Hindawi Publishing Corporation
ISRN Stroke
Volume 2013, Article ID 704526, 6 pages
http://dx.doi.org/10.1155/2013/704526

Clinical Study

Computed Tomography Angiography before Intravenous Thrombolysis Does Not Increase the Risk of Renal Dysfunction

Pilar Sobrino García, Andrés García Pastor, Juan Pablo Cuello, Silvia Gil Navarro, Gema Vicente Peracho, Pedro María Rodriguez Cruz, Javier Ricardo Pérez Sánchez, Fernando Díaz Otero, Pilar Vázquez Alen, Jose Antonio Villanueva Osorio, and Antonio Gil Nuñez

Stroke Unit, Neurology Department, General University Hospital Gregorio Marañón, 46 Dr Esquerdo Street, 28007 Madrid, Spain

Correspondence should be addressed to Andrés García Pastor; angarpas@yahoo.es

Received 1 October 2013; Accepted 10 November 2013

Academic Editors: F. Corea, A. Ducruet, and R. Totaro

Our aim is to determine whether computed tomography angiography (CTA) before intravenous thrombolysis (IVT) affects renal function in acute ischemic stroke (AIS) patients. We performed an observational analysis of AIS patients treated with IVT for three years. Patients were classified into 2 groups: those who underwent CTA (CTA-group) and those who did not (control-group). Differences in creatinine levels between baseline and 24–72 hours after IVT were calculated. Acute renal dysfunction (ARD) was defined as an increase in serum creatinine level of ≥0.5 mg/dL and/or ≥25% above baseline within 24–72 hours after IVT. 190 patients were treated with IVT. Renal function (before and after IVT) was assessed in 162 (115 in control-group; 47 in CTA-group). Nine patients (5.5%) developed ARD (2 (4.2%) in CTA-group and 7 (6.1%) in control-group; $P = 0.6$). CTA was not associated with a higher risk of ARD and did not affect the efficacy or safety of IVT. Previous chronic renal insufficiency, baseline creatinine levels, and previous use of nonsteroidal anti-inflammatory drugs were associated with a significant increase in creatinine levels, independently of contrast use. In conclusion, CTA does not seem to increase the risk of renal dysfunction. This technique may be used safely without knowledge of baseline creatinine levels.

1. Introduction

Computed tomography angiography (CTA) is commonly used in patients with acute ischemic stroke (AIS) to diagnose cerebral arterial occlusion before thrombolysis. This technique makes it possible to identify intracranial and extracranial vascular stenoses or occlusions, which are a relevant prognostic factor indicating intra-arterial interventions such as thrombolysis or mechanical thrombectomy [2–4].

Computed tomography perfusion (CTP) has proven useful for assessing the extent of brain ischemia and for identifying "tissue at risk" that is potentially salvageable with recanalization. CTP also enables clinicians to optimize acute stroke therapy and to predict clinical outcome [5, 6].

The advantages of CTA and CTP over magnetic resonance-based techniques are that they are accessible in the emergency department, inexpensive, fast, and well tolerated. In addition, the spatial resolution of both techniques is high [6].

However, administration of nonionic contrast agents can lead to elevated serum creatinine levels, which are associated with poor outcome and increased mortality in patients with AIS [4, 7, 8], and contrast-induced nephropathy (CIN), which has been associated with higher morbidity and mortality in patients undergoing cardiovascular interventions [4, 9]. Mehran et al. [1] developed a risk score to predict CIN in patients undergoing percutaneous coronary intervention. However, data on CIN in patients with AIS are limited.

In many centres, CTA is only indicated after ruling out preexisting renal disease [10], since it has been identified as the main risk factor for CIN [11]. In some hospitals, CTA, CTP, and thrombolysis are administered without knowledge of baseline creatinine levels [4, 6] in order to avoid delays. The safety of such procedures is not well known.

The aims of our study were as follows: (1) to investigate whether CTA before intravenous thrombolysis (IVT) affects renal function in patients with AIS; (2) to identify factors that

can impair renal function; and (3) to determine whether the use of contrast agents interferes with the efficacy and safety of IVT.

