

Contrast Nephropathy, myth thereof

May 1, 2019 by [Josh Farkas](#)

CONTENTS

- Venous injection of contrast (e.g. for CT scan)
 - [The birth of the contrast nephropathy myth](#) ([#contrast_nephropathy: a myth is born](#))
 - [Current lack of evidence regarding contrast nephropathy](#) ([#current_lack_of_evidence_regarding_contrast_nephropathy](#))
 - [Weighing the risks vs. benefits of using contrast \(Renalism\)](#) ([#weighing_the_risks_vs._benefits_of_using_contrast_\(Renalism\)](#))
 - [The attention given to contrast nephropathy is insane](#) ([#the_attention_given_to_contrast_nephropathy_is_disproportionately_insane](#))
- [Intra-arterial contrast \(e.g. cardiac catheterization\)](#) ([#intra-arterial_contrast](#))
- [Algorithm](#) ([#algorithm](#))
- [Podcast](#) ([#podcast](#))
- [Questions & discussion](#) ([#questions_&_discussion](#))
- [Pitfalls](#) ([#pitfalls](#))

contrast nephropathy: a myth is born

[\(back to contents\)](#) [\(#top\)](#)

Acute Anuria Following Intravenous Pyelography in a Patient with Myelomatosis.

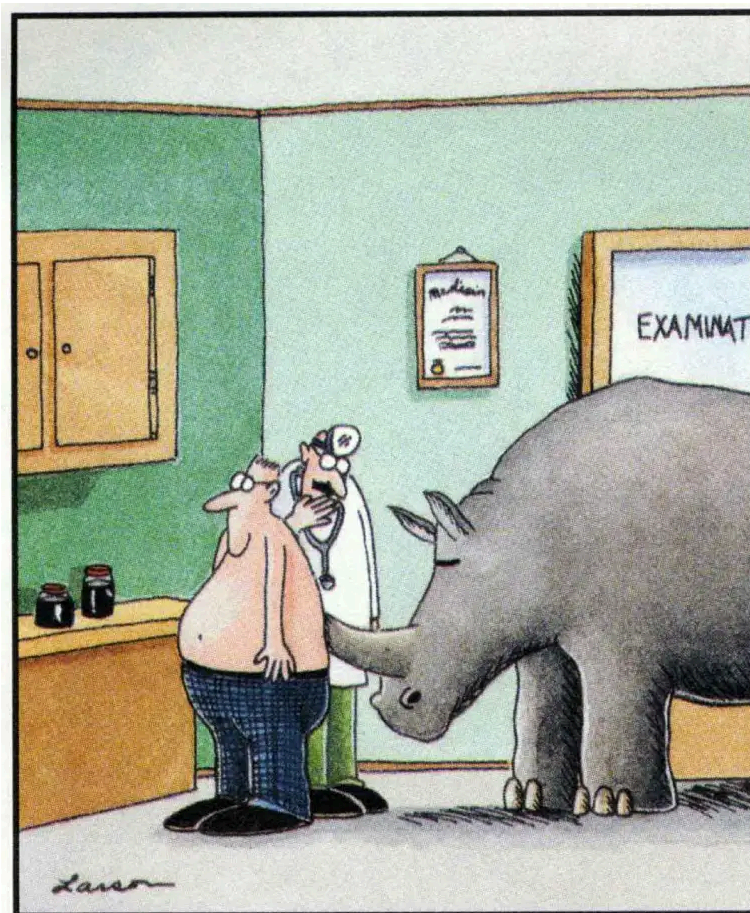
By

ERIK D. BARTELS, G. C. BRUN, A. GAMMELTOFT and POUL A. GJØRUP.

(Submitted for publication June 9, 1954.)

