

# Kontrast Nefropatisinde NAC ve Bikarbonat Gerçekten İşe Yarıyor mu?

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KARABÜK ÜNİVERSİTESİ



**ATUDER**

Acil Tıp Uzmanları Derneği

TIP FAKÜLTESİ

ACİL TIP ABD



**EPAT**

Emergency Physicians Association of Turkey

# Tanımlar

- ▶ Kontrastla indüklenen akut böbrek hasarı (nefropati(CIN)), kontrastlı görüntüleme prosedürleri yapılan hastalarda en yaygın komplikasyondur.
- ▶ Genellikle kontrasta maruz kaldıktan 2-7 gün sonra, başlangıca göre en az % 25 serum kreatinin artışı veya 0.5 mg/dL (44  $\mu$ mol/L) mutlak artış olarak tanımlanır.
- ▶ İyotlu kontrast maddenin intravasküler (IV veya intra-arteriyel) uygulanmasını gerektiren tüm hastalarda önceden var olan böbrek fonksiyon bozukluğu veya akut böbrek hasarı için diğer risklerin değerlendirilmesi gerekmektedir.

# Risk

BT de;

- ▶ Acil olmayan BT'de <% 1
- ▶ Acil durumdaki hastaların >% 10'u (altta yatan ciddi klinik duruma bağlı olabilir)

PTCA sonrası

- ▶ Böbrek fonksiyon bozukluğu olmayan hastaların <% 3'ü
- ▶ kronik böbrek hastalığı olan hastaların % 40'a kadarı

# Risk Durumları?

- ▶ Önceden var olan böbrek yetmezliği (erkeklerde serum kreatinin  $\geq 1.3$  mg/dL [ $\geq 115$  mmol / L] ve kadınlarda  $\geq 1$  mg/dL [ $\geq 88.4$  mmol/L] veya tahmini glomerüler filtrasyon hızı 1.73 m<sup>2</sup> başına  $<60$  mL/dk)
- ▶ Hipertansiyon
- ▶ Hemodinamik anstabilite
- ▶ İntravasküler volüm azlığı
- ▶ >75 yaş
- ▶ Konjestif kalp yetmezliği
- ▶ Yüksek hacimde kontrast madde verilmesi



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## CIN Calculator

NOTE: An updated version of this calculator can be found here: [Current PCI risk calculator \(SCAI\)](#)

Age: \*

Age of patient at the time of care.

Height: \*

Indicate the patient's height in centimeters.

Weight: \*

Indicate the patient's weight in kilograms.

CAD Presentation: \*

Indicate the patient's coronary artery disease (CAD) presentation. Choose the worst status.

PCI Indication: \*

Indicate the reason the PCI is being performed.

### A Risk Score To Predict Contrast-Induced Nephropathy

Risk Factors	Select Values Here	Risk Score
Age (yrs)	50	0
Gender	Female	See GFR
Is The Patient African-American?	No	See GFR
Is Hypotension Present?*	No	0
Is Intra-Aortic Balloon Pump Present?	No	0
Congestive Heart Failure**	Yes	5
Hematocrit	30	3
Diabetes	Yes	3
Volume Of Contrast Medium Used in cc	0-100	1
Serum Creatinine in mg/dl	0.9	See GFR
Glomerular Filtration Rate Index (GFR)	70.4	0
<b>Risk of Contrast-Induced Nephropathy</b>	<b>26.1%</b>	<b>12</b>
<b>Risk of Need For Dialysis</b>	<b>1.09%</b>	<b>12</b>

Mehran R et al. J. Am. Coll. Cardiol. 2004;44:1393-1399.

Data Source: Columbia University Medical Center Interventional Cardiology Data Base

\*Hypotension = systolic blood pressure <80 mmHg for at least 1 hr requiring inotropic support or intra-aortic balloon pump support within 24 hr periprocedurally.

\*\*CHF = congestive heart failure class III/IV by New York Heart Association and/or history of pulmonary edema.

Web calculator design and HTML transfer by Dr. John Coyle, 2006.

