

PROTOCOLLO DI PROFILASSI DELLA NEFROPATIA DA MEZZO DI CONTRASTO NEL PAZIENTE CON INSUFFICIENZA RENALE CRONICA OSPEDALIZZATO

H. Kulurianu, D.Rossi, C.Savignani, D. Ricciardi

❖ IDENTIFICAZIONE DEL PAZIENTE CON IRC E PROFILO DI RISCHIO PER LO SVILUPPO DI NMC

Nella pratica clinica la creatininemia viene usata come indice della funzione renale; la creatininemia varia in maniera inversamente proporzionale al GFR ma tale relazione dipende in gran parte dalla massa muscolare e dalla produzione della creatinina: l'età, il sesso, ed il peso corporeo. Nei pazienti che hanno ridotto tessuto muscolare (anziani e donne) un minimo aumento della creatininemia può corrispondere ad una significativa riduzione della funzione renale.

La misurazione della clearance della creatinina richiede la raccolta delle urine delle 24 ore che non è sempre di semplice realizzazione. La formula di Cockroft-Gault stima con sufficiente attendibilità la clearance, tiene conto del peso corporeo, del sesso e dell'età e correla con il GFR.

Clearance della creatinina ml/min

(Maschi) (140-età) x peso corporeo/(creatinina serica x 72)

(Femmine) (140-età) x peso corporeo/(creatinina serica x 72) X 0.85

Pazienti ad alto rischio.

1. Clearance della creatinina stabile < 25ml/min
2. Clearance della creatinina 25-50ml/ min + uno dei seguenti fattori di rischio
 - Diabete mellito
 - Scompenso cardiaco congestizio
 - Recente somministrazione di mdc
 - Necessità di alte dosi di mdc

Pazienti a rischio moderato

1. Clearance della creatinina stabile 25-50 ml/min
2. Clearance della creatinina stabile 50-75 ml/min + un fattore di rischio:
 - Diabete mellito
 - Scompenso cardiaco congestizio
 - Recente somministrazione di mdc
 - Necessità di alte dosi di mdc

❖ MISURE DI PROFILASSI DA ATTUARE

Per tutti i pazienti con funzione renale ridotta:

- Segnalare nella richiesta dell'esame contrastografico la riduzione della funzione renale
- Sospendere i diuretici (se non controindicato clinicamente), i FANS, il dipiridamolo, gli aminoglicosidi, gli ACE-inibitori e sartanici e la metformina.
- Prescrivere acetilcisteina (600mg x 2) a partire dal giorno prima dell'esame avendo cura di somministrare una dose un' ora prima dell'esame.
- Teofillina in infusione di 30 min prima dell'esame se non ci sono controindicazioni.
- Usare mezzi di contrasto a bassa osmolalità preferibilmente l'iodixanolo.
- Idratazione
- Ottenere un buon controllo glicemico (glicemia 200-250mg/dl)

1. Per i pazienti a rischio moderato:

Idratazione orale con almeno 1 Lit di acqua nelle 10 ore precedenti l'esame.

Idratazione parenterale a partire da 4 ore prima dell'esame e per 8-12 ore dopo alla velocità di infusione di 1-1.5 ml/Kg/min.

2. Per i pazienti ad alto rischio:

Idratazione parenterale a partire da 12 ore prima e per 12-24 ore dopo alla velocità di 1-1.5ml/Kg/min.

La scelta della soluzione salina (ipotonica vs normale) può variare in base alla sodiemia e soprattutto alla tollerabilità del carico di sodio. E' comunque preferibile usare l'ipotonica almeno nell'immediato periodo periprocedurale.

❖ CONTROLLO DELLA FUNZIONE RENALE: A 24 ORE PER IMPOSTARE ULTERIORE IDRATAZIONE SE NECESSARIO.

❖ CONTROLLO DELLA FUNZIONE RENALE A 72 ORE.

Cronin R. Radiocontrast media-induced acute renal failure. Diseases of the kidney. Fifth Edition. Vol II:1187-1202.

¹ Kramer BK, Kammerl M, Schweda F, Schreiber M. A primer in radiocontrast-induced nephropathy. Nephrol Dial Transplant. 1999;14:2830-2834.