2. Materials and Methods

We performed a retrospective observational analysis of a prospectively collected cohort of consecutive AIS patients treated with IVT and admitted to our stroke unit from January 2009 to December 2011.

Intravenous tissue plasminogen activator (tPA) was administered at a standard dose (0.9 mg/kg) according to recommendations for ischemic stroke treatment. Since the publication of the European Cooperative Acute Stroke Study III and data from the Safe Implementation of Treatment in Stroke registry, patients have been treated within the 4.5-hour time window [12, 13]. All patients or next of kin signed an informed consent document before IVT. Clinical data were included in a database approved by the local ethics committee.

Neurological examination and cranial CT scans were performed on admission in order to establish the stroke subtype and indication for treatment. Stroke severity was assessed at baseline according to the National Institutes of Health Stroke Scale (NIHSS). All evaluations were performed by NIHSS-certified neurologists. A posttreatment CT scan was performed after 24 hours or in cases of neurological deterioration.

We prospectively recorded the following parameters: (1) demographic data (age, gender); (2) vascular risk factors (e.g., history of hypertension, diabetes mellitus, dyslipidaemia, previous diagnosis of atrial fibrillation, previous diagnosis of congestive heart failure, smoking, previous diagnosis of chronic renal disease, and previous diagnosis of stroke); (3) previous treatments (antiplatelet therapy, anticoagulants, nonsteroidal anti-inflammatory drugs (NSAIDs), and metformin); (4) symptom onset-to-treatment time; (5) blood pressure on admission; (6) baseline NIHSS score; (7) laboratory parameters at baseline and within 24–72 hours after IVT (e.g., serum glucose, serum creatinine, serum nitrogen urea, C-reactive protein, hemoglobin, hematocrit, platelets, international normalised ratio, fibrinogen, and homocysteine).

CT studies were carried out using a multislice CT scanner (Toshiba Aquilion 64, Toshiba Medical Systems Corporation, Japan). CTA was performed using a low osmolar nonionic contrast agent (ioversol; Optiray 300 ultraject, Covidien Pharmaceuticals, Hazelwood, Missouri, USA). The dose of contrast agent was 80 mL for the circle of Willis study and 115 mL for the combined study of the circle of Willis and supra-aortic trunks. For CTP, we used 40 mL of nonionic contrast agent with a flow rate of 4 mL/sec. For conventional cerebral arteriography, the total dose of nonionic contrast agent was 150 mL. We did not apply any specific hydration protocol or specific management before or after contrast administration.

Patients were classified into 2 groups: the CTA group (patients who underwent CTA before IVT) and the control group (patients studied only with plain cranial CT). Performance of CTA depended on the availability of the technique and the advice of the physician attending to the patient at the time. All patients in the CTA group underwent CTA before baseline creatinine levels were available.

We calculated differences between creatinine levels at baseline (before CTA and IVT) and within 24–72 hours after IVT. Acute renal dysfunction (ARD) was defined as an increase in the serum creatinine level of ≥0.5 mg/dL and/or ≥25% above baseline within 24–72 hours after IVT [14]. We considered the patient to have CIN when ARD occurred after administration of the contrast agent [14].

The risk score for prediction of CIN developed by Mehran et al. [1] was calculated for patients in the CTA group. The score includes the following variables: hypotension after administration of the contrast agent (systolic blood pressure < 80 mmHg for at least 1 hour requiring inotropic medication) (score 5); intra-aortic balloon pump within 24 hours after administration of contrast agent (score 5); congestive heart failure ≥ NYHA III (score 5); age > 75 years (score 4); anemia (baseline hematocrit < 39% for men and <36% for women) (score 4); diabetes (score 3); contrast media volume > 100 cc (score 1 for each 100 cc); and serum creatinine >1.5 mg/dL (score 4). The risk of CIN is 7.5% when the total score is ≤5, 14% with a score of 6–10, 26.1% with a score of 11–16, and 57.3% with a score of >16.

