IODINATED CONTRAST MEDIA CAN DAMAGE THE KIDNEYS. HOW DO WE KNOW?

- History
- We know the normal physiologic effects from the nephrotoxic ones
- Evidences from experiments on
  a) cells
  b) animals
  c) human beings
- Coincidence in time to other potentially injurious incidences does not rule out some nephrotoxic effects of the contrast agent

GUIDELINES AND NEW FACTORS

- Guidelines, - definitions of Contrast-Induced Nephropathy (CIN)
- Guidelines, - high-risk patients for CIN defined in detail
- Guidelines, - hydration and other preventive measures/efforts outlined
- Old CIN definition is sensitive for renal damage
- CI-AKI, PC-AKI introduced
- KDIGO (Kidney Disease: Improving Global Outcomes) definition should be used
- What about renal reserves and accumulated sub-clinical damage?
CONTRAST MEDIA RESEARCH

Pre-clinical

Clinical

On the market

- Meta-analyses
- Large post-marketing studies
- Special indications
- Phase IV

INTERPRETING RESULTS OF CLINICAL TRIALS

"No statistical significant difference" only means that the null-hypothesis is not falsified. That does not prove similarity between the products tested. Claiming so is not possible within the hypothesis testing theory of the hypothetico-deductive method.

Absence of evidence is not equal to evidence of absence. Superiority study design has been the common design up to now. Non-inferiority design has to be used if we want to prove similarity.


SELECTIVE CORONARY ARTERIOGRAPHY:
Dilution of CM from the coronary arteries and back to the aortic bulb

After CM injection into the coronary arteries, the kidney receives highly diluted CM into their arteries. What about left ventriculography?

Intravenous and arterial neurointerventional procedures

True arterial contrast exposure to the kidney

Selective visceral arteriography is an intravenous procedure for the kidney, except for the initial abdominal aorta survey.

PTA on iliac and femoral arteries is an intravenous procedure for the kidney, except for the abdominal aorta survey.

THE GOOD WORK OF REDUDING THE RISK OF CIN

Definition of CIN

Knowledge of risks

Guidelines

Refinement of guidelines

Retrospective studies done now and for the last 10-15 years include the effect that present guidelines had the last 15 years.
NEPHROLOGIC CRITERIA FOR ACUTE KIDNEY INJURY

An iterative process over years:
- 2004: The Acute Dialysis Qualitative Initiativ (ADQI) group developed the RIFLE criteria
- 2007: The Acute Kidney Injury Network (AKIN) revised the criteria

RENAL FUNCTIONAL RESERVE AND KIDNEY INJURIES

DETECTING SUBCLINICAL CI-AKI WITH BIOMARKERS

- Urine β-microglobulin
- Brush border enzymes
  - ALP (alkaline phosphatase)
  - AAP (alanin aminopeptidase)
- Lysosomal enzyme
  - NAG (N-acetylglycosaminidase)
- NGAL (Neutrophil Gelatinase-Associated Lipocalin)
- Cystatin C
- And a lot of other.

EXPERIENCE WITH BIOMARKERS AND DIFFERENT CONTRAST AGENTS

Some tubular biomarkers measured after IV 1.2 g I/kg bw to healthy volunteers, measured in 0-4 h collection period of urine post injection. Values are changes in per cent from baseline. All changes from baseline were statistically significant, and the two monomers caused significantly more changes than the dimeric iodixanol.

RENAL FUNCTION AND AGE

HIERARCHY OF EVIDENCE

"the higher up a methodology is ranked, the more robust and closer to objective truth it is assumed to be"
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**WHAT IS NEW ABOUT RENAL EFFECTS?**

- Accessible guidelines do describe a risk of renal adverse effects after iodinated contrast media (eg, no myth!)
  - ESRV r. 10 (2018) risk level include:
    - **4** less than 65 ml/min/1.73 m² before m contrast medium administration with first pass renal exposure or in ICU patient.
    - **4** less than 50 ml/min/1.73 m² in medium or in arterial contrast medium administration with second pass renal exposure.
    - **4** less than 65 ml/min/1.73 m² in medium or in arterial contrast medium administration with second pass renal exposure.
    - Known or suspected acute renal failure.
  - **n**
    - Other guidelines risk level include:
      - **4** less than 65 ml/min/1.73 m² in IV 60 ml/min/1.73 m² for tk.
    - **ESL** guidelines assessment of level of evidence
      - Risk PC-AKI ≥0.5, Prevention effective for GFR<30 after IV: C, Prevention of VEB after IV (first pass): C

**WHICH CONTRAST AGENT?**

Intravenous Administration of Iodinated Associated with Increased Risk of Acute Kidney Injury, Dialysis, or Mortality? A Propensity Score-Matched Study

**HYDRATION**

Prophylactic hydration to protect renal function from intravascular administered contrast material in patients at high risk of contrast induced nephropathy (AMONG) a prospective, randomised, phase 3, controlled, open-label, non-inferiority trial

**THE McDOXAL STUDY AND COMMENTS**

The McDoxal group (1) used RCM for patients with acute cor-

myocardial infarction, greater than 1 ml/min/1.73 m² in the first pass, and 0.5 ml/min/1.73 m² in the second pass.

Although the average timed dosage of exposure, the authors suggest that there is a marked decrease in the risk of RCM in the presence of acute renal failure. Risk in the group seen at 600 ml showed a higher incidence of complications even in IC
do-in patients, as compared to controls (OR 2.20; 95% CI 1.14–4.24). The incidence of AKI was lower in the group of patients who received RCM and had an acute renal failure due to AKI (OR 0.58; 95% CI 0.40–0.94, p = .022).

McDonald et al. have reported the results of this study (1) and that RCM may have been applied on patients who were not considered as such by the guidelines. However, in this study, the incidence of AKI was lower in the group of patients who received RCM and had an acute renal failure due to AKI (OR 0.58; 95% CI 0.40–0.94, p = .022).

**Risk of AKI after contrast media injection:**

**Myth or reality?**

- Iodinated contrast media (I-CM) can cause kidney injuries
- I-CM can cause subclinical injuries that diminish the functional renal reserve of the kidney
- Adhering to guidelines seems to have a good preventive effect
- The risk of AKI after I-CM may become higher in the future due to high age, cancer drugs, increasing use of I-CM, etc.
- New studies on renal effects, of risks, on differences between products, and clinically, should use the KDIGO definition of AKI
- Risk of AKI after contrast media injection is a reality so evident that we have to continue protecting the kidney