Incidence of Acute Kidney Injury After Computed Tomography Angiography±Computed Tomography Perfusion Followed by Thrombectomy in Patients With Stroke Using a Postprocedural Hydration Protocol

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Background—The risk of contrast-induced acute kidney injury (AKI) in patients with stroke receiving both computed tomography (CT) angiography and mechanical thrombectomy has been investigated only in small case series. No studies have investigated whether additional CT perfusion or chronic kidney disease (CKD) are associated with higher rates of AKI.

Methods and Results—Retrospective analysis of the AKI incidence in 1089 consecutive patients receiving CT angiography and mechanical thrombectomy from 2015 to 2017 and in subgroups with CKD (n=99) and CT perfusion (n=104) was performed. Patients received a standardized hydration protocol. Data on kidney function after mechanical thrombectomy were available in 1017 patients. A total of 59 (5.8%) patients developed AKI, and only 4 (6.8%) patients needed hemodialysis, all with known CKD. Patients with AKI significantly more often had known CKD (20.3% versus 8.4%, P=0.002), diabetes mellitus (33.9% versus 20.9%, P=0.018), and tandem occlusion (32.2% versus 16.2%, P=0.003) and a significantly higher in-hospital mortality (20.3% versus 7.0%, P<0.001) compared with patients without AKI. However, there were no significant independent predictors for AKI in multivariable logistic regression analysis. Sex (odds ratio [OR], 2.03; 95% CI, 1.17–3.52 [P=0.012]), higher National Institutes of Health Stroke Scale (OR, 1.10; 95% CI, 1.05–1.14 [P<0.001]), AKI (OR, 3.52; 95% CI, 1.63–7.64 [P=0.001]), diuretic use (OR, 1.80; 95% CI, 1.02–3.19), futile or incomplete recanalization (OR, 0.19; 95% CI, 0.09–0.40 [P<0.001]), and total volume of contrast agent volume (OR, 1.007; 95% CI, 1.002–1.011 [P=0.004]) were independently associated with in-hospital death. Two thirds of the patients with AKI died of severe brain damage and not AKI itself.

Conclusions—Post-contrast AKI rarely occurs in patients with stroke receiving a contrast agent for CT angiography/CT perfusion and subsequent mechanical thrombectomy. Patients with known CKD had higher rates of AKI and only these patients needed hemodialysis, but CKD was not independently associated with AKI or in-hospital mortality. (*J Am Heart Assoc.* 2020;9:e014418. DOI: 10.1161/JAHA.119.014418.)

Key Words: acute kidney injury • computed tomography angiography • computed tomography perfusion • contrast agent • ischemic stroke • thrombectomy

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Contrast-associated acute kidney injury (AKI) is characterized by a decrease in kidney function that occurs within days after intravascular administration of an iodinated

contrast agent.[1] Incidence of contrast-associated AKI in hospitalized patients is high and related to increased mortality.[2,3] In a systematic review and meta-analysis including 14 studies with 5727 patients with acute ischemic stroke (AIS) receiving computed tomography (CT) angiography (CTA) and/or computed tomography perfusion (CTP) and 981 patients with AIS receiving nonenhanced CT, contrast administration was not associated with a statistically significant increased risk of AKI.[4] The overall rate of AKI in patients with CTA/CTP was 3% (95% CI, 2%–4%), and hemodialysis had to be performed in only 0.07%.[4] Advanced CT of the brain with CTA and CTP is now increasingly used to detect large vessel occlusion (LVO) in patients with AIS up to 24 hours after symptom onset to identify candidates for mechanical thrombectomy (MT).[5] During the MT procedure, patients with AIS receive additional intra-arterial contrast agent for digital

Clinical Perspective

What Is New?

- Using a standardized hydration protocol with Ringer solution, acute kidney injury rarely occurred after intravenous and intra-arterial iodinated contrast application for computed tomography angiography/perfusion and mechanical thrombectomy in patients with acute ischemic stroke and large vessel occlusion.
- Additional computed tomography perfusion did not increase the incidence of post-contrast acute kidney injury.
- Patients with known chronic kidney disease had significantly higher rates of post-contrast acute kidney injury and only these patients needed transient hemodialysis.

