MANAGEMENT PROTOCOL

PREVENTION OF CONTRAST-INDUCED ACUTE KIDNEY INJURY (CI-AKI) FOLLOWING THE INTRAVASCULAR ADMINISTRATION OF IODINATED CONTRAST MEDIA
EXPERT PANEL

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MESSAGE FROM THE EXECUTIVE DIRECTOR

It is with great pleasure that NKTi, through its Department of Adult Nephrology in cooperation with the Department of Radiology and the Section of Cardiology present to you a very vital clinical risk management guideline, “Management Protocol for the Prevention of CI-AKI”.

We strongly believe that the healthcare sector’s biggest asset lies in its ability to learn from one another and to build strong partnerships in supporting the delivery of safe care. Hence, this multi-disciplinary approach to protect our patients from Contrast-Induced Acute Kidney Injury (CI-AKI) has come about.

We thank the Department of Adult Nephrology for spearheading this initiative.

Through this protocol, we hope that you will partner with us in making healthcare safer.

AILEEN RIEGO-JAVIER, MD, FPSP, CESO IV
Executive Director
National Kidney and Transplant Institute

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In the last year, with the commencement of services by the cardiac catheterization laboratory of the NKTI Diagnostics Center, more than a hundred coronary angiographic procedures have been done. Majority of them are performed on elderly, diabetic patients, and many with varying stages of chronic kidney disease. This is on top of the radiologic procedures of all organ systems using the most highly advanced equipment of the Department of Radiological Sciences, such as the 256-slice CT scan and 3-Tesla MRI as well as the vascular procedures of the Department of Organ Transplantation and Vascular Surgery.

Majority of these procedures involve the use of contrast agents to better visualize the organs and vascular system. Thus it is timely that the NKTI, under the Departments of Adult Nephrology, Radiological Sciences and Cardiovascular and Catheterization and Radiology Unit recommend a management protocol to guide all medical physicians in prescribing the radiologic procedures with the appropriate contrast agent to prevent the development of contrast-induced-acute kidney injury.

We learn about the pathophysiology of CI-AKI and how contrast agents can lead to CI-AKI because of their inherent properties. We look into the value of different contrast agents, recently made available in the country, that may help prevent its occurrence.

As the major referral center for diagnostic and therapeutic intervention for renal and urologic diseases and organ transplantation of the Department of Health, the NKTI takes the lead for all hospitals under the DOH, to guide physicians on measures to decrease the incidence of CI-AKI, starting with the recognition of the risk factors for its development, therapeutic modalities to prevent its occurrence and the strategies to monitor its development.

Included in this Management Protocol is an algorithm, tools to assist in predicting the risk for the development of CI-AKI, and even a physician order sheet to ensure that the physician takes all the necessary precautions to prevent CI-AKI.

This Protocol is dedicated to all the patients whom we treat every day, who have to go through a diagnostic modality or intervention involving contrast. It is the NKTI's way to ensure PATIENT SAFETY!

My congratulations to all who were involved in the development of this very handy protocol book! Kidneys will be saved!
Foreword

Pathophysiology of CI-AKI

Guideline 1 – Definition of CI-AKI

Guideline 2 – eGFR computation

Guideline 3 – Iodinated Contrast Media

Guideline 4 – Withdrawal of Concomitant Medications

Guideline 5 – Preventive Measures (Hydration, Medications)

Guideline 6 – Supportive Measures

Guideline 7 – Algorithm

Guideline 8 – Management of Low Risk Patients

Guideline 9 – Management of Moderate Risk Patients

Guideline 10 – Management of High Risk Patients

Guideline 11 – Management of Patients on RRT

Guideline 12 – Emergency Procedures

Guideline 13 – Monitoring

Guideline 14 – Doctor’s Orders

References
Reduced Nephron Mass Vulnerable To Injury
Associated Factors: Diabetes, Poor Renal Perfusion, Others

Contrast Enters Renal Vasculature
Endothelium-independent Transient Vasodilation (minutes)