1 Barrett BJ, Parfrey PS. Prevention of nephrotoxicity induced by radiocontrast agents. N Engl J Med 331: 1449-1450.

1 Nash K, Hafee ZA, Abrinko P, Hou S: Hospital acquired acute renal failure. J Am Soc Nephrol. 1996; 7:1376.

1 Hospital acquired renale failure Am J Kidney Dis May 2002

1 Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, Best PJ, Singh M, Bell MR, Barsness GW, Mathew V, Garratt KN, Holmes DR Jr. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. Circulation 2002 May 14;105(19):2259-64.

1 Abizaid AS, Clark CE, Mintz GS, Dosa S, Pompa JJ, Pichard AD, Satler LF, Harvey M, Kent KM, L MB. Effects of dopamine and aminophylline on contrast-induced renal failure after coronary angioplasty in patients with preexisting renal insufficiency. 1999; Am J Cardiol 83: 260-263.

1 Levy EM, Viscoli CM, Horwitz RI. High mortality in contrast-associated renal failure is not explained by comorbidity. J Am Soc Nephrol. 1996; 5: 400-408

1 Freeman RV, O'Donnell M, Ke-Rogers E, Clark VL, De Franco AC, Eagle KA, McGinnity JG, Patel K, Maxwell-Eward A, Bondie D, Moscucci M; Blue Cross-Blue Shield of Michigan Cardiovascular Consortium (BMC2). Nephropathy requiring dialysis after percutaneous intervention and the critical role of an adjusted contrast dose. Am J Cardiol 2002 Non 15;90 (10):1068-73.

1 Berg KJ, Nephrotoxicity related to contrast media. Scand J Urol Nephrol. 2000; 34:317-22.

¹ Gruberg L, Mehran R, Dangas G, Mintz GS, Waksman R, Kent KM, Pichard AD, Satler LF, Wu H, Leon MB. Acute renal failure requiring dialysis after percutaneous coronary interventions. Catheter Cardiovasc Interv. 2001;52:409-416.

¹ McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neil WW. Acute renal failure after coronary intervention: Incidence, risk factors and relationship to mortality. Am J. Med. 1997;103:368-375.

¹ Folley RN, Parfrey PS, Harnett JD. Clinical and echocardiographic disease in patients starting end-stage renal disease therapy. Kidney Int. 1995;47:186-192.

¹ Ting HH, Tahirkheli NK, Berger PB. Evaluation of long-term survival after successful percutaneous coronary intervention among patients with chronic renal failure. Am J Cardiol. 2001; 87:630-633, A9.

¹ Berns AS. Nephrotoxicity of contrast media. Kidney Int 1989;36:730-740.

1 Davidson CJ, Hlattry M, Morris KG, Pierer K, Skleton TN, Schwab SJ, Bashore TM. Cardiovascular and renal toxicity of a non-ionic radiographic contrast agent after cardiac catheterization. A prospective trial. Ann Intern Med 1989;110:119-124.

