a saline chaser to decrease the amount of contrast media, by using the contrast medium that otherwise would remain in the dead space of the arm veins; this may save 10–20 ml of contrast media.
- Use 80 kVp; contrast-medium dose may be reduced by a factor of 1.5–1.7 compared to the dose used at 120 kVp since iodine attenuation increases, and combine with increased tube loading (mAs) to maintain signal-to-noise ratio.
- Further reduction of contrast media may be instituted in patients with known decreased cardiac output (not unusual in patients with renal impairment) undergoing CT-angiographic studies.

Some angiographic strategies in patients at risk of CI-AKI

- Use biplane when appropriate.
- Avoid test injections; the same amount may be enough for a diagnostic digital-subtraction angiography run.
- Scrutinize each series before performing the next; avoid unnecessary projections.
- Decrease kilovoltage in a thin patient; a lower iodine concentration may be used.
- Assess the physiologic significance of a stenosis by measurement of translesional pressure gradient and fractional flow reserve, a technique well accepted and validated for the coronary circulation. For different arterial beds, perform manometry of a questionable stenosis instead of multiple projections.
- Avoid ventriculography: echocardiography (and "echo contrast") is always a reasonable alternative.
- Use plasma isotonic contrast-media concentrations for renal artery injections.
- When renal artery stenosis is suspected, map the origin of major renal arteries with noninvasive procedures (e.g., CT without contrast media) for proper initial renal angiographic projections to avoid unnecessary runs, or perform primary manometry.
- CO_2 may be used as contrast medium in venous examinations and below the diaphragm for arterial examinations or alternatively use iodinated contrast media with the same contrast effect, i.e., about 40 mg iodine per milliliter.
- Since the contrast effect of 0.5 M Gd-contrast media has been regarded as diagnostic by many investigators (coronary, renal, aortofemoral arteriography, etc.), iodinated contrast media may be diluted to the same density, i.e., about 75 mg iodine per milliliter.
- Use selective or superselective catheterizations when appropriate, e.g., "single leg run-off".
- Reduce aortic flow and amount of contrast medium by temporal occlusion of femoral arteries with tourniquets when performing aortography.

Gd, gadolinium; kVp, peak kilovoltage.

4.3.2: We recommend using either iso-osmolar or lowosmolar iodinated contrast media, rather than high-osmolar iodinated contrast media in patients at increased risk of CI-AKI. (1B)
Soovitus põhineb randomiseeritud kontrollitud uuringutelja metaanalüüsidel mille alusel on madala osmolaarsusega kontrastained eelneva neerufunktsiooni vähenemisega patsientidele vähem nefrotoksilised. Ravijuhendi raames läbi viidud mõõduka tõenduse kvaliteediga süstemaatilise ülevaate alusel ei leitud madala osmolaarsusega ainete olulist eelist isoosmolaarstete ainete ees.

4.4.1: We recommend i.v. volume expansion with either isotonic sodium chloride or sodium bicarbonate solutions, rather than no i.v. volume expansion, in patients at increased risk for CI-AKI. (1A)
Soovitus põhineb mitmetel hea tasemega randomiseeritud kontrollitud uuringutel ja süstemaatilistel ülevaadetel. Täärühm soovitab i/v vedelikuasendust vähemalt 1.0–1.5 ml/kg/h 3–12 tundi enne ja 6–12 pärast kontrastaine manustamist. Eesmärgiks on diurees üle 150 ml/h.
Võrdlusuuringud isotoonilise bikarbonaadi ja 0,9% NaCl kasutamise osas on vastuolulised. Uuringute alusel või bikarbonaadi kasutamisel olla eelis kontrastnefropaatia ennetamisel, kuid töörühm rõhutab, et arvestada tuleb laguse valmistamise keerukust. Isotoonilise bikarbonaadi lahuse valmistamiseks tuleb lisada 154 ml 8.4% Na-bikarbonaati 846 ml-le 5% glükoosi lahusele. Lahuse valmistamiseks tekkivat ajakulu ja võimalikke vigu arvesse võttes ei leia töörühm, et Na-bikarbonaadi lagus omaks 0,9%-lise NaCl lahuse ees olulist eelist.

4.4.2: We recommend not using oral fluids alone in patients at increased risk of CI-AKI. (1C)
4.4.3: We suggest using oral NAC, together with i.v. isotonic crystalloids, in patients at increased risk of CI-AKI. (2D)
Töörühm leiab, et siiani ei ole piisavat tõendust, et KA-nefropaatia vältimiseks oleks vedeliku suukaudne manustamine sama efektiivne kui i/v manustamine.
N-atsetüültsüsteiini toimet KA-nefropaatia ennetamisel on tõestatud mitmes väikese valimiga RCT-s ja nende põhjal koosattud metaanalüüsides. Siiski on tõenduse kvaliteet madal, uuringutes esineb vasturääkivusi. Samas arvestades N-atsetüültsüsteiini väikest kõrvaltoimete riski ja võrdlemisi madalat hinda, soovitab töörühm seda KA-nefropaatia ennetamiseks kasutada.

4.5.1: We suggest not using prophylactic intermittent hemodialysis (IHD) or hemofiltration (HF) for contrast-media removal in patients at increased risk for CI-AKI. (2C).
Contrast media can be efficiently removed from blood by IHD and a single session effectively removes 60–90% of contrast media. On the basis of these observations, several studies have explored the prophylactic value of IHD in patients at high risk, but most of these studies have not demonstrated a reduced incidence of CI-AKI. It could theoretically be anticipated that high-flux membranes used in HF or hemodiafiltration (HDF) modalities should be able to remove contrast media more efficiently than low-flux membranes used in routine IHD. However, recent publications on this topic have added to the controversy about the role of IHD or HF to prevent

CI-AKI. In summary, the evidence profile for IHD vs. HF showed low-quality evidence and an uncertain benefit vs. harm balance of HF/IHD in preventing CI-AKI in patients with severe CKD. Given the costs and logistical difficulties, the use of HF modalities for CI-AKI prevention can only be advocated if future studies will convincingly show clear benefit.

Ravijuhendite soovitused on kooskõlas Ameerika ÜhendriikideToidu- ja ravimite ameti (FDA) ja Euroopa ravimiameti (EMA) piirangutega gadoliiniumiga kontrastainete kasutamise kohta neerufunktsiooni langusega patsientidel.