Adenosine Release from Macula Densa
(Tubulo-glomerular Feedback)

Endothelin Release

Prostaglandin Dysregulation
Decreased Nitric Oxide Synthesis/Release

Sustained Intrarenal Vasoconstriction (hours)

Prolonged contrast transit time in kidneys
Increased contrast exposure to renal tubular cells

Medullary hypoxia

Contrast Direct Cellular Injury And Death
Ischemic Injury And Death
Oxidative Stress, Inflammation, Other Organ Injury Processes

Acute Kidney Injury
1. DEFINITION OF CI-AKI

Contrast-Induced AKI (CI-AKI) is defined as a rise in serum creatinine of ≥0.5 mg/dl (≥44 μmol/L) or a 25% increase from baseline value, assessed at 48 hours after a radiological procedure without an alternative etiology.


2. RISK STRATIFICATION (RENAL)

- **Low Risk**: eGFR > 60 ml/min
- **Moderate Risk**: eGFR 30-59 ml/min
- **High Risk**: eGFR < 30ml/min

- Estimated Glomerular Filtration Rate (eGFR) should be computed using the CKD-EPI formula which has been validated locally.

SERUM CREATININE DETERMINATION

- For outpatient procedures and for patients with no change in health status/meds: use serum creatinine taken within 30 days
- For inpatient procedures and patients with known risk factors: use serum creatinine taken within 7 days

Sebastian E. 2012. Validation of equations to estimate GFR among Filipinos.
Osmolality and Nephrotoxicity

How osmolality might influence the development of contrast-induced nephropathy (CIN)\(^1\text{-}^4\)

Adapted from Berg 2000\(^1\), Gleeson 2004\(^2\), Kerl 2008\(^3\), Jung 2008\(^4\)

References
3. CONTRAST MEDIUM

We recommend the use of either *Isosmolar or Low Osmolar* iodinated contrast media, rather than High Osmolar iodinated contrast media in patients at increased risk of CI-AKI.


- **ISOSMOLAR Iodinated** contrast media is recommended for the following groups of patients:
  - All high risk patients (eGFR <30 mL/min)
  - Dialysis patients
  - Moderate Risk (eGFR <60 mL/min) patients for intra-arterial procedures
- Use the lowest possible dose of contrast medium in patients at risk for CI-AKI.

4. WITHDRAWAL OF CONCOMITANT MEDICATIONS

- The following drugs should be discontinued 24 hours before until 48 hours after contrast media administration.
  - NSAIDs
  - Aminoglycosides
  - Metformin
  - Anti-virals (Acyclovir and Foscarnet)
  - Amphotericin B

- Consider discontinuing the following drugs 24 hours before until 48 hours after contrast media administration.
  - High dose diuretics
  - ACE-inhibitors
  - ARBs


5. PREVENTIVE MEASURES: MEDICATIONS

- N-Acetylcysteine (NAC) may be given to prevent CI-AKI
  - NAC 600-1200 mg PO BID for 3 days (1 day before until 1 day after the procedure)

- The following drugs have no role in the prevention of CI-AKI.
  - Theophylline, Fenoldopam

Mc Cullough PA. Contrast-Induced Acute Kidney Injury. JACC 2008;51:1419-28
5. PREVENTIVE MEASURES: HYDRATION PROTOCOL

• ORAL: Low risk patients should be instructed to take 1-2 liters of water 12 hours before the procedure. Patients should be placed on NPO 4 hours before the procedure and IV fluids may be started if additional hydration is needed.

• * IV: ≥ 1.0–1.5 ml/kg/h of NSS has to be administered for 3–12 hours before and up to 6–12 hours after contrast media exposure.

  – Example: For a 60 kg patient, 60 – 90 cc/hour for 3-12 hours prior to the procedure and up to 6-12 hours after the procedure.

• CAUTION: In patients with poor systolic function use lower dose and/or rate of hydration.