The incidence of symptomatic intracerebral hemorrhage (SICH) according to the definition of the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) [15] and 3-month mortality was recorded. Functional outcome (rated using the modified Rankin scale) at 3 months was assessed. Favourable functional outcome was defined as a modified Rankin scale score of 0 or 2 at the 3-month visit.

The statistical analysis was performed using SPSS version 15.0. The results were expressed as proportions for categorical variables and as mean and standard deviation or median and interquartile range for continuous variables. Categorical variables were compared using the χ^2 test or 2-tailed Fisher exact test. Continuous variables were compared using a 2-sample t-test or the Mann-Whitney U test. A multiple linear regression analysis was performed to identify independent variables associated with an increase in creatinine levels. The adjusted R^2 was calculated to assess whether the independent variables were good predictors for the observed differences. For the comparison between the CTA group and the control group, P values were adjusted for age, history of diabetes, hypertension, previous diagnosis of chronic renal disease, baseline NIHSS score, previous use of metformin, and previous treatment with NSAIDs. P values < 0.05 were considered statistically significant.

3. Results

Between January 2009 and December 2011, we treated 190 AIS patients with IVT in our stroke unit. Baseline and control creatinine levels were determined in 162 patients. CTA was performed in 47 patients (29.6%), a circle of Willis study in 21 patients, a combined circle of Willis and supra-aortic trunk

Table 1: Patient characteristics in the CTA group and control group.

	Control group (n = 115)	CTA group (n = 47)	P
Age (y), mean (±SD)	71.5 (10.7)	65.3 (16.2)	0.05
Male sex, n (%)	63 (54.8)	29 (61.7)	0.4
History of diabetes, n (%)	28 (24.3)	11 (23.4)	0.9
History of hypertension, n (%)	70 (60.9)	30 (63.8)	0.7
History of chronic renal insufficiency, n (%)	8 (7)	1 (2.1)	0.2
Previous stroke, n (%)	10 (8.7)	2 (4.3)	0.3
Previous use of metformin, n (%)	20 (17.4)	8 (17)	0.9
Previous use of nonsteroidal anti-inflammatory drugs, n (%)	15 (13)	3 (6.4)	0.2
Baseline NIHSS score, median (IQR)	13 (8–17)	14 (7–18)	0.9
Baseline creatinine >1.5 mg/dL, n (%)	5 (4.3)	4 (8.5)	0.3
Baseline glucose levels (in mg/dL), mean (±SD)	132.3 (43.8)	136 (57.1)	0.6
Baseline creatinine levels (in mg/dL), mean (±SD)	0.99 (0.75)	0.93 (0.33)	0.5
Creatinine levels within 24–72 hours after IVT (in mg/dL), mean (±SD)	0.96 (0.90)	0.86 (0.32)	0.3
Risk score of CIN (Mehran et al.) [1], mean (±SD)	NA	5.6 (4)	NA
Total contrast dose (mL), mean (±SD)	NA	105.2 (33.4)	NA

CTA: computed tomography angiography; SD: standard deviation; NIHSS: National Institutes of Health Stroke Scale; IQR: interquartile range; IVT: intravenous thrombolysis; CIN: contrast-induced nephropathy; NA: not applicable.

CTA in 21 patients, a combination of CTP and circle of Willis and supra-aortic trunks CTA in 4 patients, and conventional cerebral arteriography following contrast-enhanced CT in 1 patient.

The characteristics of the patients in both groups are shown in Table 1. The distribution of risk factors and baseline parameters was similar, except for age: CTA patients were younger than control patients. Nine patients (5.5%) developed ARD, 7 patients (6.1%) in the control group and 2 patients (4.2%) in the CTA group ($P = 0.6$). No patients required dialysis.

CTA did not affect the risk of developing ARD or the probability of death, SICH, or favourable functional outcome at 3 months (Table 2).