The concept of contrast nephropathy was born in the 1950's, when it was observed that some patients developed renal failure following injection of IV contrast dye for intravenous pyelography. ([13217726 \(https://pubmed.ncbi.nlm.nih.gov/13217726/\)](https://pubmed.ncbi.nlm.nih.gov/13217726/)) This might have represented a true nephrotoxic reaction. The contrast dye used at that time probably *was* poisonous (50% diodone, a high-osmolar contrast dye which nobody would imagine using today). However, none of these early studies had adequate control groups, so it's impossible to know for sure. This was before the establishment of evidence-based medicine.

Regardless, a myth was born. Over time, fear of contrast nephropathy blossomed and took root. Any renal failure which occurred following the administration of contrast was likely to be labeled as "contrast nephropathy." Over the ensuing decades, well over a thousand publications were written about contrast nephropathy.

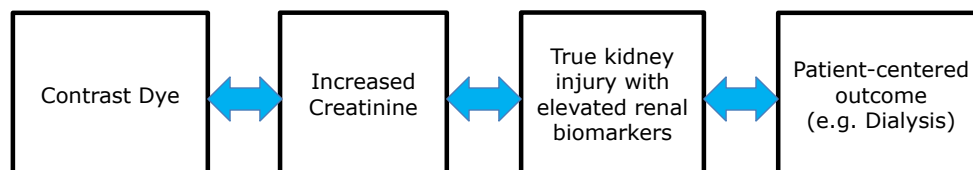


"Hmmm... You got a CT scan last week?
Another case of contrast nephropathy!"

current lack of evidence regarding contrast nephropathy

(back to contents) (#top)

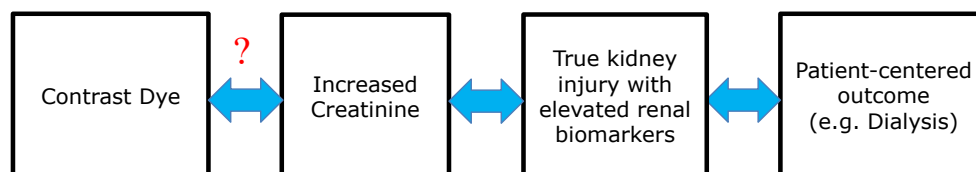
Older contrast dyes probably *were* nephrotoxic. However, modern contrast dyes (with lower osmolality) don't seem to cause renal failure.



"Contrast nephropathy" is usually defined as a small increase in creatinine within the days following contrast administration (e.g. 0.3 mg/dL). The *assumption* driving this is that even

small bumps in creatinine reflect *genuine* renal damage, which in turn is clinically relevant. However, upon closer examination, this chain of reasoning doesn't hold up...

(1) does contrast dye cause an increase in creatinine?