Mc Cullough PA. Contrast-Induced Acute Kidney Injury. JACC 2008;51:1419-28

6. SUPPORTIVE MEASURES

• Maintain BP at least 90/60

• Maintain hydration measures while the procedure is ongoing

• For patients on coronary angiography, obtain a measure of the Left Ventricular filling pressure to guide hydration
7. ALGORITHM FOR CLASSIFICATION AND INTERVENTION

CALCULATE eGFR USING CKD-EPI

DISCONTINUE NSAIDS, AMINOGLYCOSIDES, METFORMIN, ANTI-VIRALS, AMPHOTERICIN B, ACE-INHIBITORS, ARBS IF POSSIBLE

High Risk
eGFR < 30ml/min
- Consider admission
- Refer to Nephrology service
- Start IV hydration (see Guideline 5)
- Preferred Contrast Media (CM): ISOSMOLAR
- Limit and specify CM volume: < 30 ml for diagnostic procedures and <100 ml for diagnostic procedures + interventional procedures
- Give NAC 600-1200 mg PO BID for 3 days (1 day before until 1 day after the procedure)

Moderate Risk
eGFR 30-59 ml/min
- Consider Nephrology referral
- Start IV hydration (see Guideline 5)
- Preferred Contrast Media (CM): ISOSMOLAR
- for intra-arterial procedures.
- Limit and specify CM volume: < 30 ml for diagnostic procedures and <100 ml for diagnostic procedures + interventional procedures
- Give NAC 600-1200 mg PO BID for 3 days (1 day before until 1 day after the procedure)

Low Risk
eGFR > 60 ml/min
- Oral hydration should be advised (see Guideline 5).
- May give NAC 600-1200 mg PO BID for 3 days (1 day before until 1 day after the procedure).

Modified from McCullough PA. Contrast-Induced Acute Kidney Injury. JACC 2008;51:1419-28
8. MANAGEMENT OF LOW RISK PATIENTS

- Oral hydration should be advised (see Guideline 5).
- May give NAC 600-1200 mg PO BID for 3 days (1 day before until 1 day after the procedure)

9. MANAGEMENT OF MODERATE RISK PATIENTS

- Consider Nephrology referral
- Start IV hydration (see Guideline 5)
- Preferred Contrast Media (CM): ISOSMOLAR for intra-arterial procedures.
- Limit and specify CM volume: < 30 ml for diagnostic procedures and <100 ml for diagnostic procedures + interventional procedures
- Give NAC 600-1200 mg PO BID for 3 days (1 day before until 1 day after the procedure)
11. MANAGEMENT OF PATIENTS ON RRT

- For dialysis patients, use of **Isosmolar** contrast media is recommended to minimize the risk of potential volume overload from the performance of angiographic studies.
- If with residual renal function, may give NAC 600-1200 mg PO BID for 3 days (1 day before until 1 day after the procedure)
- Contrast media are dialyzable (HD and PD)
  - Schedule HD after the procedure.
  - Additional PD exchange/s should be done immediately after the procedure.

10. MANAGEMENT OF HIGH RISK PATIENTS

- Consider admission
- Refer to Nephrology service
- Start IV hydration (see Guideline 5)
- Preferred Contrast Media (CM): **ISOSMOLAR**
- Limit and specify CM volume: < 30 ml for diagnostic procedures and <100 ml diagnostic procedures + interventional procedures.
- Give NAC 600-1200 mg PO BID for 3 days (1 day before until 1 day after the procedure)
12. EMERGENCY PROCEDURES

• In the setting of emergency procedures or when renal function data are unavailable, we still recommend getting a baseline serum creatinine level and repeating after 24-48 hours.