# Patogenez

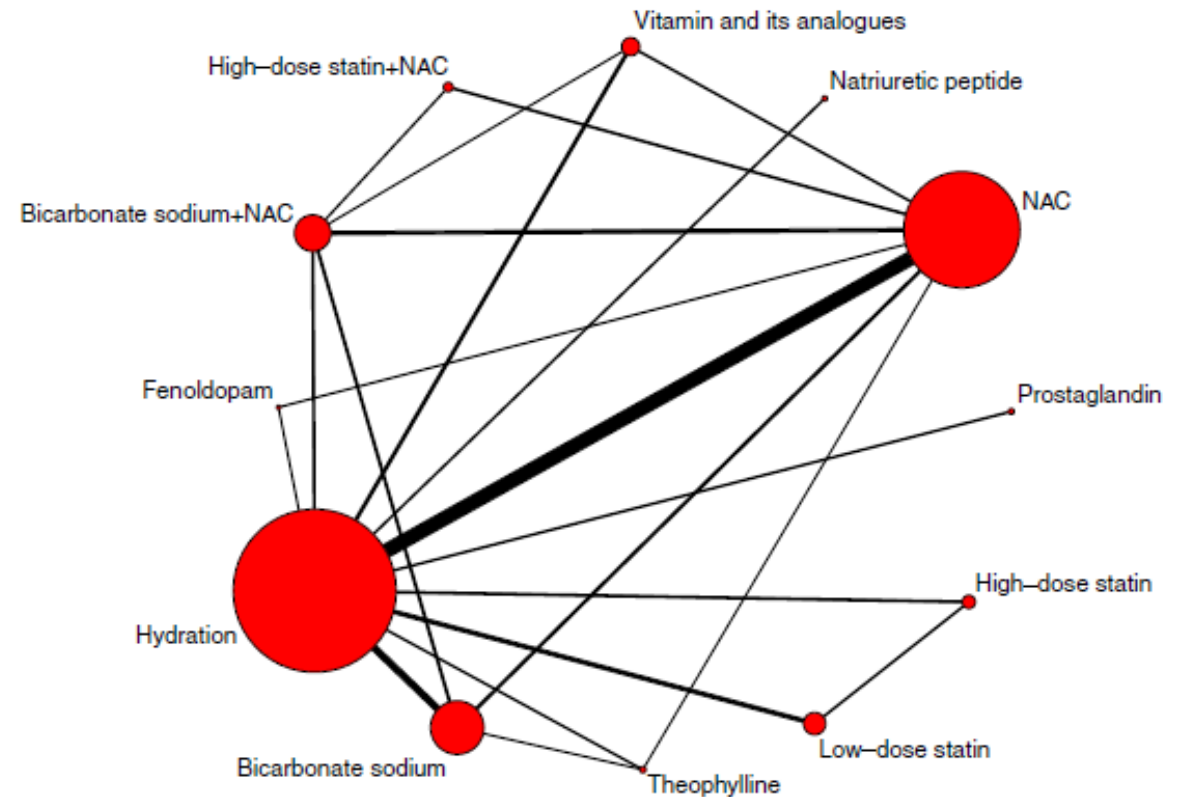
- ▶ Esas suçlanan mekanizma vazodilatör ve vazokonstriktör faktörler arasında oluşan dengesizlik sonucunda meydana gelen renal iskemidir.
- ▶ Akut tübüler nekroz
- ▶ Hipoksemiye neden olan renal vazokonstrüksiyon
- ▶ Kontrastın direkt sitotoksik etkisi
- ▶ Yüksek osmolalite

# Kontrast Nefropatisinin Önlenmesi

- ▶ Mümkünse nefrotoksik ilaçları kesilmesi
- ▶ Yüksek riskli hastalarda
  - Alternatif görüntüleme metodunun seçilmesi
  - Mümkün olan en düşük dozda iyot bazlı kontrast madde
  - İzo-osmolar veya düşük osmolar kontrast kullanımı
- ▶ İşlem öncesi hidrasyon
  - Tek başına oral sıvılar kullanmamalı
  - Volüm genişletmek için IV izotonik sodyum klorür solüsyonları
  - IV sodyum bikarbonat ile hidrasyon, IV salinden daha etkili olabilir???