The clinical and baseline characteristics of patients who developed ARD and patients who did not are compared in Table 3. Patients who developed ARD more frequently had a previous history of diabetes or chronic renal insufficiency, were more frequently exposed to NSAIDs, and presented higher baseline creatinine levels. Total contrast dose and risk score for CIN were not different between patients who developed nephropathy and patients who did not.

The univariate regression analysis revealed previous history of chronic renal insufficiency, baseline creatinine levels, and previous use of NSAIDs as predictors of increased creatinine at 24–72 hours. In a multiple regression model, history of chronic renal insufficiency, baseline creatinine levels, and previous use of NSAIDs remained significant ($F = 7.29$, adjusted $R^2 = 0.33$, $P < 0.001$) (Table 4).

4. Discussion

Our study evaluated the safety of performing CTA in patients with AIS treated with IVT before baseline creatinine levels are available. We found that CTA was not associated with a higher risk of developing ARD or with increased creatinine levels within 24–72 hours. These results did not change after adjustment for the most common predictors of ARD and increased creatinine levels.

Two patients out of 47 (4.2%) had CIN. In previous studies, CIN occurred in 2% to 5% of patients with AIS after administration of nonionic contrast agents, although no patients required dialysis or developed permanent kidney dysfunction [6, 10, 16]. In contrast, the incidence of CIN after percutaneous coronary intervention is much higher (13.1%, reaching 20–30% in high-risk patients) [9]. This difference could be because conditions associated with reduced kidney perfusion are more common in patients with coronary heart disease than in those with AIS. The risk score developed by Mehran et al. [1] has proven to be an accurate tool for predicting CIN. However, the risk score of the 2 patients with CIN in our study was low, as observed elsewhere [17]. This finding may be because the score comprises variables frequently observed in patients with coronary heart disease (e.g., hypotension, intra-aortic balloon pump, congestive heart failure, and anemia), although these variables are rarely present in AIS patients. Therefore, the risk score developed by Mehran et al. may not be useful for predicting CIN in patients with AIS.

The difference in the incidence of CIN between patients with AIS and patients with coronary heart disease could be due to the higher volume of contrast media used in patients undergoing cardiac interventions (usually >150 mL) [1] than in patients with AIS [4].

We found that variables other than exposure to contrast agents (e.g., history of chronic renal insufficiency, baseline creatinine levels, and previous use of NSAIDs) predicted an increase in creatinine levels within 24–72 hours. A previous study identified baseline creatinine levels and baseline C-reactive protein as predictors of increased creatinine levels independently of CTA in patients with AIS [4]. The acute

Table 2: Risk for ARD, SICH, mortality, and favourable functional outcome in patients who underwent computed tomography angiography.

	Unadjusted	P	Adjusted	P^*
Acute renal dysfunction, OR (95% CI)	0.69 (0.14–3.43)	0.60	0.88 (0.14–5.39)	0.89
Symptomatic intracerebral hemorrhage, OR (95% CI)	1.84 (0.55–6.1)	0.30	1.39 (0.28–6.93)	0.69
Mortality, OR (95% CI)	1.08 (0.41–2.83)	0.87	0.63 (0.19–2.08)	0.45
mRS score at 3 months ≤2, OR (95% CI)	1.06 (0.54–2.09)	0.86	1.05 (0.46–2.39)	0.90

OR: odds ratio; CI: confidence interval; mRS: modified Rankin scale.
*Adjusted for age, history of diabetes, hypertension, previous diagnosis of chronic renal disease, baseline National Institutes of Health Stroke Scale score, and previous treatment with nonsteroidal anti-inflammatory drugs.

Table 3: Patient characteristics according to the presence or absence of acute renal dysfunction.