- 1 Moore RD, Steinberg EP, Powe NR, Brinker JA, Fishman EK, Graziano S, Gopalan R. Nephrotoxicity of high osmolarity versus low-osmolarity contrast media: a randomized clinical trial. *Radiology* 1992;182:649-655.
- ¹ VavZee BE, Hoy WE, Talley TE, Jaenike JR: Renal injury associated with intravenous pyelography in nondiabetics and diabetic patients. *Ann Intern Med* 1978;51-54.
- 1 Parfrey PS, Griffiths SM, Barrett BJ. Contrast material induced renal failure in patients with diabetes mellitus, renal insufficiency, or both. *N Engl J Med*. 1989; 320: 143-9.
- 1 Manske CL, Sprafka JM, Strony JT, Wang Y. Contrast nephropathy in azotemic diabetic patients undergoing coronary angiography. *Am J Med* 1990;89:615-20.
- ¹ Myers GH, Witten DM: Acute renal failure after excretory urography in multiple myeloma. *Am J Roentgenol Rad Ther Nucl Med*. 1971; 113:583-588.
- ¹ Schwartz RH, Berdon WE, Wagner HE. Tamm-Horsfall urinary microprotein precipitation by urographic contrast agents. *Am J Roentgenol* 1970; 100:698-701.
- ¹ McCarthy CS, Becker JA: Multiple myeloma and contrast media. *Radiology* 1992;183:519-521.
- 1 Deray G. Nephrotoxicity of contrast media. *Nephrol. Dial. Transplant.* 1999; 14:2602-2606.
- ¹ Taliercio CP, Vlietstra RE, Fisher LD, Burnett JC. Risks for renal dysfunction with cardiac angiography. *Ann Int Med* 1986;104:501-504.
- 1 Cigarroa RG, Lange RA, Williams RH, Hillts LD: Dosing of contrast material to prevent contrast nephropathy in patients with renal disease. *Am J Med*. 1989;86:649-652.
- 1 Katayama H, Yamaguchi K, Kozuka T, Takashima T, Seez P, Matsuura K,. Adverse reactions to ionic and non ionic contrast media: a report from the Japanese Committee on the Safety of Contrast media. *Radiology* 1990; 175:621-8.
- 1 Barrett BJ, Carlisle EJ: Meta analysis of the relative nephrotoxicity of high and low osmolality iodinated contrast media. *Radiology* 1993; 188:171-178.
- 1 Rudnik MR, Goldfarb S, Wexler L. Nephrotoxicity of ionic and non ionic contrast media in 1196 patients: a randomized trial. *Kidney Int* 1995;47:254-61.
- 1 Katholi RE, Taylor GJ, Woods WT. Nephrotoxicity of non-ionic low-osmolality versus high-osmolality contrast media: a prospective double-blind randomized comparison in human beings. *Radiology*, 1993 ;186:183-187.
- 1 Rich MW, Creselius CA. Incidence, risk factors and clinical course of acute renal insufficiency after cardiac catheterization in patients 70 years and older. 1990 *Arch Intern Med* 150: 1237-1242.
- 1 Guitterez NV, Diaz A, Timmis GC, O'Neill WW, Stevens MA, Sandberg KR, McCullough PA. Determinants of serum creatinine in acute contrast nephropathy. *J Intev Cardiol* 2002 Oct; 15(5):349-54.
- 1 Kolonko A, Kokot F Wiecek A. Contrast associated nephropathy – old clinical problem and new therapeutic perspectives. *Nephrol. Dial. Transpalnt.* 1998; 13: 803-806.
- 1 Heyman SN, Brezis M, Epstein et al. Early medullary hypoxic injury from radiocontrast and indometacin. *Kidney Int.*; 1991;40: 632-642.
- 1 Russo D, Minutolo R, Giancaruso B et al. : Early effects of contrast media on renal hemodynamics and tubular function in chronic renal failure. *J Am Soc Nephrol*. 1995; 6: 1451-1458.
- ¹
- ¹ Arend LJ, Bakris GL, Burnett JCJ, Megerian C, Spielman WS. Role for intrarenal adenosine in the renal hemodynamic response to contrast media. *J Lab Clin Med* 1987;110:406-411.
- ¹ Deray G, Martinez F, Cacoub P, Baumelou B, Baumelou A, Jacobs C. A role for adenosine calcium and ischemia in radiocontrast-induced intrarenal vasoconstriction. *Am J Nephrol*. 1990;10:316-322.
- ¹ Arakawa K, Suzuki H, Naith M, Matsumoto A, Hayashi K, Matsuda H, Ishihara A, Kubota E, Saruta T. Role of adenosine in the renal responses to contrast medium. *Kidney Int.* 1996;49:1199-1206.
- ¹ Margulies KB, McKinley LJ, Burnett JC. Endothelin in human and canine radiocontrast-induced nephropathy. *J Vasc Res*. 1992;29:163-4
- ¹ Heyman SN, Clark BA, Kaiser N. Radiocontrast agents induce endothelin release in vivo and in vitro. *J Am Soc Nephrol* 1992;3:58-65.
- ¹ Margulies KB, Hildebrand FLJ, Heublein DM, Burnett JCJ. Radiocontrast increases plasma and urinary endothelin. *J Am Soc Nephrol*. 1991;2:1041-1045.
- ¹ Katzberg RW, Meggs LG, Schulman G, Hollenberg NK. Contrast medium induced renal vasoconstriction and endogenous vasoconstrictor hormones. *Br J Radiol*. 1982;55:266-8.
- ¹ Cadicott WJH, Hollenberg NK, Abrams HL. Characteristics of response of renal vascular bed to contrast media: evidence of vasoconstriction induced by renin-angiotensin system. *Invest Radiol*. 1970;5:539-47.