## Medikasyon

- ▶ NAC
- ▶ teofilin (aminofilin),
- ▶ fenoldopam,
- ▶ iloprost, alprostadil, prostaglandin E1,
- ▶ statinler, statinler artı NAC,
- ▶ bikarbonat sodyum, bikarbonat sodyum artı NAC,
- ▶ askorbik asit (C vitamini), E vitamini veya benzerleri (tokoferol),
- ▶ α-lipoik asit atriyal natriüretik peptid, B-tipi natriüretik peptid, karperitid.





# Neden NAC veya Bikarbonat?

## ► NAC

- Antioksidan ve vazodilatör etki
- Ucuz ve yan etki az

## ► Bikarbonat

- Alkalinizasyon serbest oksijen hasarından koruyucu

Received May 26, 2016; accepted August 17, 2016.

## Effectiveness of *N*-Acetylcysteine for the Prevention of Contrast-Induced Nephropathy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Renfan Xu, MD, PhD; Anyu Tao, MD; Yang Bai, MD; Youbin Deng, MD, PhD; Guangzhi Chen, MD, PhD

- ▶ 1. grup NAC+-Hidrasyon
- ▶ 2. grup Placebo veya Hidrasyon
- ▶ KAG ve BT de daha faydalı
- ▶ Periferik Anjiyografide faydasız??
- ▶ Verilen kontrast miktarları ve türü bilinmiyor
- ▶ NAC dozu 600-7200 mg

**Methods and Results**—PubMed, EMBASE, and the Cochrane Library were electronically searched from inception to January 2016 for all relevant studies. The weighted relative risk (RR) and corresponding 95% CI for incident CIN were estimated using random effects models. Standard methods for assessing statistical heterogeneity and publication bias were used. The study included 11 480 participants and 1653 cases of CIN. The incidence of CIN was 12.8% in the NAC group versus 16.0% in the control group (RR: 0.76, 95% CI: 0.66–0.88,  $P=0.0002$ ). In the patients undergoing coronary angiography, the incidence of CIN in the NAC group versus the control group was 13.7% versus 17.2% (RR: 0.74, 95% CI: 0.63–0.87,  $P=0.0002$ ); in those undergoing peripheral angiography, the incidence was 6.4% versus 5.8% (RR: 1.00, 95% CI: 0.42–2.40,  $P=1.00$ ); in those undergoing computed tomography, the incidence was 7.7% versus 14.8% (RR: 0.51, 95% CI: 0.29–0.89,  $P=0.02$ ).

**Conclusions**—Our meta-analysis showed an inverse and significant association between NAC supplementation and risk of CIN in patients undergoing coronary angiography and computed tomography, while a protective role for NAC in patients undergoing peripheral angiography was not obvious. (*J Am Heart Assoc.* 2016;5:e003968 doi: 10.1161/JAHA.116.003968)

# N-Acetylcysteine Plus Intravenous Fluids Versus Intravenous Fluids Alone to Prevent Contrast-Induced Nephropathy in Emergency Computed Tomography

Stephen J. Traub, MD; Alice M. Mitchell, MD, MS; Alan E. Jones, MD; Aimee Tang, MD; Jennifer O'Connor, BS; Teresa Nelson, MS; John Kellum, MD; Nathan I. Shapiro, MD, MPH

**Results:** The data safety and monitoring board terminated the study early for futility. Of 399 patients enrolled, 357 (89%) completed follow-up and were included. The N-acetylcysteine plus saline solution group contrast-induced nephropathy rate was 14 of 185 (7.6%) versus 12 of 172 (7.0%) in the normal saline solution only group (absolute risk difference 0.6%; 95% confidence interval -4.8% to 6.0%). The contrast-induced nephropathy rate in patients receiving less than 1 L intravenous fluids in the emergency department (ED) was 19 of 147 (12.9%) versus 7 of 210 (3.3%) for greater than 1 L intravenous fluids (difference 9.6%; 95% confidence interval 3.7% to 15.5%), a 69% risk reduction (odds ratio 0.41; 95% confidence interval 0.21 to 0.80) per liter of intravenous fluids.