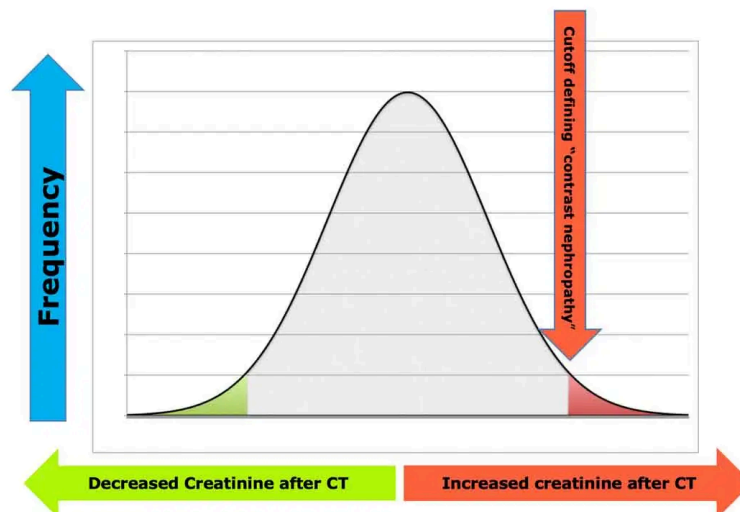
Unfortunately, it would be unethical to perform a prospective RCT to evaluate this. Consequently, we are limited to retrospective, propensity-matched studies (which attempt to eliminate confounding variables). Recently, *numerous* studies and meta-analyses have emerged which don't detect any relationship between contrast dye administration and elevation of creatinine. ([23319662](https://pubmed.ncbi.nlm.nih.gov/23319662/) (<https://pubmed.ncbi.nlm.nih.gov/23319662/>), [24475854](https://pubmed.ncbi.nlm.nih.gov/24475854/) (<https://pubmed.ncbi.nlm.nih.gov/24475854/>), [23360742](https://pubmed.ncbi.nlm.nih.gov/23360742/) (<https://pubmed.ncbi.nlm.nih.gov/23360742/>), [28131489](https://pubmed.ncbi.nlm.nih.gov/28131489/) (<https://pubmed.ncbi.nlm.nih.gov/28131489/>), [30798098](https://pubmed.ncbi.nlm.nih.gov/30798098/) (<https://pubmed.ncbi.nlm.nih.gov/30798098/>), [28197679](https://pubmed.ncbi.nlm.nih.gov/28197679/) (<https://pubmed.ncbi.nlm.nih.gov/28197679/>), [28811122](https://pubmed.ncbi.nlm.nih.gov/28811122/) (<https://pubmed.ncbi.nlm.nih.gov/28811122/>), [24656402](https://pubmed.ncbi.nlm.nih.gov/24656402/) (<https://pubmed.ncbi.nlm.nih.gov/24656402/>), [20651198](https://pubmed.ncbi.nlm.nih.gov/20651198/) (<https://pubmed.ncbi.nlm.nih.gov/20651198/>), [25203000](https://pubmed.ncbi.nlm.nih.gov/25203000/) (<https://pubmed.ncbi.nlm.nih.gov/25203000/>), [30480553](https://pubmed.ncbi.nlm.nih.gov/30480553/) (<https://pubmed.ncbi.nlm.nih.gov/30480553/>))

One clever study examined creatinine changes in patients who had received both a contrasted CT scan and also a non-contrasted CT scan at different points in time. ([23360742](https://pubmed.ncbi.nlm.nih.gov/23360742/) (<https://pubmed.ncbi.nlm.nih.gov/23360742/>)) Changes in creatinine following both scans were the *same*, regardless of whether the patient had received a contrasted or non-contrasted CT scan. This demonstrates that creatinine levels normally bounce a certain amount. If we examine only creatinine *elevations* and *assume* that these represent “contrast nephropathy,” then we may manufacture a disease – when in fact we are looking at random statistical noise.

Indeed, several studies have found that the *average* creatinine of a group of patients exposed to IV contrast *doesn't change at all*. ([24656402](https://pubmed.ncbi.nlm.nih.gov/24656402/) (<https://pubmed.ncbi.nlm.nih.gov/24656402/>), [20707658](https://pubmed.ncbi.nlm.nih.gov/20707658/) (<https://pubmed.ncbi.nlm.nih.gov/20707658/>), [17317065](https://pubmed.ncbi.nlm.nih.gov/17317065/) (<https://pubmed.ncbi.nlm.nih.gov/17317065/>), [25183538](https://pubmed.ncbi.nlm.nih.gov/25183538/) (<https://pubmed.ncbi.nlm.nih.gov/25183538/>))

Some patients experience an *increase* in creatinine, while an equal number experience a *decrease*. By focusing on the former patients and ignoring the latter, we convert statistical noise into a clinical “disease.”

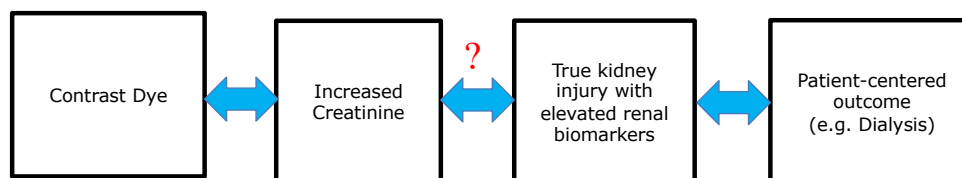
Random changes in creatinine can create the appearance of “contrast nephropathy”



Creatinine values are continually fluctuating over time (e.g. due to changes in hydration status). Several studies have found similar numbers of patients with *increased* or *decreased* creatinine following contrast dye administration (due to random statistical noise). Unfortunately we often label patients with increased creatinine as having “contrast nephropathy,” whereas patients with decreased creatinine are ignored.