What Are the Clinical Implications?

- Fear of post-contrast AKI should not result in delay or omission of diagnostic computed tomography angiography and computed tomography perfusion imaging, or the endovascular procedure itself, in patients with stroke with large vessel occlusion.
- Kidney function in patients with stroke with known chronic kidney disease should be closely monitored after mechanical thrombectomy.

subtraction angiography dependent on procedure time. It is generally believed that intra-arterial administration of a contrast agent with second-pass renal exposure has a higher risk of AKI than venous CTA/CTP, and that repeated administration of a contrast agent with higher volumes is also associated with an increased AKI risk.[1,6] Furthermore, pre-existing chronic kidney disease (CKD) was the strongest patient-related risk factor for developing AKI in patients undergoing percutaneous coronary intervention.[7,8] As a consequence, CTA/CTP might be postponed until laboratory information of kidney function is available, resulting in a delay of the MT procedure, or CTA/CTP and MT might not be performed in patients with AIS with known CKD.

To date, incidence of contrast-associated AKI in patients with AIS receiving CTA followed by MT has been investigated in only 3 small case series with a combined total of fewer than 250 patients.[9–11] No studies have systematically investigated whether endovascular-treated patients with AIS receiving additional CTP or with pre-existing CKD have higher rates of AKI. We therefore assessed the incidence of post-contrast AKI in 1089 consecutive patients with AIS who received CTA±CTP and MT, followed by a standardized hydration protocol with physiological Ringer solution, at our large tertiary neurovascular center over a period of 3 years.

Methods

All data that support the findings of this study are available from the corresponding author upon reasonable request. We conducted a retrospective chart review in all consecutive patients with AIS undergoing MT after CTA/CTP at our tertiary neurovascular center from January 2015 to December 2017. The study was approved by the local ethics committee of the University Duisburg-Essen and consent requirement was waived.

Demographic and baseline characteristics including age, sex, cardiovascular risk factors (arterial hypertension, diabetes mellitus, current smoking), pre-stroke treatment with diuretics and angiotensin-converting enzyme inhibitors, known CKD (defined as a history of CKD using the Kidney Disease: Improving Global Outcomes [KDIGO] criteria by chart review[12]), prior dialysis, baseline serum creatinine value before CTA/CTP, referral status, bridging intravenous thrombolysis (IVT), stroke severity at admission in our neurovascular center using the National Institutes of Health Stroke Scale (NIHSS), and arterial occlusion site were assessed.

Contrast Agent for Imaging and Hydration Protocol

For CTA of the head and neck, 60 mL to 100 mL of non-ionic iodinated contrast agent (Accupaque 300 or 350 [GE Healthcare] and Imeron 300 or 400 [Bracco Imaging]) was injected depending on local protocols, and for CTP an additional 40 mL of Accupaque 300 was injected. Periprocedural MT variables included x-ray exposure time, volume of intra-arterial-administered non-ionic iodinated contrast agent used during MT procedure (Visipaque 270 [GE Healthcare], in 50 mL steps), and rate of successful recanalization, defined as a thrombolysis in cerebral infarction score of 2b or 3. Total volume of contrast agent used for CTA, CTP, and MT in milliliters was calculated in each individual patient. Control CT of the brain was routinely performed between 20 and 30 hours after MT procedure or immediately in case of clinical worsening. Symptomatic intracranial hemorrhage (SICH) was defined as intracranial hemorrhage seen on brain imaging associated with an increase of ≥ 4 points on the NIHSS.

After the MT procedure, all patients were kept under continuous medical surveillance in the stroke or intensive care unit of our neurovascular center for at least 48 hours and received a standardized hydration protocol with continuous intravenous infusion of Ringer solution at an infusion rate of 80 mL per hour (Jonosteril 1/1 E, Fresenius Kabi).

