**Evidence Table I-4. Summary of studies of N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy and other outcomes**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author, year** | **Comparison** | **Number randomized (Number analyzed if differerent)** | **Population**  | **Age, years (or range of means**¶) | **No. female (%)**§ | **Total follow-up** | **CM****Route\*** | **Definition** **of CIN\*** | **Study limitations†** |
| Allaqaband, 2002 [5](#_ENREF_5) | IV 0.45% saline vs. oral NAC + IV 0.45% saline vs. IV IV fenoldopam + 0.45% saline + | 126 (123) | CKD (SrCr ≥ 1.6 mg/dl or an estimated creatinine clearance ≤ 60 ml/min) | 71 | 52 (42) | 48 hours | LOCMIA | A2a | M |
| Baskurt, 2009[8](#_ENREF_8) | IV normal saline vs. oral NAC + IV normal saline vs. Oral NAC + oral theophylline + IV normal saline | 217 | Moderate degree (stage 3) CKD (eGFR between 30 and 60 ml/min/1.73 m2) | 67 | 87 (40) | 12 months | LOCM (Ioversol)IA | A2b | H |
| Briguori, 2004 [10](#_ENREF_10) | Oral NAC + IV 0.45% saline vs. IV fenoldopam + IV 0.45% saline | 192 | CKD (stable SrCr ≥ 1.5 mg/dl and/or creatinine clearance < 60 mL/min) | 68-69 | 29 (15) | 48 hours | IOCM (Iodixanol),IA | A2b | M |
| Briguori, 2004[11](#_ENREF_11) | Oral NAC single-dose (600 mg bid) + IV 0.45% saline vs. Oral NAC double-dose (1200 mg bid) + IV 0.45% saline | 223 | CKD (stable SrCr ≥table SrCr ed/or creatinineclearance <60 ml/min) | 66-67 | 41 (18) | 48 hours | IobitriolIA | A2b | M |
| Briguori, 2007[12](#_ENREF_12) | Oral NAC + IV normal saline vs. Oral NAC + IV NaHCO3 in dextrose and water vs Oral NAC + IV ascorbic acid + IV normal saline | 351 (326) | CKD (SrCr ≥2.0 mg/dl and/or estimated GFR < 40 ml/min/1.72m2 | 69-71 | 57 (17) | 48 hours | IodixanolIA | A1b | M |
| Brueck, 2013 [78](#_ENREF_78) | IV normal saline + placebo vs. IV NAC + IV normal saline vs. IV ascorbic acid + IV normal saline | 520 (499) | SrCr ≥ 1.3 mg/dl | 74-75 | 181 (36) | 72 hours | Iopromide(LOCM)IA | A2b | L |
| Castini, 2010[79](#_ENREF_79) | IV normal saline vs. + IV normal saline vs. IV NaHCO3 | 156 |  SrCr ≥ 1.2 mg/dl | 70-72 | 19 (12) | 5 days | Iodixanol(IOCM)IA | A1b | M |
| Chen, 2008 [14](#_ENREF_14) | If SrCr <1.5 mg/dL:No intravenous fluids vs. IV 0.45% saline.If SrCr ≥1.5 mg/dL, then NAC + IV 0.45% saline vs. NAC without intravenous fluids  | 936 | Myocardial Ischemia, scheduled for percutaneous coronary intervention (PCI)  | 56-67 | 84 | 6 months | IOCMIA | A2a | H |
| Demir, 2008 [16](#_ENREF_16) | IV normal saline vs. NAC + IV normal saline vs. misoprostol + IV normal saline + vs. theophylline+ IV normal saline vs. nifedipine + normal saline |  97 | Non-diabetic, no CKD | 43-78 | 43 (44) | 72 hours | Iomeprol, IopamidolIV | A3b | H |
| Gunebakmaz, 2012[21](#_ENREF_21) | normal saline vs. normal saline + nebivolol vs. NAC + normal saline | 120 | SrCr ≥ 1.2 mg/dl | 64-66 | 38 (31) | 5 days | IopromideIA | A3b | H |