	No acute renal dysfunction (n = 153)	Acute renal dysfunction (n = 9)	P
Age, mean (±SD)	69.9 (12.9)	66.1 (10.9)	0.4
Male sex, n (%)	87 (56.9)	5 (55.6)	0.9
History of diabetes, n (%)	34 (22.2)	5 (55.6)	0.02
History of hypertension, n (%)	92 (60.1)	8 (88.9)	0.08
History of chronic renal insufficiency, n (%)	6 (3.9)	3 (33.3)	<0.001
Previous stroke, n (%)	10 (6.5)	2 (22.2)	0.08
Previous use of metformin, n (%)	25 (16.3)	3 (33.3)	0.2
Previous use of nonsteroidal anti-inflammatory drugs, n (%)	15 (9.8)	3 (33.3)	0.03
Baseline NIHSS score, median (IQR)	14 (8–17.5)	13 (7–16.5)	0.4
Baseline creatinine >1.5 mg/dL, n (%)	7 (4.6)	2 (22.2)	0.02
Baseline glucose levels (in mg/dL), mean (±SD)	131.7 (42.2)	160.7 (106.2)	0.08
Baseline creatinine levels (in mg/dL), mean (±SD)	0.94 (0.3)	1.67 (2.5)	0.001
Creatinine levels within 24–72 hours after IVT (in mg/dL), mean (±SD)	0.85 (0.31)	2.16 (2.92)	<0.001
Performance of CTA, n (%)	45 (29.4)	2 (22.2)	0.6
Risk score of CIN (Mehran et al.) [1], mean (only applicable in CTA group)	5.6 (4.1)	6.5 (2.1)	0.7
Total contrast dose (mL), mean (±SD) (only applicable in CTA group)	104.8 (34.1)	115 (0)	0.68

SD: standard deviation; NIHSS: National Institutes of Health Stroke Scale; IQR: interquartile range; IVT: intravenous thrombolysis; CTA: computed tomography angiography; CIN: contrast-induced nephropathy.

Table 4: Univariate and multivariate linear regression analyses to predict creatinine increase in 24–72 hours compared with baseline.

	Univariate analysis		Multivariate analysis	
	Standardised coefficient	P	Standardised coefficient	P
Age	−0.097	0.22		
Male sex	0.081	0.30		
History of diabetes	0.071	0.37		
History of hypertension	0.02	0.78		
History of chronic renal insufficiency	0.41	<0.001	0.20	0.01
Previous stroke	0.05	0.56		
Use of metformin	−0.038	0.64		
Baseline glucose levels	−0.04	0.62		
Baseline NIHSS score	−0.092	0.25		
Baseline creatinine	0.46	<0.001	0.30	<0.001
Baseline systolic blood pressure	−0.022	0.78		
Use of nonsteroidal anti-inflammatory drugs	0.29	<0.001	0.19	0.008
CTA performance	−0.081	0.31		
Risk score of CIN (Mehran et al.) [1]	−0.175	0.24		
Contrast dose	−0.191	0.19		

NIHSS: National Institutes of Health Stroke Scale; CTA: computed tomography angiography; CIN: contrast-induced nephropathy.

nephrotoxicity of NSAIDs is well known and seems to affect elderly patients with coexisting renal disease receiving concomitant treatments (especially antihypertensive drugs) [18].

Multiple predisposing risk factors for the development of CIN have been identified. The most important predictor of CIN is a history of chronic kidney disease, which has a reported incidence of up to 50% in patients with advanced chronic kidney disease [4, 6, 19–21]. Another important predictor is a history of diabetes, which is mostly attributable to diabetic nephropathy [6, 21]. Some studies suggested that the risk of CIN increased with higher doses of contrast agent [22–24]. In AIS patients, NIHSS scores ≥ 15 seem to increase the risk for CIN [25].

In our study, CTA did not affect mortality, the rate of SICH, or functional outcome. Previous experimental studies reported that contrast agents could disrupt the blood-brain barrier; this finding has been associated with an increased risk of SICH in patients with AIS treated with IVT [4, 26]. We did not find differences in the SICH rate between the CTA group and the control group. Similar results have been reported elsewhere [4]. Our results imply that contrast agents probably do not interfere with the safety and efficacy of IVT.