**Conclusion:** We did not find evidence of a benefit for N-acetylcysteine administration to our ED patients undergoing contrast-enhanced CT. However, we did find a significant association between volume of intravenous fluids administered and reduction in contrast-induced nephropathy. [Ann Emerg Med. 2013;62:511-520.]

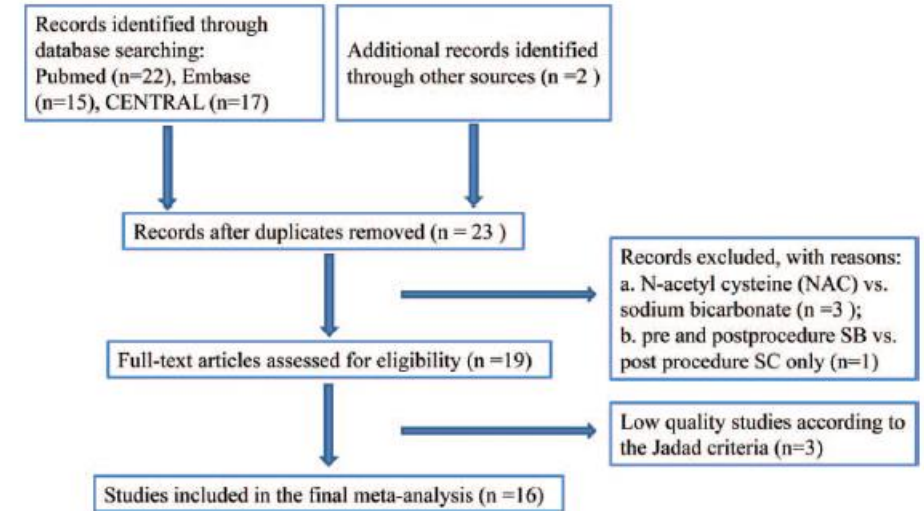
- ▶ RCT, Çift kör, 2 Merkezli çalışma
- ▶ 357 hasta
- ▶ NAC+sıvı %7,6, Sadece sıvı %7 CIN gelişmiş
- ▶ 1 L den az sıvı verilenlerde %12,9, fazla verilenlerde %3,3

OPEN

# How Strong Is the Evidence for Sodium Bicarbonate to Prevent Contrast-Induced Acute Kidney Injury After Coronary Angiography and Percutaneous Coronary Intervention?

Yuhao Dong, MD, Bin Zhang, MD, Long Liang, MD, Zhouyang Lian, MD, Jing Liu, MD, Changhong Liang, PhD, and Shuixing Zhang, PhD

- ▶ 16 RCT, 3537 hasta, 2 grup
- ▶ Sivi+HCO<sub>3</sub> vs NaCl
- ▶ Birincil sonlanım CIN, anlamlı fark gösterilmiş
- ▶ HCO<sub>3</sub>, Kreatinin düşüşü ve GFR artışında faydalı
- ▶ Mortalite, diyaliz ihtiyacı, yatış süresinde anlamlı etki yok



# Effect of No Prehydration vs Sodium Bicarbonate Prehydration Prior to Contrast-Enhanced Computed Tomography in the Prevention of Postcontrast Acute Kidney Injury in Adults With Chronic Kidney Disease The Kompas Randomized Clinical Trial

Rohit J. Timal, MD; Judith Koolman, MD, PhD; Yvo W. J. Sijpkens, MD, PhD; Jean-Paul P. M. de Vries, MD, PhD; Iris J. A. M. Verberk-Jonkers, MD, PhD; Harald F. H. Brulez, MD, PhD; Marjolijn van Buren, MD, PhD; Aart J. van der Molen, MD, PhD; Suzanne C. Cannegieter, MD, PhD; Hein Putter, PhD; Wilbert B. van den Hout, PhD; J. Wouter Jukema, MD, PhD; Ton J. Rabelink, MD, PhD; Menno V. Huisman, MD, PhD, FESC