- ¹ Cantley LG, Spokes K, Clark B, McMahon EG, Carter J, Epstein FH. Role of endothelin and prostaglandin in radiocontrast-induced renal artery constriction. *Kidney Int.* 1993;44:1217-23.
- ¹ Touati C, Idee JM, Deray G. Modulation of renal effects of contrast media by endothelium-derived nitric oxide in the rat. *Invest Radiol* 1993;28:814-20.
- ¹ Bakris GL, Lass N, Gaber AO, Jones JD, Burnett JC Jr. Radiocontrast medium-induced declines in renal function: a role for oxygen free radicals. *Am J Physiol* 1990;258:F115-F120.
- ¹ Yoshioka T, Fogo A, Beckman JK. Reduced activity of antioxidant enzymes underlies contrast-media-induced renal injury in volume depletion. *Kidney Int* 1992;41:1008-1015.
- ¹ Margulies KB, McKinley LJ, Cavero PG, Burnett JCJ. Induction and prevention of radiocontrast induced nephropathy in dogs with heart failure. *Kidney Int*. 1990;38:1101-08.
- ¹ Morkos SK. Contrast media-induced nephrotoxicity-questions and answers. *Br J Radiol* April 71;1998:357-365.
- ¹ Van Amringe M, Shannon TE. Awareness, assimilation and adoption: the challenge of effective dissemination and the first AHCPR-sponsored guidelines. *QRB Qual Rev Bull* 1992;18:397-404.
- ¹ Heyman SN, Brezis M, Greenfeld Z, Rosen S. Protective role of furosemide and saline in radiocontrast-induced acute renal failure in the rat. *Am J Kidney Dis*. 1989;14(5):377-385.
- ¹ Brown RS, Ransil B, Clark BA. Prehydration protects against contrast nephropathy in high risk patients undergoing cardiac catheterization (abstract), *Am Soc Nephrol* 1990;1:330.
- ¹ Eisenberg RL, Bank WO, Hedcock MS. Renal failure after major angiography. *Am J Med* 1980;68:43-46.
- ¹ Teruel JL, Marcen R, Herrero JA, Felipe C, Ortuno J. An easy and effective procedure to prevent radiocontrast agent nephrotoxicity in high-risk patients. *Nephron* 1989;51:282.
- ¹ Solomon R. Contrast medium induced renal failure. *Kidney Int*, 1998; 53:230-42.
- ¹ Solomon R, Werner C, Mann, Silva P. Effects of saline, mannitol and furosemide to prevent acute decreases in renal function induced by radiocontrast agents. *N Engl J Med*. 1994;331:1416-1420.
- ¹ Taylor A, Hotchkiss D, Morse RW, McCabe J. PREPARED: PREParation for Angiography in Renal Dysfunction. A Randomized Trial of Inpatient vs Outpatient Hydration Protocols for Cardiac Catheterization in Mild-to-Moderate Renal Dysfunction. *Chest* 1998;114:1570-1574.
- ¹ Mueller C, Buerkle G, Buettner HJ, Petersen J, Perruchoud AP, Eriksson U, Marsch S, Roskamm H. Prevention of contrast media-associated nephropathy. Randomised comparison of 2 hydration regimens in 1620 patients undergoing coronary angioplasty. *Arch. Intern. Med* 2002, Feb. 11: 329-336.
- ¹ ACP Journal Club. September/October 2002, Vol 137, 2-044.
- ¹ Weinstein JM, Heyman S, Brezis M. Potential deleterious effect of furosemide in radiocontrast nephropathy. *Nephron* 1992;62(4): 413-5.
- ¹ Erley CM. Does hydration prevent radiocontrast-induced acute renal failure? *Nephrol Dial Transplant*. 1999;14:1064-1066.
- ¹ Waaler A, Svaland M, Fauchald P. Elimination of ioexol, a low osmolar nonionic contrast medium, by hemodialysis in patients with chronic renal failure. *Nephron*. 1990;56:81-85
- ¹ Ueda J, Fukurawa T, Takahashi S, Sakaguchi K. Elimination of ioversol by hemodialysis. *Acta Radiol*. 1996; 37:826-829.
- ¹ Fukurawa T, Ueda J, Takahashi S, Sakaguchi K. Elimination of low-osmolality contrast media by hemodialysis. *Acta Radiol*. 1996; 37:966-971
- ¹ Matzkies FK, Reinecke H, Tombach B. Influence of dialysis procedure, membrane surface and membrane material on iopromide elimination in patients with reduced kidney function. *Am J Nephrol*. 2000;20:300-304
- ¹ Schindler R, Stahl C, Venz S, Ludat K, Krause W, Frei U. Removal of contrast media by different extracorporeal treatments. 2001; *Nephrol Dial Transplant* Jul; 16(7):1471-4
- ¹ Matzkies FK, Reinecke H, Tombach B, Koeneke J, Hohage H, Kisters K, Schaefer RM. Reduced iopromide elimination in hemodialysis with cuprophan membranes. *Acta Radiol* 2000 Nov;41(6):671-3
- ¹ Donally PK, Burwell N, McBurney A, Ward JW, Wals J, Warkin EM. Clearance of iopamidol, a non ionic contrast medium, by CAPD in patients with end-stage renal failure. *Br J Radiol*; 65:1108-1113.
- ¹ Iwamoto M, Hiroshige K, Suda T, Ohta T, Ohtani A, Nakashima Y. Elimination of iomeprol in patients undergoing continuous ambulatory peritoneal dialysis. *Perit Dial Int* 1999 Jul-Aug;19(4):380-5
- ¹ Brooks MH, Barry KG. Removal of iodinated contrast material by peritoneal dialysis *Nephron*; 12:10-14.
- ¹ Lehnert T, Keller E, Gondolf K, Schaffner T, Pavenstadt H, Schollmeyer P. Effect of haemodialysis after contrast medium administration in patients with renal insufficiency. *Nephrol Dial Transplant* 1998 Feb;13(2):358-62