There are several limitations to our study. First, its retrospective nonrandomized design may have produced selection biases in the CTA group; CTA performance could have been avoided in patients with extremely elevated baseline creatinine levels. However, the proportion of patients with creatinine levels >1.5 mg/dL was higher in the CTA group than in the control group (8.5% Versus 4.3%). Also, CTA group patients were younger than the control patients, but in the multivariate analysis age did not affect creatinine levels within 24–72 hours. Second, it has a small sample size, with a low proportion of patients baseline creatinine levels >1.5 mg/dL ($n = 9$), which restricted the statistical power to detect small differences in this subgroup. Third, the study was performed at a single centre; therefore, CTA study protocol, contrast agent, and doses may not be generalized for other institutions. The main strengths of our study are that CTA was always performed without knowledge of baseline creatinine levels and that the CTA group and control group were evaluated simultaneously: in contrast with other studies, we did not use a historical control group [4, 27].

In conclusion, our study showed that performing a CTA in AIS patients without knowledge of their baseline creatinine levels is not associated with an increased risk of developing ARD or elevated creatinine levels within 24–72 hours. However, a history of chronic renal insufficiency, baseline creatinine levels, and previous use of NSAIDs were associated with a significant increase in creatinine levels within 24–72 hours, independent of the use of contrast agents. Moreover, CTA did not affect the probability of death, SICH, or favourable functional outcome at 3 months and, therefore, did not interfere with the safety and efficacy of IVT.

References

[1] R. Mehran, E. D. Aymong, E. Nikolsky et al., "A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation," *Journal of the American College of Cardiology*, vol. 44, no. 7, pp. 1393–1399, 2004.

[2] W. S. Smith, H. C. Roberts, N. A. Chuang et al., "Safety and feasibility of a CT protocol for acute stroke: combined CT, CT angiography, and CT perfusion imaging in 53 consecutive patients," *American Journal of Neuroradiology*, vol. 24, pp. 688–690, 2003.

[3] J. R. Sims, G. Rordorf, E. E. Smith et al., "Arterial occlusion revealed by CT angiography predicts NIH stroke score and acute outcomes after IV tPA treatment," *American Journal of Neuroradiology*, vol. 26, no. 2, pp. 246–251, 2005.

[4] P. Aulický, R. Mikulík, D. Goldemund, M. Reif, M. Dufek, and T. Kubelka, "Safety of performing CT angiography in stroke patients treated with intravenous thrombolysis," *Journal of Neurology, Neurosurgery and Psychiatry*, vol. 81, no. 7, pp. 783–787, 2010.

[5] S. P. Kloska, R. Dittrich, T. Fischer et al., "Perfusion CT in acute stroke: prediction of vessel recanalization and clinical outcome in intravenous thrombolytic therapy," *European Radiology*, vol. 17, no. 10, pp. 2491–2498, 2007.

[6] J. J. Hopyan, D. J. Gladstone, G. Mallia et al., "Renal safety of CT angiography and perfusion imaging in the emergency evaluation of acute stroke," *American Journal of Neuroradiology*, vol. 29, no. 10, pp. 1826–1830, 2008.

[7] R. S. MacWalter, S. Y. S. Wong, K. Y. K. Wong et al., "Does renal dysfunction predict mortality after acute stroke? A 7-year follow-up study," *Stroke*, vol. 33, no. 6, pp. 1630–1635, 2002.

[8] Z. Hao, B. Wu, S. Lin et al., "Association between renal function and clinical outcome in patients with acute stroke," *European Neurology*, vol. 63, no. 4, pp. 237–242, 2010.

[9] P. J. M. Best, R. Lennon, H. H. Ting et al., "The impact of renal insufficiency on clinical outcomes in patients undergoing percutaneous coronary interventions," *Journal of the American College of Cardiology*, vol. 39, no. 7, pp. 1113–1119, 2002.

[10] A. L. Krol, I. Dzialowski, J. Roy et al., "Incidence of radiocontrast nephropathy in patients undergoing acute stroke computed tomography angiography," *Stroke*, vol. 38, no. 8, pp. 2364–2366, 2007.