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(2) do creatinine bumps reflect genuine renal injury?

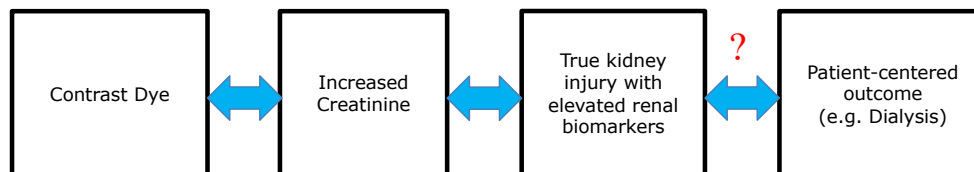


Let's imagine for a moment that contrast dye *does* cause a transient elevation in creatinine. Creatinine is an inert molecule, with no physiological effect. The next question is whether small elevations in creatinine actually reflect genuine kidney injury (or whether they might simply reflect transient reductions in creatinine secretion). It's crucial to realize that some drugs cause transient reductions in creatinine secretion *without* actually damaging the kidneys – such drugs are termed *pseudo-nephrotoxins*.

There is no evidence in the literature that small increases in creatinine sometimes seen following contrast dye administration reflect actual kidney injury. Studies using renal biomarkers have found no signal of renal injury following contrast dye exposure – *even* in patients with elevated creatinine levels meeting the definition of “contrast

nephropathy.”(25773936 (<https://pubmed.ncbi.nlm.nih.gov/25773936/>)) Thus, the definition of “contrast nephropathy” in terms of small creatinine bumps is flawed, as these elevations don't seem to reflect any genuine renal injury.

(3) what is the impact on patient-oriented clinical endpoints?



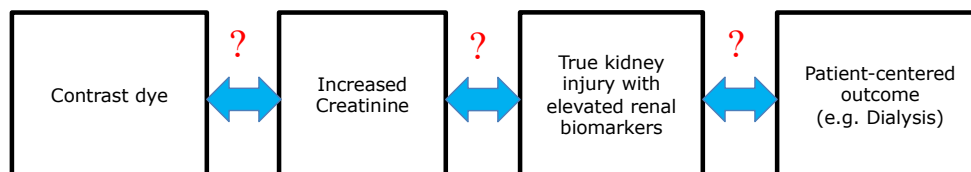
Let's be honest though – what everyone worries about most is *dialysis*. We're not really worried about causing a small bump in the patient's creatinine, or even causing transient renal injury. We're worried about a *severe* renal insult which would require dialysis. And, of course, we worry about mortality.

Virtually every study has found *no evidence* that contrast increases the risk of dialysis or death.(23319662 (<https://pubmed.ncbi.nlm.nih.gov/23319662/>), 28131489 (<https://pubmed.ncbi.nlm.nih.gov/28131489/>), 28811122 (<https://pubmed.ncbi.nlm.nih.gov/28811122/>), 25203000 (<https://pubmed.ncbi.nlm.nih.gov/25203000/>), 26250726 (<https://pubmed.ncbi.nlm.nih.gov/26250726/>), 26001222 (<https://pubmed.ncbi.nlm.nih.gov/26001222/>)) One study focusing on ICU patients *did* find that contrast correlated with an increased likelihood of requiring dialysis among patients with a GFR<45 ml/min. Bizarrely, this same study found *no* signal that contrast correlated with increased creatinine levels. How could contrast dye increase the risk of dialysis, *without* affecting renal function? The answer might be an increased rate of dialysis due to the *volume overload* associated with contrast dye (which may largely reflect fluid given to prevent “contrast nephropathy”).(28213620 (<https://pubmed.ncbi.nlm.nih.gov/28213620/>))