- 1 Sterner G, Frennby B, Kurkus J, Nyman U. Dose post-angiographic hemodialysis reduce the risk of contrast-medium nephropathy? *Scand J Urol Nephrol.* 2000;Oct; 34(5):323-6
- 1 Vogt B, Ferrari P, Schonholzer C, Mart HP, Mohaupt M, Wiederkehr M, Cereghetti C, Serra A, Huynh-Do U, Uehlinger D, Frey F. Prophylactic hemodialysis after radiocontrast media in patients with renal failure insufficiency is potentially harmful. *JAMA.* 2001, Dec. 15:692-698.
- 1 Berger ED, Bader BD, Bosker J, Risler T, Erley CM. Contrast medium-induced renal failure can not be prevented by hemodialysis. *Dtsch Med Wochenschr.* 2001 Feb 16;126(7):162-6.
- 1 Huber W, Jeschke B, Kreymann B, Hennig M, Page M, Salmhofer H, Eckel F, Schmidt U, Umgelter A, Schweigart U, Classen M. Haemodialysis for the prevention of contrast-induced nephropathy: outcome of 31 patients with severely impaired renal function, comparison with patients at similar risk and review. *Invest Radiol* 2002 Sep;37(9):471-81
- ¹ Gabutti L, Marone C, Monti M, Malfanti M, Zwahlen U, Pasotti E, Colucci G, Schonholzer C. Does continuous hemodiafiltration comitant with radiological procedures provide a significant and safe removal of the iodinated contrast ioversol? *Blood Purif* 2003; 21(2):152-7.
- 1 Acetylcysteine: Drug Information. UpToDate Vol. 10 No 1.
- ¹ Arstall MA, Yang J, Stafford I, Betts WH, Horowitz JD. N-acetylcysteine in combination with nitroglycerin and streptokinase for treatment of evolving acute myocardial infarction: safety and biochemical effects. *Circulation* 1995;92:2855-2862.
- ¹ DiMari J, Megyesi J, Udvarheyi N, Price P, Davis R, Safirstein RL, N-acetylcysteine ameliorates ischemic renal failure. *Am J Physiol.* 1997;272:F292-F298.
- ¹ Weinbroum AA, Rudick V, Ben-Abraham R, Karchevski E. N-acetyl-L-cysteine for preventing lung reperfusion injury after liver ischemia-reperfusion; a possible dual protective mechanism in a dose-response study. *Transplantation* 2000;69:853-859.
- 1 Tepel M, Van Der Giet M, Schwarfeld C, Laufer U, Liermann D, Zidek W. Prevention of radiocontrast agent induced reductions in renal function by acetylcysteine. *NEJM,* July 2000: 180-184.
- 1 Diaz-Sandoval L, Kosowsky B, Losordo DW. Acetylcysteine to prevent angiography-related renal tissue injury (the APART trial. *The American Journal of Cardiology.* 2002 Vol 89, Issue 3, 356-358.
- 1 Shyu KG, Cheng JJ, Kuan P. Acetylcysteine protects against acute renal damage in patients with abnormal renal function undergoing a coronary procedure. *J Am Coll Cardiol* 2002 Oct 16;40(8):1383-8