**Evidence Table I-4. Summary of studies N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy and other outcomes (continued)**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author, year** | **Comparison** | **N** | **Population**  | **Age, range of means**¶  | **No. female (%)**§ | **Total follow-up** | **CM Route\*** | **Definition** **of CIN\*** | **Study limitations†** |
| Hafiz, 2012 [22](#_ENREF_22) | IV normal saline with or without oral NAC vs. IV NaHCO3 in 5% dextrose in water with or without oral NAC | 320 | SrCr >1.6 mg/dl in non-diabetics and >1.4 mg/dl in diabetics or an estimated glomerular filtration rate (eGFR) of <50 ml/min/1.73 m2 | 73 | 138 (43) | 48 hours | LOCMIA | A3a | M |
| Heguilen, 2013 [25](#_ENREF_25) | IV NaHCO3 vs. NAC + IV NaHCO3 vs. NAC + IV normal saline | 133 (123) | Stable SrCr ≥1.25 mg/dl or estimated creatinine clearance > 45 ml/min, but SrCr must be ≤ 4.5 mg/dl | 64-69 | 34 (25) | 72 hours | IoversalIA  | A1b | M |
| Holscher, 2008[26](#_ENREF_26) | IV normal saline + glucose vs. + hemodialysis IV normal saline +glucose vs. oral NAC + IV normal saline + g glucose | 412  | SrCr 1.3-3.5 mg/dl | 67 | 68 (16.5)  | 30 days | IopromideIA | A2b | H |
| Huber, 2006[27](#_ENREF_27) | IV ttheophylline vs. IV NAC vs. IV theophylline + IV NAC | 91 | At least one risk factor for CIN; stable renal function | 58.5 | 31 (34) | 48 hours | Iomeprol (LOCM)IA and IV | See footnote ‡ | M |
| Kinbara, 2010[29](#_ENREF_29) | IV normal saline vs. + IV aminophylline + normal saline vs. NAC + normal saline | 45 | Stable coronary artery disease and stable SrCr | 70-71 | 17 (37) | 48 hours | IopamidolIA | A2a | M |
| Kotlyar, 2005[34](#_ENREF_34) |  IV normal saline vs IV NAC 300mg in 5% dextrose + IV normal saline + vs. IV NAC 600mg in 5% dextrose + IV normal saline  | 65 (60) | Stable SrCr concentrations ≥0.13 mmol/l (1.47 mg/dl) | 66-69 | 7 (11) | 30 days | IopromideIA | A2b | M |
| Kumar, 2014[36](#_ENREF_36) | Oral NAC + IV Saline vs. Allopurinol + IV Saline | 95 | Coronary block | 65 | 110 (22) | 5 days | LOCM (Iohexol)IOCM (Iodixanol)IA | Oral | NR |
| Marenzi, 2006 [46](#_ENREF_46) | IV normal saline + placebovs. standard-dose NAC (600 mg IV NAC before the procedure, then 600 mg twice a day for 48 h after the contrast) + normal saline vs. High-dose NAC + (1200 mg IV NAC before the contrast, then 1200 mg orally twice a day for 48 hours after) + IV normal saline | 354 | ST elevation acute myocardial infarction | 62-62 | 50 (14) | NR | IohexolIA | A1b | M |
| Ng, 2006 [50](#_ENREF_50) | Oral NAC + IV normal saline vs. IV fenoldopam + IV normal saline | 95 (84) | Stable renal disease, SrCr >1.2 mg/dl | 68 | 24 (25) | 72 hours | Only non-ionic LCOM or IOCMIA | A3a | M |
| Ozcan, 2007[80](#_ENREF_80) | IV normal saline vs NAC + IV normal saline vs IV NaHCO3 in dextrose  | 264 | SrCr > 1.2 mg/dl and ≤ 4 mg/dl | 69 | 67 (25) | 48 hours | Ioxaglate (LOCM)IA | A3a | H |
| Ozhan, 2010[52](#_ENREF_52) | NAC + IV saline vs. NAC + atorvastatin + IV saline | 130 | No renal insufficiency (SrCr ≤ 1.5 and GFR ≥ 70 ml/min) | 54-55 | 53 (41) | 48 hours | IopamidolIA | A3a | M |

**Evidence Table I-4. Summary of studies N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy and other outcomes (continued)**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author, year** | **Comparison** | **N** | **Population**  | **Age, range of means**¶  | **No. female (%)**§ | **Total follow-up** | **CM****Route\*** | **Definition** **of CIN\*** | **Study limitations†** |
| Ratcliffe, 2009 [54](#_ENREF_54) | IV normal saline in 5% dextrose vs. NAC + IV normal saline in 5% dextrose vs. IV NaHCO3 in 5% dextrose vs. NAC + IV NaHCO3 in 5% dextrose | 118 (78)  | CKD and/or diabetes mellitus | 66 | 31(40) | 7 days | Iodixanol (IOCM)IA | A1a | H |
| Recio-Mayoral, 2007 [55](#_ENREF_55) |  Oral NAC post-contrast + IV normal saline vs. IV NAC pre- contrast oral NAC post-contrast+ IV sodium bicarbonate in 5% glucose and water | 111 | Patients with myocardial infarction treated with PCI or high-risk non-ST segment elevation acute coronary syndrome needing urgent revascularization (no GFR inclusion criteria other than the exclusion of dialysis patients) | 65 | 34 (31) | 7 days | Iomeprol (LOCM)IA | A2b | H |
| Reinecke, 2007 [56](#_ENREF_56) | IV normal saline +5% glucose vs. one session of hemodialysis + IV normal saline + 5% glucose vs. oral NAC + IV normal saline + 5% glucose | 424 (412) | SrCr 1.3-3.5 mg/dl | 67-68 | 73 (17) | Mean follow-up: 553 days (63 to 1316 days) | Iopromide (IOCM)IA | A2b | H |

%=percent; CIN=contrast induced nephropathy; CKD=chronic kidney disease; CM=contrast media; dL=deciliter; eGFR=estimated glomerular filtration rate; IA=intrarterial; IV=intravenous; LOCM=low-osmolar contrast media; m2=meter squared; mg=milligram; min=minute; ml=milliliter; mmol/l=millimole per liter; N=sample size; NAC=N-acetylcysteine; NaHCO3=sodium bicarbonate; NR=not reported; PCI=percutaneous coronary intervention; SrCr=serum creatinine

\* CIN definitions: rise in serum creatinine relative to baseline: >25% (A1a); ≥25% (A1b); >0.5 mg/dl (A2a); ≥0.5 mg/dl (A2b); >25% or > 0.5 mg/dl (A3a); ≥25% or ≥0.5 mg/dl (A3b); ≥50% (A4) B: >25% reduction in creatinine clearance

† Study limitations: L=low risk of bias; M=medium risk of bias; H=high risk of bias

‡Barrett BJ, Parfrey PS. Prevention of nephrotoxicity induced by radiocontrast agents, N Engl J Med 1994;331:1449–1450.

§ Percent females in entire study population

¶ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms if the mean age for the whole population is not reported