How to prevent contrast-induced nephropathy and manage risk patients: Practical recommendations

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In this study, the contributions of each of the authors have been collected and reviewed by the entire group of participants.

The recommendations that follow are supported by clinical and experimental data. Wherever possible, prospective randomized trial data formed the basis for the recommendation. In some cases, a single trial with a relatively small number of subjects constituted the only such data. Less rigorous but more encompassing data from observational studies and systematic analyses were used to provide context and robustness to the recommendations.

RECOMMENDATION NO. 1

All patients receiving contrast should be evaluated for their risk of contrast-induced nephropathy

A number of risk stratification methods have been developed in interventional cardiology and radiology. These strategies use the present and past history of the patient together with knowledge of renal function to identify 'high risk for contrast-induced nephropathy (CIN)' individuals. Renal function is usually assessed with a serum creatinine, which is used in either the Cockcroft–Gault or modification of diet on renal disease formula to estimate glomerular filtration rate. The risk of CIN increases as the estimated glomerular filtration rate falls, particularly below 60 ml/min. When the serum creatinine is not known (as is often the case in outpatient radiologic examinations), the present and past history of the patient (hypertension, renal disease, dyslipidemia, hyperuricemia, diabetes, heart failure, myeloma, treatment with nephrotoxic drugs) can be used to identify those patients who require further assessment of renal function by measurement of serum creatinine. This is particularly important in patients receiving suprarenal intraarterial contrast where the risk of CIN appears to be increased.

A baseline level of serum creatinine is necessary to estimate renal function and to be compared to serum creatinine levels following contrast exposure. The baseline level should be obtained prior to maneuvers which themselves might affect serum creatinine, such as intravenous (i.v.) volume expansion.

Future research

Adequate, prospective, cohort studies should be conducted to:

- Compare the incidence of CIN following intraarterial and i.v. administration of contrast.
- Assess the attributable risk of end-stage renal disease following contrast *vis a vis* other patient-related and procedure-related factors.

RECOMMENDATION NO. 2

All patients receiving contrast should be in optimal volume status at the time of exposure to contrast

There was no consensus on how one defines 'optimal volume status' although it was recognized that there is increased risk in those with dehydration, extracellular volume depletion, and reduced risk with a variety of volume expansion protocols. To minimize the risk, all patients should be encouraged to drink water liberally in the 12 h before contrast exposure when possible. This is particularly useful in the outpatient setting. For the inpatient setting, i.v. volume expansion should be standard of care for all patients identified as high risk for CIN. The specific volume expansion protocol will depend on patient characteristics such as low ejection fraction and symptomatic congestive heart failure, and the amount of time available for volume expansion prior to contrast exposure. In general, the shorter the interval of time between starting i.v. fluids and contrast exposure, the more vigorous the volume expansion, and this will increase the risk of precipitating congestive heart failure. Therefore, each patient should be evaluated and the most appropriate volume expansion protocol applied. The various protocols are reviewed in the article by Mueller.[1]

All the volume expansion protocols continued i.v. fluids for at least 6 h after contrast exposure. In the absence of any data with a shorter duration of i.v. fluids postcontrast, i.v. fluids should be continued at a rate of 1 ml/kg/h for at least 6 h.

Urine output is one reflection of volume status. Urinary output should be monitored before and after contrast exposure. Urinary output should not be pharmacologically enhanced by diuretics because of a risk of exacerbating CIN.

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[3]The Consensus Panel for CIN, see Appendix A.

Future research

Clinical studies are needed to:

- Determine how to best assess the efficacy of volume expansion protocols, that is, through measurement of urine osmolality (to reach osmolality <300 mOsm/kg) or some other measure of euvolemia.
- Determine the most effective solution to be used in emergency situations when there is less than 1 h before contrast media (CM) exposure.

RECOMMENDATION NO. 3

High-risk patients should only be considered for pharmacologic prophylaxis with therapies supported by clinical evidence

Although the meta-analysis of *N*-acetylcysteine (NAC) efficacy have shown equivocal benefit, some recent data reviewed by Briguori and Marenzi[2] suggest benefit with higher doses (1200 mg b.i.d. $\times$ 4 doses). The latest metaanalysis[3] still finds NAC use of equivocal benefit however. Therefore, despite the low cost and low side effect profile of NAC, the lack of compelling evidence in favor of a beneficial effect prevents a firm recommendation to use this agent. The consensus group found, however, no evidence to prevent its use at the discretion of the physician. Its use should not substitute for the application of appropriate volume expansion strategies to prevent CIN. There is little evidence supporting an interaction between NAC and serum creatinine measurements performed on autoanalyzers used in most hospital laboratories.