- 1 Kay J, Chow WH, Chan TM, Lo SK, Kwok OH, Yip A, Fan K, Lee CH, Lam WF. Acetylcysteine for prevention of acute deterioration of renal function following elective coronary angiography and intervention: a randomized controlled trial. *JAMA.* 2003 Feb 5;289(5):606-8.
- 1 Briguori C, Manganeli F, Scarpato P, Elia PP, Golia B, Riviezzo G, Lepore S, Librera M, Villari B, Colombo A, Ricciarelli B. Acetylcysteine and Contrast Agent-Associated nephrotoxicity. *Journal of American College of Cardiology.* 2002, Vol 40 No 2: 298-303.
- 1 Vallero A, Cesano G, Pozzato M, Garbo R, Minelli M, Quarello F, Formica M. Contrast nephropathy in cardiac procedures: no advantages with prophylactic use of N-acetylcysteine (NAC). *G Ital Nefrol* 2002 Sep-Oct;19(5):529-33
- 1 Caputo C, Dokko JH, Durham JH. Pahlavan M, Keltz J, Dutka P, Marzo K, Zaharakis T, Fisbane S. A randomized controlled trial of N- acetylcysteine to prevent contrast nephropathy following coronary angiography. *Am J Kidney Dis* 2002;39(4):A14.
- 1 Erickson C, Erickson J, Wilsker G, Brunner L. A retrospective analysis of oral acetylcysteine intervention to prevent radiographic contrast-induced nephropathy in patients undergoing coronary angiography with elevated serum creatinine. *Am J Kidney Dis* 2002;39(4):A14.
- ¹ Kellum JA, Janine M, Decker RN. Use of dopamine in acute renal failure: a meta-analysis. *Crit Care Med* 2001 Vol.29, N8:15261531.
- ¹ Hans B, Hans SS, Mittal VK, Khan TA, Patel N, Dahn MS. Renal functional response to dopamine during and after arteriography in patients with chronic renal insufficiency. *Radiology.* 1990;Sep;176(3):651-4.
- ¹ Hans SS, Hans B, Dhillon R, Dmuchowski C, Glover J. Effect of dopamine on renal function after arteriography in patients with pre-existing renal insufficiency. *Am Surg.* 1998 May;64(5):432-6
- ¹ Weisberg LS, Kurnik PB, Kurnik BR. Dopamine and renal blood flow in radiocontrast-induced nephropathy in humans. *Ren Fail.* 1993;15(1):61-8.
- ¹ Gare M, Haviv YS, Ben-Yehuda A, Rudinger D, Bdolah-Abram T, Fuchs S, Gat O, Popovtzer MM, Gotsman MS, Mossner M. The renal effect of low-dose dopamine in high risk patients undergoing coronary angiography. *J Am Coll Cardiol.* 1999 Nov 15;34(6):1682-8
- ¹ Diez T, Bagilet D, Damos M, Jolly H, Diab M, Marcucci R, Rojo L. Evaluation of two methods to avoid the nephropathy associated with radiologic contrast. *Medicina (B Aires).* 1999;59(1):55-8.