[11] N. Pannu, N. Wiebe, and M. Tonelli, "Prophylaxis strategies for contrast-induced nephropathy," *Journal of the American Medical Association*, vol. 295, no. 23, pp. 2765–2779, 2006.

[12] W. Hacke, M. Kaste, E. Bluhmki et al., "Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke," *The New England Journal of Medicine*, vol. 359, no. 13, pp. 1317–1329, 2008.

[13] N. Wahlgren, N. Ahmed, A. Dávalos et al., "Thrombolysis with alteplase 3-4·5 h after acute ischaemic stroke (SITS-ISTR): an observational study," *The Lancet*, vol. 372, no. 9646, pp. 1303–1309, 2008.

[14] M. Tepel, P. Aspelin, and N. Lameire, "Contrast-induced nephropathy: a clinical and evidence-based approach," *Circulation*, vol. 113, no. 14, pp. 1799–1806, 2006.

[15] N. Wahlgren, N. Ahmed, A. Dávalos et al., "Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study," *The Lancet*, vol. 369, pp. 275–282, 2007.

[16] A. Oleinik, J. M. Romero, K. Schwab et al., "CT angiography for intracerebral hemorrhage does not increase risk of acute nephropathy," *Stroke*, vol. 40, no. 7, pp. 2393–2397, 2009.

[17] R. Dittrich, S. Akdeniz, S. P. Kloska et al., "Low rate of contrast-induced Nephropathy after CT perfusion and CT angiography

in acute stroke patients," *Journal of Neurology*, vol. 254, no. 11, pp. 1491–1497, 2007.

[18] M. Musu, G. Finco, R. Antonucci et al., "Acute nephrotoxicity of NSAID from the foetus to the adult," *European Review for Medical and Pharmacological Sciences*, vol. 15, no. 12, pp. 1461–1472, 2011.

[19] I. Goldenberg and S. Matetzky, "Nephropathy induced by contrast media: pathogenesis, risk factors and preventive strategies," *Canadian Medical Association Journal*, vol. 172, no. 11, pp. 1461–1471, 2005.

[20] E. M. Lautin, N. J. Freeman, A. H. Schoenfeld et al., "Radiocontrast-associated renal dysfunction: incidence and risk factors," *American Journal of Roentgenology*, vol. 157, no. 1, pp. 49–58, 1991.

[21] S. D. Weisbord and P. M. Palevsky, "Radiocontrast-induced acute renal failure," *Journal of Intensive Care Medicine*, vol. 20, no. 2, pp. 63–75, 2005.

[22] P. A. McCullough, R. Wolyn, L. L. Rocher, R. N. Levin, and W. W. O'Neill, "Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality," *American Journal of Medicine*, vol. 103, no. 5, pp. 368–375, 1997.

[23] C. S. Rihal, S. C. Textor, D. E. Grill et al., "Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention," *Circulation*, vol. 105, no. 19, pp. 2259–2264, 2002.

[24] R. V. Freeman, M. O'Donnell, D. Share et al., "Nephropathy requiring dialysis after percutaneous coronary intervention and the critical role of an adjusted contrast dose," *American Journal of Cardiology*, vol. 90, no. 10, pp. 1068–1073, 2002.

[25] O. Mir, T.-C. Wu, D. S. Canseco, H. Peng, J. C. Grotta, and S. Savitz, "Contrast induced nephropathy is associated with poor outcomes in IV-tPA treated patients," *Stroke*, vol. 43, Article ID A2696, 2012.

[26] N. Hjort, O. Wu, M. Ashkanian et al., "MRI detection of early blood-brain barrier disruption: parenchymal enhancement predicts focal hemorrhagic transformation after thrombolysis," *Stroke*, vol. 39, no. 3, pp. 1025–1028, 2008.

[27] F. O. Lima, M. H. Lev, R. A. Levy et al., "Functional contrast-enhanced CT for evaluation of acute ischemic stroke does not increase the risk of contrast-induced nephropathy," *American Journal of Neuroradiology*, vol. 31, no. 5, pp. 817–821, 2010.