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Reference: The high risk of contrast-induced nephropathy in patients with suspected pulmonary embolism despite three different prophylaxis: a randomized controlled trial. *Academic Emergency Medicine.* (2016) 23:1136-1145.

Question/Objective: “The objective was to compare the protective effects of *N*-acetylcysteine (NAC) plus normal saline (NS), sodium bicarbonate plus NS, and NS alone in the prevention of contrast-induced nephropathy (CIN) after computed tomography pulmonary angiography (CTPA) in emergency patients.”

Introduction: How often do we order CTPA in our emergency patients? I would say pretty often. How often do we consider the aftermath of the contrast bolus our patients receive during this commonplace procedure? I would argue less often. CIN is defined as new onset or increasing renal deficiency or failure within 48 hours of exposure to contrast without any other definable cause, and it is one of the main causes of iatrogenic renal insufficiency in hospital patients today. CTPA, in addition to coronary angiography, are highly associated with CIN. We are ordering these studies more and more, and why not? The benefits of obtaining each are drastic, but we sometimes forget that with great positives, negatives lurk eerily in the underworld. Apart from hydration, very few studies have studied the effectiveness of pharmacologic prophylactic options in avoiding CIN. This study aims to do exactly this. Can we prevent or at least decrease the morbidity of CIN in patients specifically undergoing CTPA with certain IV concoctions?

Methods: This randomized, controlled study was performed at one tertiary care university hospital in Turkey. Inclusion criteria were as follows: patients undergoing contrast-enhanced thoracic CT due to suspected PE, 18 years or older, measurable serum creatinine levels prior to and 48-72 hours after CTPA, and at least one risk factor for CIN (pre-existing renal dysfunction, DM, HTN, hypotension, CAD, history of nephrotoxic drug use, liver disease, CHF, age 75 or over, anemia). Patients on peritoneal or hemodialysis, pregnant women, subjects with known allergy to NAC or sodium bicarbonate, subjects already on NAC or sodium bicarbonate therapy, previous exposure to contrast within the last 10 day or during hospital follow-up period, or patients refusing to participate were excluded. The three groups were as follows: 3 ml/kg IV NAC + NS, sodium bicarbonate + NS, or NS alone, 1 hour before CTPA and 1 ml/kg IV per hour for a minimum of 6 hours after CTPA. The primary outcome measure was serum creatinine increase $\geq 25\%$ or 0.5 mg/dL in 48-72 hours after contrast exposure compared to baseline levels. Secondary outcomes were moderate renal injury or severe renal failure during hospitalization and in-hospital mortality.

Results: A total of 281 patients were enrolled, 257 patients underwent randomization, and 231 patients were included in the final analysis. The following table demonstrates materialization of CIN, renal injury, several renal injury, and in-hospital mortality for the three individual groups.

	NAC (n = 85)	Sodium bicarbonate (n = 85)	NS (n = 87)	p-value
CIN	20	18	23	0.719
Renal injury	8	9	15	0.244
Severe renal injury	8	9	15	0.244
In-hospital mortality	11	10	12	0.923

Discussion: As can be clearly seen from the table above, the p-values never reached statistical significance. There appears to be no difference among the three treatment arms. The overall level of CIN was 23.7%, despite the various prophylactic options administered. Multiple studies in the last several years have provided varied recommendations in terms of effectiveness of prophylaxes in patients undergoing contrast-aided imaging studies. A study by Klima et al. in 2012 concluded that NS may be superior to sodium bicarbonate in preventing CIN. A meta-analysis by Wu et al. in 2013 determined that NAC therapy was superior to other prophylaxis regimens. This study demonstrates that no such benefit exists, especially in the specific patient population where PE is considered. Therefore, clinicians may select any prophylaxes deemed feasible to their specific patient. For me, judicious fluid administration with solely NS seems like a viable option. The initiation of other components within NS seems unnecessary in light of this particular study.

Limitations: This study did not have a traditional control group, and thus, results may be skewed. When reviewing the data, the basal creatinine levels were significantly higher in the sodium bicarbonate group. Despite this fact, the rates of CIN did not seem to differ among the groups. Perhaps if the basal creatinine levels were closer to the NAC and NS group, we may have seen a statistically significant difference in the sodium bicarbonate group? It is difficult to say. Also, it appears that CIN is a diagnosis of exclusion made at the 48-72 hours rate post-contrast administration. Ostensibly, other pathologic renal entities may ensue in this period. The rates of CIN may have been underestimated or overestimated accordingly. This study was performed at a single, teaching hospital, which may limit the applicability to other realms. Most importantly, while the pre-contrast and immediate post-contrast administration of prophylaxes could be accurately recorded, the patients were then transferred to many other departments; the fluids administered until the second measurement of serum creatinine at 48-72 hours could not be accurately recorded. This seems like the most egregious deficit in the design of this study.