- ▶ 523 hasta, stage 3 KBY , RCT
- ▶ 2 grup; hidrasyon yapılmayan vs 250 ml izotonik+bikarbonat
- ▶ CIN gelişimi toplam 11 (%2,1) (7 vs 4)
- ▶ Diyaliz ihtiyacı olmamış

**RESULTS** Of 554 patients randomized, 523 were included in the intention-to-treat analysis. The median (interquartile range) age was 74 (67-79) years; 336 (64.2%) were men and 187 (35.8%) were women. The mean (SD) relative increase in creatinine level 2 to 5 days after contrast administration compared with baseline was 3.0% (10.5) in the no prehydration group vs 3.5% (10.3) in the prehydration group (mean difference, 0.5; 95% CI, -1.3 to 2.3;  $P < .001$  for noninferiority). Postcontrast acute kidney injury occurred in 11 patients (2.1%), including 7 of 262 (2.7%) in the no prehydration group and 4 of 261 (1.5%) in the prehydration group, which resulted in a relative risk of 1.7 (95% CI, 0.5-5.9;  $P = .36$ ). None of the patients required dialysis or developed acute heart failure. Subgroup analyses showed no evidence of statistical interactions between treatment arms and predefined subgroups. Mean hydration costs were €119 (US \$143.94) per patient in the prehydration group compared with €0 (US \$0) in the no prehydration group ( $P < .001$ ). Other health care costs were similar.

**CONCLUSIONS AND RELEVANCE** Among patients with stage 3 CKD undergoing contrast-enhanced computed tomography, withholding prehydration did not compromise patient safety. The findings of this study support the option of not giving prehydration as a safe and cost-efficient measure.

# Comparison of combination therapy of high-dose oral N-acetylcysteine and intravenous sodium bicarbonate hydration with individual therapies in the reduction of Contrast-induced Nephropathy during Cardiac Catheterisation and Percutaneous Coronary Intervention (CONTRAST): A multi-centre, randomised, controlled trial☆

Eric Chong<sup>a,b,1</sup>, Kian-Keong Poh<sup>a,c,\*</sup>, Qingshu Lu<sup>d</sup>, James Jun-Jie Zhang<sup>e</sup>, Ning Tan<sup>f</sup>, Xu Min Hou<sup>g</sup>, Hean-Yee Ong<sup>h</sup>, Aizai Azan<sup>i</sup>, Shao-Liang Chen<sup>e</sup>, Ji-Yan Chen<sup>f</sup>, Rosli Mohd Ali<sup>i</sup>, Wei-Yi Fang<sup>g</sup>, Titus Wai Leong Lau<sup>j</sup>, Huay-Cheem Tan<sup>a,c,\*</sup>



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- ▶ 3 grup toplam 548 hasta
- ▶ NAC vs Bikarbonat vs Kombine
- ▶ Birincil sonlanım CIN
- ▶ Kombinasyon üstün değil
- ▶ NAC da insidans Bikarbonattan düşük
- ▶ 12 saat HCO<sub>3</sub> infüzyonu 1 saatten üstün



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International Journal of Cardiology

journal homepage: [www.elsevier.com/locate/ijcard](http://www.elsevier.com/locate/ijcard)

**Methods:** In a multi-centre, open-label, randomised, controlled trial (NCT00497328), we prospectively enrolled 548 patients with at least moderate renal impairment undergoing cardiac catheterisation with or without percutaneous coronary intervention. Patients were randomly assigned to 3 groups: 1) NAC: 154 mEq/L sustained sodium chloride regime (1 mL/kg/h 12 h before, during and 6 h after the procedure) with oral NAC at 1.2 g bid for 3 days (n = 185); 2) SOB: 154 mEq/L abbreviated SOB regime at 3 mL/kg/h 1 h before the procedure, and 1 mL/kg/h during and 6 h after the procedure (n = 182); and 3) COM: combination of abbreviated SOB regime and oral NAC (n = 181). The primary end point was incidence of CIN. The secondary end points were rise in serum creatinine, hospitalisation duration, haemodialysis, morbidity and mortality within 30 days.