- ¹ Kappor A, Sinha N, Sharma RK, Shrivastava S, Radhakrishnan S, Goel PK, Bajaj R. Use of dopamine in prevention of contrast induced acute renal failure – A randomised study. *Int J Cardiol* 1996;53:233-236.
- 1 Murphy M B, Murray C, Shorten G. Fenoldopam – A selective peripheral dopamine-receptor agonist for the treatment of severe hypertension. *NEJM* 2001 November 22, Vol 345:1548-1557.
- 1 Mathur VS, Swan SK, Lambrecht LJ. The effects of fenoldopam, a selective dopamine receptor agonist, on systemic and renal hemodynamics in normotensive subjects. *Crit. Care Med* 1999; 27: 1832-1837.
- 1 Bakris GL, Lass NA, Glock D. Renal hemodynamics in radiocontrast medium-induced renal dysfunction: A role for dopamine-1 receptors. *Kidney Int*. 1999 Jul;56(1):206-10.
- 1 Kini AS, Mitre C, Kamran M, Suleman J, Kim M, Duffy M, Marmur JD, Sharma SK. Changing trends in incidence and predictors of radiographic contrast nephropathy after percutaneous coronary intervention with use of fenoldopam. *The American Journal of Cardiology*. 2002 April 15: 999-1002.
- 1 Madyoon H, Croushore L, Weaver D, Mathur V. Use of fenoldopam to prevent radiocontrasts nephropathy in high-risk patients. *Cath. Cardiovasc. Interv.* 2001; 53: 341-345.
- 1 Tumlin JA, Wang A, Murray PT, Mathur VS. Fenoldopam mesylate blocks reductions in renal plasma flow after radiocontrast dye infusion: A pilot trial in the prevention of contrast nephropathy. *Am. Heart J.* 2002; Vol 143, No 5:894-903.
- 1 Stone G, McCullough P, Tumlin J, Lepor N, Madyoon H, Murray P, Wang A, Chu AA, Schaer G, Stevens M, Wilensky R, O'Neill WW. A prospective, randomized Placebo-controlled multicenter trial evaluating fenoldopam mesylate for the prevention of contrast induced nephropathy: The CONTRAST Trial.
- 1 Kien N, Moore P, Jaffe R. Blood flow distribution during controlled hypotension induced by fenoldopam in anaesthetised dogs. *Anesth Analg* 1990; 70 S203.
- 1 Lapenna D, De Gioia S, Mezzetti A, Ciofani G, Fetsi D, Cuccurullo F. Aminophylline: could it act as an antioxidant in vivo? *Eur J Clin Invest* 1995;25:464-470.
- 1 Calhoun WJ, Stevens CA, Lambert SB,. Modulation of superoxide production of alveolar macrophages and peripheral blood mononuclear cells by beta-agonists and theophylline. *J Lab Clin Med*. 1991;117:514-522
- 1 Katholi RE, Taylor GJ, McCann WP, Woods WT, Womack KA, McCoy CD, Katholi CR, Moses HW, Mishkel GJ, Lucore CL, Holloway RM, Miller BD, Woodruff RC, Dove JT, Mikell FL, Schneider JA. Nephrotoxicity from contrast media: Attenuation with theophylline. *Radiology* 1995;195:17-22.
- 1 Kapoor A, Kumar S, Gulati S, Gambhir S, Sethu R, Sinha N. The role of theophylline in contrast-induced nephropathy: a case control study. *Nephrol Dial Transplant*. 2002;17:1936-1941
- 1 Erley CM, Duda S, Rehfuss D, Scholtes B, Bock J, Muller C, Osswald H, Risler T. Prevention of radiocontrast-media-induced nephropathy in patients with pre-existing renal insufficiency by hydration in combination with the adenosine antagonist theophylline. *Nephrol Dial Transplant* 1999;14:1146-1149.
- 1 Erley CM, Duda SH, Schlepkow S, Koehler J, Huppert PE, Strohmaier WL, Bohle A, Risler T, Osswald H. Adenosine antagonist theophylline prevents the reduction of glomerular filtration rate after contrast media application. *Kidney Int*. 1994;45(5):1425-1431.
- 1 Kolonko A, Wiecek A, Kokot F. The nonselective antagonist theophylline does prevent renal dysfunction induced by radiographic contrast agents. *J Nephrol*. 1998;11(3):151-156.
- 1 Shamas NW, Kapalis MJ, Harris M, McKinney D, Coyne EP. Aminophylline does not protect against radiocontrast nephropathy in patients undergoing percutaneous angiographic procedures. *J Invasive Cardiol*. 2001 Nov;13(11):738-40.
- 1 Abizaid A, Clark CE, Mintz GS, Dosa S, Pompa JJ, Pichard AD, Sattler LF, Harvey M, Kent KM, Leon MB. Effects of dopamine and aminophylline on contrast-induced acute renal failure after coronary angioplasty in patients with pre-existing renal insufficiency. *Am J Cardiol* 1999;83(Jan 15):260-263.
- 1 Huber W, Ilgmann K, Page M, Hennig M, Schweigart U, Jeschke B, Lutilsky, L, Weiss W, Salmhofer H, Classen M. Effect of theophylline on contrast material-induced nephropathy in patients with chronic renal insufficiency: Controlled, Randomized, Double-blinded Study. *Radiology* 2002;223:772-779.
- 1 Carraro M, Mancini W, Artero M, Stacul F, Grotto M, Cova M, Faccini L. Dose effect of nitrendipine on urinary enzymes and microproteins following non-ionic radiocontrast administration. *Nephrol Dial Transplant* 1996 Mar;11(3):444-8
- 1 Spangberg-Viklund B, Berglund J, Nikonoff T, Nyberg P, Skau T, Larsson R. Does prophylactic treatment with felodipine, a calcium antagonist, prevent low-osmolar contrast-induced renal dysfunction in hydrated diabetic and