Statistical Analysis

The incidence of contrast-mediated, postprocedural contrast AKI in patients undergoing CTA/CTP and subsequent MT was

the primary study objective. Post-contrast AKI was defined as an increase of serum creatinine $\geq$25% or $\geq$0.5 mg/dL from baseline at 1 of the following 5 days after the MT procedure.[13] We dichotomized the study cohort in patients with AIS who developed AKI and those who had unchanged kidney function after MT procedure. Furthermore, we compared the incidence of AKI in subgroups of patients with AIS with and without known CKD, and between patients receiving combined CTA/CTP and those receiving only CTA before MT. NIHSS at discharge from our neurovascular center (to home, rehabilitation facility, or back to the primary referring neurological hospital) and in-hospital mortality were assessed. The cause of in-hospital death was judged by an experienced stroke neurologist (R.W.).

Groups were compared using Mann-Whitney U test or chi-square test, as appropriate. Univariable logistic regression analyses for the primary outcome parameter post-contrast AKI and the secondary outcome parameter in-hospital death were performed using each of the variables age, sex, referral status, history of hypertension, history of diabetes mellitus, current smoker, known CKD, angiotensin-converting enzyme inhibitor use, diuretic use, bridging IVT, CTP use, serum creatinine $\geq$1.2 mg/dL at baseline, NIHSS at baseline, total contrast agent volume used for CTA, CTP and digital subtraction angiography, contrast agent volume $\geq$150 mL during MT procedure, successful recanalization, and AKI (only for in-hospital mortality). Covariables with $P<0.2$ in the univariable analysis were included in multivariable logistic regression analysis to identify independent predictors for AKI and in-hospital death (model 1). We additionally forced CTP use and known CKD (both with $P>0.2$ in univariable analysis) in a second multivariable logistic regression model. All statistical analyses were performed with SPSS (version 21.0, IBM).

Results

A total of 1089 patients with AIS received CTA$\pm$CTP before MT for large vessel occlusion in the anterior or posterior circulation at our tertiary neurovascular center from January 2015 to December 2017. The mean age was 72.9 ($\pm$13.1) years, 51.9% of the patients were women, and the median NIHSS at admission was 13 (interquartile range, 7–18). CTA alone was performed in 985 (90.4%) patients before the MT procedure, while 104 (9.6%) patients received multimodal imaging with both CTA and CTP. The majority of patients were secondarily referred for MT (84.4%), and bridging IVT before MT was performed in 467 (43%) patients. Ninety-nine (9.1%) patients had known CKD, and 259 (23.8%) patients had a serum creatinine $\geq$1.2 mg/dL at baseline.

All MT procedures were performed under general anesthesia. The median intra-arterial contrast agent volume administered during the MT procedure was 100 mL (interquartile range, 100–150 mL; maximum volume, 600 mL). Data on kidney function after CTA$\pm$CTP and the MT procedure were available in 1017 (93.4%) patients. Of these, 59 (5.8%) patients developed AKI, 4 (0.4%) of whom needed transient hemodialysis. All 4 patients who needed transient hemodialysis had known CKD and functionally improved after stroke treatment and hemodialysis.

Patients with AKI significantly more often had known CKD ($P=0.002$) and diabetes mellitus ($P=0.018$) and received MT for tandem occlusion of the internal carotid and middle cerebral artery ($P=0.003$) (Table 1). There were no significant differences in age, sex, bridging IVT, referral status, rate of arterial hypertension, current smoking, use of diuretics or angiotensin-converting enzyme inhibitors at admission, additional CTP performed, volume of contrast media used for MT, and successful recanalization between patients with and without AKI (Table 1). The total volume of iodinated contrast agent for CTA, CTP, and MT also did not significantly differ between patients with and without AKI (190$\pm$60 mL versus 190$\pm$53 mL, $P=0.275$) (Table 1). Incidence of AKI did not differ significantly between patients with AIS receiving $\geq$150 mL of the contrast agent volume during the MT procedure and patients receiving <150 mL (6.1% versus 5.8%, $P=0.834$) (Table 1).

The rate of SICH was not significantly different between patients with (4/59, 6.8%) and without AKI (35/958, 3.7%; $P=0.460$). The medium NIHSS at discharge was nonsignificantly higher in patients with AKI (median 6 versus 4, $P=0.052$). In-hospital mortality was significantly higher in patients with AKI (12/59 [20.3%] versus 67/958 [7.0%], $P<0.001$).