**Results:** The 3 groups had similar baseline characteristics: age  $68 \pm 10$  years, 76% male, 48% diabetic and baseline glomerular filtration rate (GFR)  $47.7 \pm 13.0$  mL/min. There were 41 (8.8%) patients with GFR < 30. The CIN incidences were NAC 6.5%, SOB 12.8% and COM 10.6%. The COM regimen was not superior to either the NAC (relative risk (RR) = 1.61, 95% confidence interval (CI): 0.76 to 3.45, p = 0.225) or SOB (RR = 0.83, 95% CI: 0.44 to 1.56, p = 0.593) regimens. The CIN incidence was lower in the NAC group than the SOB group (adjusted odds ratio (OR) = 0.40, 95% CI: 0.17 to 0.92; p = 0.032). Multivariate analysis showed contrast volume (OR = 1.99, 95% CI: 1.33 to 2.96, p < 0.001 per 100 mL), female (OR = 2.47, 95% CI: 1.22 to 5.00, p = 0.012) and diabetes



# Strategies Preventing Contrast-Induced Nephropathy After Coronary Angiography: A Comprehensive Meta-Analysis and Systematic Review of 125 Randomized Controlled Trials

Sadegh Ali-Hassan-Sayegh, MD<sup>1</sup>, Seyed Jalil Mirhosseini, PhD<sup>1</sup>,  
Zahra Ghodrati-pour, MD<sup>1</sup>, Zahra Sarrafan-Chaharsoughi, MD<sup>1</sup>,

## Abstract

This systematic review with meta-analysis sought to determine the strength of evidence for the effects of hydration (sodium bicarbonate [SB] and normal saline [NS]), supplementations (*N*-acetylcysteine [NAC] and vitamin C), and some common drugs (adenosine antagonists [AAs], statins, loop diuretics, and angiotensin-converting enzyme inhibitors [ACEIs]) on the incidence of contrast-induced nephropathy (CIN) and requirement for hemodialysis after coronary angiography. After screening, a total of 125 trials that reported outcomes were identified. Pooled analysis indicated beneficial effects of SB versus NS (odds ratio [OR] = 0.73; 95% confidence interval [CI]: 0.56-0.94; *P* = .01), NAC (OR = 0.79; 95% CI: 0.70-0.88; *P* = .001), vitamin C (OR = 0.64; 95% CI: 0.45-0.89; *P* = .01), statins (OR = 0.45; 95% CI: 0.35-0.57; *P* = .001), AA (OR = 0.28; 95% CI: 0.14-0.47; *P* = .001), loop diuretics (OR = 0.97; 95% CI: 0.33-2.85; *P* = .9), and ACEI (OR = 1.06; 95% CI: 0.69-1.61; *P* = .8). Overall, hydration with SB, use of supplements, such as NAC and vitamin C, and administration of statins and AA should always be considered for the prevention of CIN after coronary angiography.

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journals.sagepub.com/home/ang  
SAGE

- Bir çok ajan incelenmiş.
  - Bikarbonat ve Salin, NAC ve placebo
  - Her ikisi de CIN gelişimine faydalı
  - Her ikisi de hemodiyaliz ihtiyacını azaltma açısından faydasız???
- (%0,77-0,82)                      (%1,9-2,2)