nondiabetic patients with normal or moderately reduced renal function? Scand J Urol Nephrol 1996 Feb;30(1):63-8

1 Khoury Z, Schlicht JR, Como J, Karschner JK, Shapiro AP, Mook WJ, Weber RJ. The effect of prophylactic nifedipine on renal function in patients administered contrast media. Pharmacotherapy 1995 Jan-Feb;15(1):59-65

1 Neumayer HH, Junge W, Kufner A, Wenning A. Prevention of radiocontrast-media-induced nephrotoxicity by the calcium channel

blocker nitrendipine: a prospective randomised clinical trial. Nephrol Dial Transplant 1989;4(12):1030-6

1 Koch JA, Sketch M, Brinker J, Bernink PJ. Prostaglandin E1 for prevention of contrast medium-induced kidney dysfunction. Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr 1999 Jun;170(6):557-63

1 Koch JA, Plum J, Grabensee B, Modder U Prostaglandin E1: a new agent for the prevention of renal dysfunction in high

risk patients caused by radiocontrast media? PGE1 Study Group. Nephrol Dial Transplant 2000 Jan;15(1):43-9

1 Sketch MH Jr, Whelton A, Schollmayer E, Koch JA, Bernink PJ, Woltering F, Brinker J; Prostaglandin E1 Study Group. Prevention of contrast media-induced renal dysfunction with prostaglandin E1: a randomized, double-blind, placebo-controlled study. Am J Ther 2001 May-Jun;8(3):155-62

1 Kurnik BR, Allgren RL, Genter FC, Solomon RJ, Bates ER, Weisberg LS. Prospective study of atrial natriuretic peptide for the prevention of radiocontrast-induced nephropathy. Am J Kidney Dis 1998 Apr;31(4):674-80

1 Kurnik BR, Weisberg LS, Cuttler IM, Kurnik PB. Effects of atrial natriuretic peptide versus mannitol on renal blood flow during radiocontrast infusion in chronic renal failure. J Lab Clin Med 1990 Jul;116(1):27-36