Fluid given to prevent “contrast nephropathy” may cause renal injury by exacerbating volume overload and systemic congestion. Volume overload is more dangerous than the contrast dye.

bottom line: no coherent evidence of harm



Despite decades of searching and literally thousands of publications, there is no coherent evidence that modern contrast dyes cause clinically meaningful harm. The vast majority of recent publications suggest that modern contrast dyes are safe. A few publications raise the possibility of harm, but these studies are overall inconsistent (e.g., increased risk of dialysis without increased risk of kidney injury).

Unfortunately, we will never be able to exclude the possibility that contrast dye is nephrotoxic with 100% certainty (this is methodologically impossible, because it would require a massive prospective RCT). However, the best available evidence indicates that contrast dye is safe. If contrast dye were nephrotoxic, then it would have to be an extremely *weak* nephrotoxin of no real clinical significance.

Overall, given the massive amount of study which has been spent on this issue, it's highly reassuring that no definitive evidence of harm has been found. The renal effects of contrast dye have probably been more intensely investigated than the renal effect of any other drug or substance in medical history.

weighing the risks vs. benefits of using contrast (Renalism)

([back to contents](#)) ([#top](#))



Clinicians are often tasked with balancing the risk-vs-benefit of the administration of IV contrast for CT scanning. Currently, this calculation would seem to be as follows:

- Risk of using contrast dye: There is no high-quality evidence that this risk exists.
- Benefit of using contrast dye: This is often quite real (although it will certainly vary, depending on the clinical scenario).

From an evidentiary standpoint, avoidance of contrast dye is difficult to justify. Physicians are often risk-averse, as we certainly want to avoid causing harm. However, the best available

evidence suggests that our patients will benefit the most if we don't shy away from using contrast dye in scenarios where it is indicated.

“Renalism” refers to the avoidance of contrast dye in patients with renal dysfunction, causing a failure to perform important studies and leading to harm.([25318756](https://pubmed.ncbi.nlm.nih.gov/25318756/) (<https://pubmed.ncbi.nlm.nih.gov/25318756/>)) In the current era of improved contrast dyes, *renalism* poses a greater risk to our patients than does “contrast nephropathy.”

Hinson et al. sums this up well in their conclusions following a trial involving septic patients at John Hopkins (CM=contrast medium):([30798098](https://pubmed.ncbi.nlm.nih.gov/30798098/) (<https://pubmed.ncbi.nlm.nih.gov/30798098/>))

Acute kidney injury following contrast media administration in the septic patient: A retrospective propensity-matched analysis

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5. Conclusions

Sepsis is a medical emergency proven to benefit from early diagnosis and rapid initiation of treatment. As such, physicians must mobilize all available resources in the care of septic patients. For too long, outsized fear of contrast-induced AKI has led to the avoidance of CM in situations where their use was warranted. Here, we report that the risk for developing AKI following CM administration was not elevated in over four thousand patients with sepsis, including those with the lowest baseline renal function. Our findings argue against the practice of withholding CM to avoid nephropathy when administration is otherwise clinically indicated.

the attention given to contrast nephropathy is disproportionately insane

([back to contents](#)) ([#top](#))

Given how much we worry about contrast nephropathy, you might think that contrast dye is the only potentially nephrotoxic substance in the hospital. In fact, contrast dye is probably

among the *least* nephrotoxic things that we prescribe. The following list includes commonly used drugs which are definitely nephrotoxic:

known nephrotoxins commonly encountered in critical care:

- Antibiotics
 - Vancomycin
 - Aminoglycosides
 - Amphotericin
 - Antivirals: Acyclovir, ganciclovir
- ACE-inhibitors, Angiotensin receptor blockers (ARBs)
- NSAIDs
- Mannitol
- Normal saline (in large volumes)

We worry a lot about *contrast nephropathy* because it has its own special name. Meanwhile, we often don't think much about other drugs, which are *proven nephrotoxins*. This is entirely illogical.