NIHSS at admission, arterial hypertension, diabetes mellitus, contrast agent use $\geq$150 mL for MT, and total volume of contrast agent volume used for CTA, CTP, and MT were variables with a $P<0.2$ according to the univariable analysis for AKI. Sex, NIHSS at admission, AKI, prior use of diuretics, futile recanalization, and total volume of contrast agent volume used for CTA, CTP, and MT had a $P<0.2$ in the univariable analysis for in-hospital death.

There were no statistically significant independent predictors for AKI in multivariable logistic regression analysis model 1 (Table 2) and model 2 with the additional covariables of known CKD and CTP (Table 3). Sex (odds ratio [OR], 2.03; 95% CI, 1.17–3.52 [$P=0.012$]), higher NIHSS at admission (OR, 1.10; 95% CI, 1.05–1.14 [$P<0.001$]), AKI (OR, 3.52; 95% CI, 1.63–7.64 [$P=0.001$]), prior use of diuretics (OR, 1.80; 95% CI, 1.02–3.19), futile or incomplete

Table 1. Comparison of Patient Characteristics and Procedural and Outcome Parameters in Patients With and Without AKI

	Patients With AKI After MT	Patients Without AKI After MT	P Value
Age, y, mean (SD, minimum–maximum)	72.7 (13.4, 28–91)	72.8 (13.0, 14–98)	0.891
Men, No. (%)	29 (49.2)	459 (47.8)	0.836
Bridging IVT, No. (%)	23 (39.7)	420 (43.9)	0.329
Secondarily referred, No. (%)	48 (81.4)	828 (86.2)	0.305
NIHSS at admission, median (IQR)	14 (8–19)	13 (7–18)	0.304
Arterial hypertension, No. (%)	49 (83.1)	724 (75.4)	0.184
Current smoker, No. (%)	8 (13.6)	137 (14.3)	0.872
Diabetes mellitus, No. (%)	20 (33.9)	200 (20.9)	0.018*
Diuretics at admission, No. (%)	21 (36.2)	288 (30.5)	0.365
ACEI use at admission, No. (%)	22 (37.9)	307 (32.7)	0.410
Known CKD, No. (%)	12 (20.3)	81 (8.4)	0.002*
Occlusion site, No. (%)			
MCA	25 (42.4)	549 (57.2)	0.003*
Terminal ICA (carotid T)	4 (6.8)	144 (15.0)	
Proximal ICA±MCA	19 (32.2)	155 (16.2)	
ACA	1 (1.7)	9 (0.9)	
BA	5 (8.5)	67 (7.0)	
VA	0 (0)	9 (0.9)	
PCA	1 (1.7)	10 (1.0)	
CT perfusion, No. (%)	6 (10.2)	81 (8.4)	0.646
Blood creatinine at admission, mg/dL, median (IQR)	1.03 (0.84–1.37)	0.98 (0.80–1.20)	0.079
Total contrast volume, mL, mean (SD, IQR)	190 (60, 178–230)	190 (53, 175–230)	0.275
Volume of contrast agent for MT, mL, median (IQR)	100 (100–150)	100 (100–150)	0.752
Volume of contrast agent during MT ≥150 mL, No. (%)	19 (32.8)	293 (31.4)	0.834
Successful recanalization, TICI 2b/3, No. (%)	54 (91.5)	901 (94.3)	0.369
New dialysis after MT, No. (%)	4 (6.8)	0 (0)	<0.001*
Symptomatic ICH, No. (%)	4 (6.8)	35 (3.7)	0.460
NIHSS at discharge, median (IQR)	6 (2–11)	4 (1–10)	0.052
In-hospital mortality, No. (%)	12 (20.3)	67 (7.0)	<0.001*

ACA indicates anterior cerebral artery; ACEI, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; BA, basilar artery; CKD, chronic kidney disease; CT, computed tomography; ICA, internal carotid artery; ICH, intracranial hemorrhage; IQR, interquartile range; IVT, intravenous thrombolysis; MCA, middle cerebral artery; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; PCA, posterior cerebral artery; TICI, thrombolysis in cerebral infarction; VA, vertebral artery.
*Significant P values.