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ESTABLISHED IN 1812

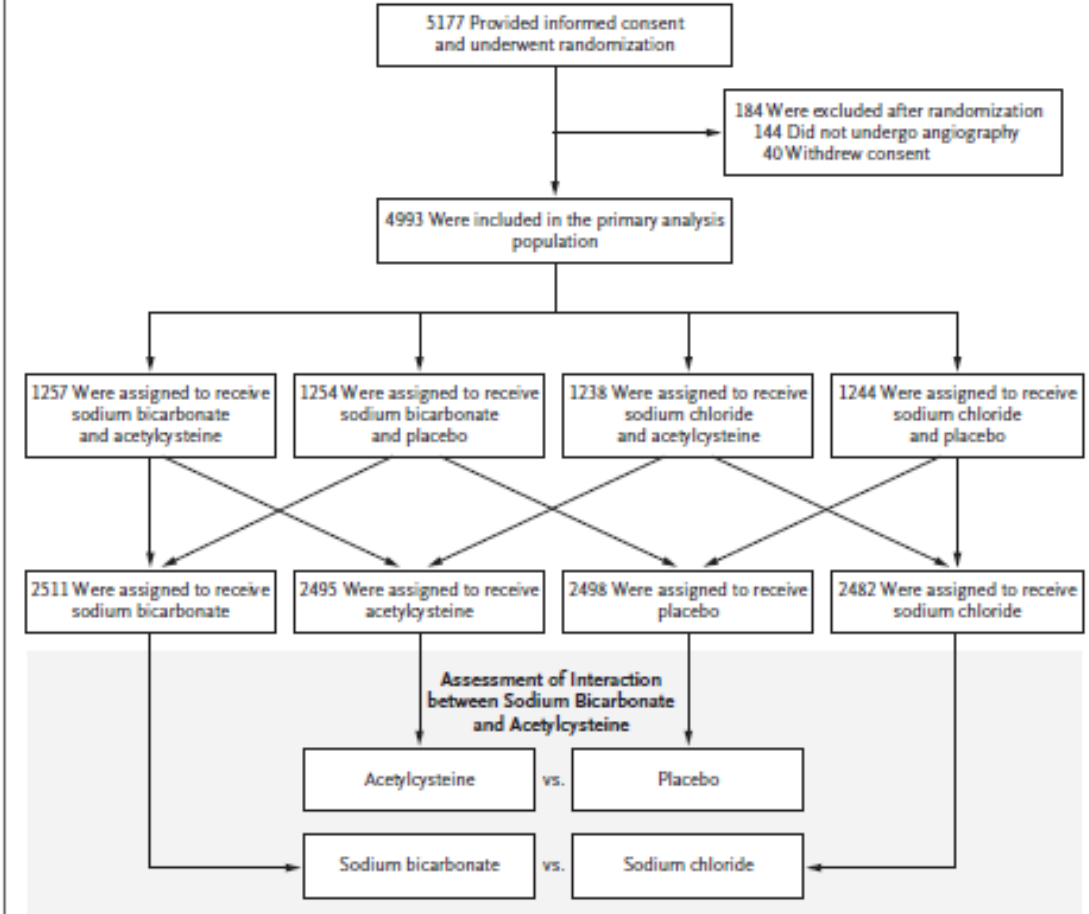
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## Outcomes after Angiography with Sodium Bicarbonate and Acetylcysteine

S.D. Weisbord, M. Gallagher, H. Jneid, S. Garcia, A. Cass, S.-S. Thwin, T.A. Conner, G.M. Chertow, D.L. Bhatt, K. Shunk, C.R. Parikh, E.O. McFall, M. Brophy, R. Ferguson, H. Wu, M. Androsenko, J. Myles, J. Kaufman, and P.M. Palevsky, for the PRESERVE Trial Group\*

- 4 yıllık süreçte 2 ye 2 randomizasyon, 4993 hasta
- Toplam 4 grup (NAC vs HCO<sub>3</sub> vs NaCl vs Placebo)
- Primer End-point anlamlı fark yok.
- 90 günlük mortalite ve diyaliz ihtiyacı, Kreatinin artışı
- Sekonder End-point CIN gelişimi
- HCO<sub>3</sub> ve NAC arasında anlamlı fark yok.
- Kombine terapiler ile 4 grubun arasında anlamlı fark yok.





# Sonuç Olarak

- ▶ NAC vs  $\text{HCO}_3$  için elde edilen net veri yok.
- ▶ Hidrasyonun faydası nispeten daha fazla gösterilmiş.
- ▶ Önleme hala en önemli basamak
- ▶ Daha çok RCT gerekli
- ▶ Elde olmayan kanıtlardan dolayı maliyet yinede ön planda tutulmalı