	Vancomycin nephrotoxicity	Contrast nephropathy
Does it exist?	Definitely, yes. (No debate about this)	Probably not. (Debatable)
Do alternatives exist?	Yes (linezolid, ceftaroline, daptomycin)	Not really.
How much do we worry about it?	Not much.	A lot.
Do concerns about nephrotoxicity delay care?	Not really.	Yes (delay in imaging due to clearance for CT scans and/or labs to return)

The Internet Book of Critical Care, by @PulmCrit

Avoiding nephrotoxins among critically ill patients is obviously important. Our efforts along this vein should be aimed at drugs which are *known nephrotoxins*. We need to stop worrying about IV contrast dye and focus more on drugs which are actually causing harm. We're wasting our time chasing a ghost, while true card-carrying nephrotoxins often pass by without much attention.

intra-arterial contrast

Renal injury can occur following intra-arterial procedures (e.g. cardiac catheterization). It's unclear why this occurs, with possible causes including the following:

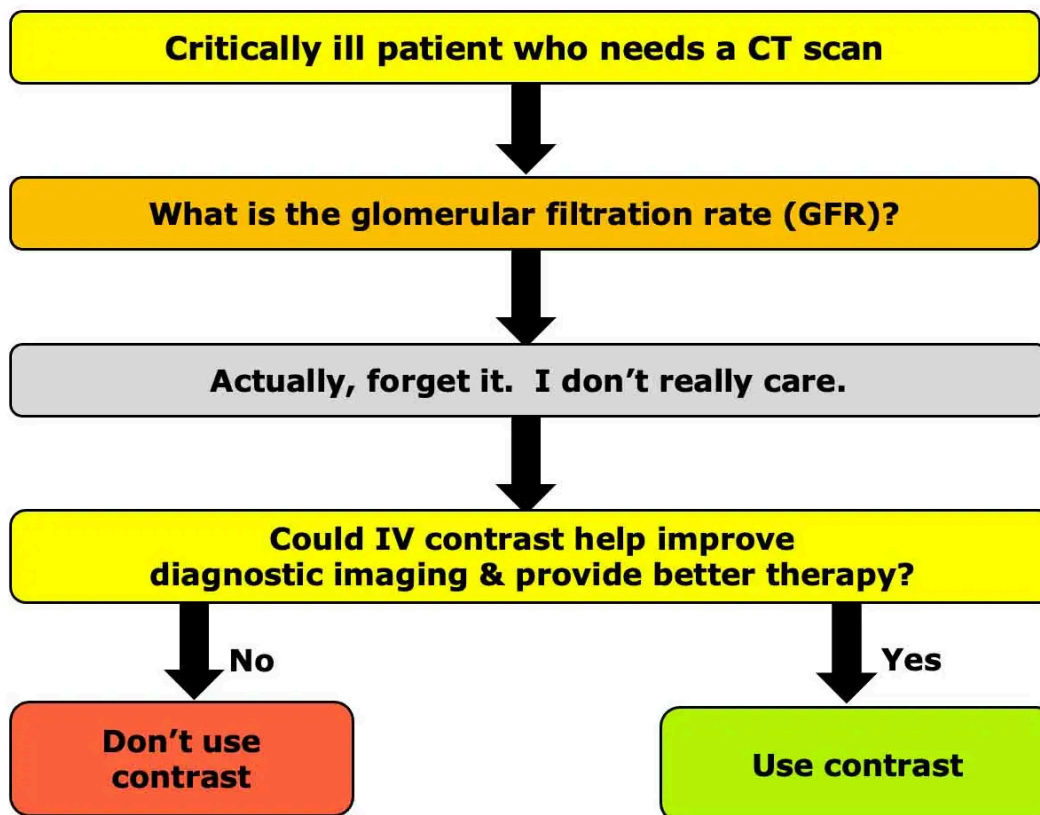
1. Patients are in heart failure or cardiogenic shock with high risk of renal failure (regardless of any intervention). The occurrence of renal failure following catheterization may merely represent *association*, not *causation*.
2. Dislodgement of cholesterol plaques with embolization to the kidneys.
3. Other periprocedural complications (e.g. arrhythmia, hemorrhage).
4. Use of intra-aortic balloon pumps (which may occlude renal blood flow when positioned incorrectly). ([20837932](https://pubmed.ncbi.nlm.nih.gov/20837932/) (<https://pubmed.ncbi.nlm.nih.gov/20837932/>))
5. Direct effect of contrast dye.