recanalization (OR, 0.19; 95% CI, 0.09–0.40 [P<0.001]), and total volume of contrast agent volume in milliliters used for CTA, CTP, and MT (OR, 1.007; 95% CI, 1.002–1.011 [P=0.004]) were independent predictors for in-hospital death in both multivariable logistic regression analysis models (Tables 2 and 3; given ORs and 95% CIs for model 2). Known CKD (OR, 1.92; 95% CI, 0.91–4.07 [P=0.087]) and additional use of CTP (OR, 0.95; 95% CI, 0.38–2.37 [P=0.919]) were not significantly independently associated with in-hospital mortality (Table 3).

Nine of the 12 (75%) patients in the AKI group were judged to have died from their malignant media or brainstem infarction (n=6) or SICH (n=3), and not the AKI itself. NIHSS at 24 hours in these 9 patients ranged from 18 and 31 points, 7 seven of these 9 patients had combined internal carotid artery (ICA)/middle cerebral artery (MCA) or MCA/anterior cerebral artery (ACA) occlusion. Death in 3 patients was judged to be possibly related to AKI, and 1 of them had additional rhabdomyolysis with crush kidney syndrome after 2 days of lying in front of her

Table 2. Multivariable Regression Analysis for AKI and In-Hospital Death for all Covariables With *P*<0.2 in Univariable Analysis (Model 1)

	AKI, OR (95% CI)	P Value	In-Hospital Death, OR (95% CI)	P Value
Sex	. . .	. . .	2.04 (1.18–3.53)*	0.011*
NIHSS at admission	1.03 (0.99–1.08)	0.094	1.10 (1.06–1.14)*	<0.001*
Arterial hypertension	1.73 (0.78–3.85)	0.176	. . .	. . .
Diabetes mellitus	1.73 (0.94–3.18)	0.076	. . .	. . .
AKI	N/A	N/A	3.59 (1.65–7.78)*	0.001*
Diuretics use	. . .	. . .	2.01 (1.16–3.49)*	0.013*
Successful recanalization	. . .	. . .	0.18 (0.09–0.38)*	<0.001*
Contrast agent ≥150 mL for DSA	0.60 (0.23–1.52)	0.280	. . .	. . .
Total contrast agent volume	1.006 (0.999–1.013)	0.109	1.006 (1.002–1.011)*	0.005*

AKI indicates acute kidney injury; DSA, digital subtraction angiography; N/A, not applicable; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio.
*Significant covariables.

bed after a fall. One patient with AKI died as a result of sepsis.

Subgroup Analysis

Ninety-nine patients had known CKD at baseline. Patients with known CKD were significantly older (77.4 versus 72.4 years, *P*<0.001), more often had diabetes mellitus (36.4% versus 21.2%, *P*=0.001), more often used diuretics at admission (64.9% versus 28.3%), and less often received bridging IVT (28.6% versus 44.4%, *P*=0.014), while other baseline characteristics did not significantly differ. The incidence of AKI in patients with known CKD was significantly higher (12.9% versus 5.1%, *P*=0.002), and all 4 patients who received new transient dialysis after MT had known CKD (*P*<0.001). While there were no significant differences in the rate of SICH (5.2% versus 3.8%, *P*=0.719) and median NIHSS at discharge (median 4.5 versus 4, *P*=0.355) between patients with and without known CKD, in-hospital mortality was significantly higher in patients with known CKD (15.2% versus 8.0%, *P*=0.016).

Patients with AIS who received additional CTP were significantly more often primarily admitted to our institution (*P*<0.001) and treated thereafter with direct MT without

Table 3. Multivariable Regression Analysis Model for the Incidence of AKI and In-Hospital Death for Covariables With *P*<0.2 in Univariable Analysis and the Covariables Known CKD and Use of CT Perfusion (Model 2)