• Presence of the following risk factors may increase the risk for developing CI-AKI:
  – Pre-existing kidney disease with renal function impairment
  – Diabetes (risk multiplier for patients with CKD)
  – Hypertension
  – CHF
  – Advanced age
  – Volume depletion
  – Hemodynamic instability
  – Use of concurrent nephrotoxic medications
  – Large volume or high osmolality of the contrast agents

12. EMERGENCY PROCEDURES  RISK SCORING

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Integer score (calculate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>5</td>
</tr>
<tr>
<td>IABP</td>
<td>5</td>
</tr>
<tr>
<td>CHF</td>
<td>5</td>
</tr>
<tr>
<td>Age &gt;75 years</td>
<td>4</td>
</tr>
<tr>
<td>Anemia</td>
<td>3</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3</td>
</tr>
<tr>
<td>Contrast-media volume</td>
<td>1 per 100 ml</td>
</tr>
<tr>
<td>SCr &gt;1.5 mg/dl (&gt;132.6 μmol/l)</td>
<td>4</td>
</tr>
<tr>
<td>or</td>
<td>2 for 40-60</td>
</tr>
<tr>
<td></td>
<td>4 for 20-39</td>
</tr>
<tr>
<td></td>
<td>6 for &lt;20</td>
</tr>
</tbody>
</table>

Note: Low risk cumulative score <5; high risk: cumulative score >16.


13. MONITORING

- Repeat serum creatinine at the following time points after CM administration to monitor for CI-AKI
  - INPATIENT: 12 hours and 48 hours
  - OUTPATIENT: 48 hours
  - If with evidence of CI-AKI, consider serial monitoring on days 3-5 post CM administration
- Clinical parameters
  - Monitor urine output and watch out for subtle signs of uremia (hiccups, tremors, nausea, decreased appetite) which may signify the onset of CI-AKI.
14. DOCTOR’S ORDERS

NAME OF PATIENT: ___________________________   AGE/SEX: ______________
ROOM NO.: ___________________________   HOSPITAL NO.: __________
ATTENDING PHYSICIAN: ___________________________

DATE OF PROCEDURE: ___________________________
PROCEDURE: ___________________________

• SERUM CREATININE: __________  RACE: ______  eGFR by CKD-EPI: ______
• RISK STRATIFICATION (Please check):
  o Low: eGFR ≥ 60 mL/min
  o Moderate: eGFR 30-59 mL/min
  o High: eGFR < 30 mL/min
• DISCONTINUE THE FOLLOWING MEDICATIONS (Please check and specify):
  o NSAIDS: ______
  o DIURETICS: ______
  o AMINOGLYCOSIDES: ______
  o ANTI-VIRALS (Foscarnet and Acyclovir): ______
  o AMPHOTERICIN B: ______
  o METFORMIN: ______
  o ACE-INHIBITORS: ______
  o ARBS: ______
  o OTHERS: ______
• START THE FOLLOWING (Please check):
  o N-Acetylcysteine1200 mg PO BID pre and post procedure
  o Others: ______
• INITIATE HYDRATION PROTOCOL (Please check):
  o Oral - 1-2 liters of water 12 hours before the procedure
  o IV ≥ 1.0-1.5 ml/kg/h of NSS has to be administered for 3-12 hours before
    and up to 6-12 hours after contrast-media exposure.
  o Others: ______
• USE THE FOLLOWING CONTRAST MEDIUM(Please check):
  o Isosmolar (Iodixanol)
  o Low osmolar (Iohexol, Iopamidol, Ioxaglate, Ioversol)
• REPEAT SERUM CREATININE (Please check):
  o After 12 hours
  o After 48 hours for OPD patients
  o Others: ________________
• NEXT HEMODIALYSIS SCHEDULE ON:_______________________
• ADDITIONAL PD EXCHANGE/S:___________________________
• REFER TO NEPHROLOGY: ______________________________

ACCOMPLISHED BY (name and signature): _______________________
DATE: __________________   TIME: __________________
REFERENCES

- Gleeson TG, Bulugahapitiya S Am J Roentgenol 2004; 183: 1673-89
- Modified from Mc Cullough PA. Contrast-Induced Acute Kidney Injury. JACC 2008;51:1419-28
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