Future research

Further investigation is needed to:

- Understand the reason behind the mixed results obtained with NAC:
  Is it a dose issue?
  Is it the route of administration (i.v. vs oral)?
  Is it effective only in subsets of patients (i.e. those with more severe compromise of renal function or receiving a larger volume of contrast)?
- Understand the possible interaction between serum creatinine values and NAC

RECOMMENDATION NO. 4

Low osmolality CM should be used in all patients

Low osmolality CM (including CM that is isoosmolar to plasma) are recommended for all patients. There is insufficient evidence at this time to recommend one specific CM over another for its potential to cause less nephrotoxicity in patients with renal insufficiency. Both head-to-head comparison trials and systematic analysis of all prospective trials suggest that the risk of CIN in high-risk patients undergoing cardiac interventions is less than 10%, particularly when recommendations no. 2 and no. 3 above are followed. There is no statistically rigorous data on the risk of CIN with different CM when the CM is given i.v.

The volume of CM administered, particularly to high-risk patients, should be the minimum amount needed for diagnosis and intervention. Strategies to minimize CM volume, such as use of CM with high iodine content, use of saline flushes or power injectors may provide additional benefit.

Removal of CM via hemodialysis has not been shown to be effective in preventing CIN. Continuous hemofiltration before and after contrast exposure was shown in two studies to offer some benefit. Because of the complexity, cost, and risk associated with this procedure, further studies exploring the potential benefits of this therapy are needed.

Removal of CM via hemodialysis in patients with severely impaired renal function or already on dialysis has not been shown to prevent the development of congestive heart failure or hyperkalemia. These patients should be followed carefully and dialysis instituted only for clear clinical indications.[3]

Future research

Clinical studies are needed to:

- Compare CM in head-to-head trials in high-risk patients to determine whether any differences exist among the various agents.
- Further define the role of hemofiltration in the prevention of CIN and the improvement in mortality.

Basic research studies are needed to:

- Define what characteristics of CM contribute to nephrotoxicity (chemical structure, osmolality, viscosity, ionicity, or other).

RECOMMENDATION NO. 5

Drugs that adversely affect renal function should be withheld prior to and immediately following contrast exposure

A number of drugs affecting renal function are reviewed in the paper by Erley.[4] In general, drugs that produce volume depletion or renal vasoconstriction should be reviewed as to their risks and benefits prior to contrast exposure. When not associated with increasing risk to the patients, these drugs could be withheld until renal function is restored to baseline levels. The data regarding the need to specifically discontinue diuretics, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers prior to contrast exposure is insufficient. It was the opinion of the Consensus Panel that these agents do not need to be discontinued prior to contrast exposure in stable patients receiving chronic therapy.

RECOMMENDATION NO. 6

In all high-risk patients, a follow-up serum creatinine should be obtained at not less than 24 h or more than 72 h following contrast exposure

Currently, serum creatinine is the most widely available marker for renal function. Despite its many limitations the serum creatinine is the laboratory test most often available to estimate renal function prior to contrast exposure.

A follow-up serum creatinine is therefore necessary to define the occurrence of CIN.

The definition of CIN has been based on both an absolute change and a relative change in serum creatinine. For the reasons discussed in the article by Solomon and Barrett,[5] a relative change in serum creatinine, that is, a 25% increase, is recommended as the definition of CIN. This definition correlates with in-hospital outcomes, identifies more patients with CIN, and is less influenced by the baseline level of serum creatinine.

The adequacy of urine output should be assessed in all high-risk patients following contrast exposure. The development of oliguria is an early and ominous sign that serious renal injury has occurred.

Future research

Clinical studies are needed to:

- Establish the role of other markers of renal function, such as cystatin C or a change in estimate glomerular filtration rate (e.g. a 25% decrease), in identifying patients with CIN.
- Determine which markers are the best indicators of future adverse events.

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Appendix A

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