This is hard to sort out because it's impossible to perform a non-contrast cardiac catheterization. Therefore, it's even *harder* to investigate this topic than it is to investigate IV contrast for CT scans.

No clear statement can be made on this topic currently. Unlike CT scans, this issue is less ubiquitous among critically ill patients. It may be best to defer management of this issue to interventional cardiologists (who will invariably be involved in the management of any patient going to the cardiac catheterization lab).

algorithm

[\(back to contents\)](#) [\(#top\)](#)

Algorithm: Is it OK to give this patient IV contrast?

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podcast

(back to contents) (#top)



(<https://i0.wp.com/emcrit.org/wp-content/uploads/2016/11/apps.40518.14127333176902609.7be7b901-15fe-4c27-863c-7c0dbfc26c5c.5c278f58-912b-4af9-88f8-a65fff2da477.jpg>)

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questions & discussion

([back to contents](#)) ([#top](#))

To keep this page small and fast, questions & discussion about this post can be found on another page [here](https://emcrit.org/pulmcrit/contrast/) (<https://emcrit.org/pulmcrit/contrast/>).









- Failing to use contrast for CT scans due to fear of nephropathy, leading to suboptimal imaging studies which impair subsequent management (a.k.a. Renalism).
- Delaying scans in critically ill patients while awaiting “clearance” to use IV contrast.
- Administration of additional fluid to prevent “contrast nephropathy” for CT scans in critically ill patients who have already been volume resuscitated (if the patient is already euvolemic, additional fluid may provoke *volume overload*, which itself is nephrotoxic!).

Key articles to cite supporting the use of IV contrast dye 🔑

- If you need some solid peer-reviewed articles to drop into the chart:
- Aycock RD, Westafer LM, Boxen JL et al. Acute Kidney Injury after CT: A meta-analysis. *Annals of Emergency Medicine* 2018. ([28811122](https://pubmed.ncbi.nlm.nih.gov/28811122/) (<https://pubmed.ncbi.nlm.nih.gov/28811122/>))
Exhaustive, modern literature review in the Annals showing no difference in acute kidney injury, mortality, or dialysis.

- Hinson JS, Jalbout NA, Ehmann MR et al. Acute kidney injury following contrast media administration in the septic patient: A retrospective propensity-matched analysis. *Journal of Critical Care* 2019. ([28131489](https://pubmed.ncbi.nlm.nih.gov/28131489/) (<https://pubmed.ncbi.nlm.nih.gov/28131489/>)) *Large study evaluating patients presenting to John Hopkins with suspected sepsis. No effect was detected from contrast dye, even among patients with GFR<30 ml/min.*
- Ehrmann S, Aronson D, Hinson JS. Contrast-associated acute kidney injury is a myth: Yes. *Intensive Care Medicine* 2017 ([29242967](https://pubmed.ncbi.nlm.nih.gov/29242967/) (<https://pubmed.ncbi.nlm.nih.gov/29242967/>))

Guide to emoji hyperlinks

-  = Link to online calculator.
-  = Link to Medscape monograph about a drug.
-  = Link to IBCC section about a drug.
-  = Link to IBCC section covering that topic.
-  = Link to FOAMed site with related information.
-  = Link to supplemental media.

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