	AKI, OR (95% CI)	P Value	In-Hospital Death, OR (95% CI)	P Value
Sex	. . .	. . .	2.03 (1.17–3.52)*	0.012*
NIHSS at admission	1.03 (0.99–1.08)	0.107	1.10 (1.05–1.14)*	<0.001*
Diabetes mellitus	1.65 (CI 0.90–3.04)	0.107	. . .	. . .
Arterial hypertension	1.72 (0.77–3.83)	0.183	. . .	. . .
AKI	N/A	N/A	3.52 (1.63–7.64)*	0.001*
Diuretics use	. . .	. . .	1.80 (1.02–3.19)*	0.043*
Successful recanalization	. . .	. . .	0.19 (0.09–0.40)*	<0.001*
Contrast agent ≥150 mL for DSA	0.55 (0.21–1.45)	0.225	. . .	. . .
Total contrast agent volume	1.007 (0.999–1.015)	0.081	1.007 (1.002–1.011)*	0.004*
Known CKD	2.00 (0.93–4.34)	0.077	1.92 (0.91–4.07	0.087
CT perfusion	0.83 (0.30–2.32)	0.721	0.95 (0.38–2.37)	0.919

AKI indicates acute kidney injury; CKD, chronic kidney disease; CT, computed tomography; DSA, digital subtraction angiography; N/A, not applicable; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio.
*Significant covariables.

bridging IVT (*P*<0.001) compared with patients who received only CTA. All other baseline characteristics including stroke severity did not differ between patients receiving both CTA/CTP and CTA alone. Incidence of AKI (6.9% versus 5.7%, *P*=0.646), successful recanalization (93.9% versus 88.6%, *P*=0.106), SICH (4.1% versus 3.0%, *P*=0770), median NIHSS at discharge (4 versus 4, *P*=0.335), and in-hospital mortality (12.4% versus 8.4%, *P*=0.175) did not differ significantly between patients with AIS receiving both CTA/CTP and CTA alone before the endovascular stroke treatment.

Additional use of CTP was not an independent predictor of either AKI or in-hospital death in multivariable regression analysis.

Discussion

Our large study of consecutive endovascular-treated patients with AIS showed an overall low incidence of AKI in patients with AIS receiving short-time repetitive intravenous and intra-arterial contrast agent application for CTA±CTP and MT with a standardized postprocedural hydration protocol using isotonic Ringer solution. Patients with pre-existing CKD had a significantly higher incidence of AKI, but known CKD was not an independent predictor for AKI in multivariable regression analysis. Additional use of CTP did not result in higher rates of AKI.

In contrast to diagnostic administration of intravenous contrast agent for diagnostic CTA/CTP alone,[4] patients with AIS with large vessel occlusion treated with MT might receive substantial extra amounts of intra-arterial iodinated contrast agent with second-pass effect during the MT procedure, thereby theoretically increasing the risk of post-contrast AKI. One third of our patients received intra-arterial contrast agent volumes of ≥150 mL during the MT procedure. Our observed AKI incidence rate of 5.8% was in the range of previous considerably smaller case series in endovascular-treated patients with AIS.[9–11] Loh and coworkers[9] first published a small study with 99 consecutive patients who had AIS undergoing endovascular therapy with the MERCI Retriever (Concentric Medical, Inc) or Penumbra System (Penumbra, Inc) from September 2002 to January 2008 and reported a contrast agent–mediated AKI in 3 of 99 (3%) patients, all of whom died. The average volume of administered contrast agent during the MT procedure was 189±71 mL in their study, which was higher compared with that in our study. The authors did not report the proportion of patients with AIS receiving prior CTA before the endovascular procedure. All MT procedures in our study were performed using modern stent retriever systems, which have been clearly shown to result in clinical benefit and lower complication rates in patients with AIS in comparison with the older retrieval systems including

MERCI.[14,15] The use of modern stent retrievers and the high experience of our neurointerventionalists 10 years later might have resulted in the use of lower contrast agent volumes.

Another retrospective study by Sharma and coworkers[10] reported a risk of contrast-induced nephropathy in 3 (1.5%) of 194 consecutive patients with AIS undergoing endovascular stroke treatment between January 2006 and January 2011. However, only 44 (22%) of the included 194 patients received additional CTA before the MT procedure, while all patients in our study had at least diagnostic CTA. The third small study evaluated the risk of AKI in 94 patients with AIS undergoing CTA and MT from September 2016 to September 2017 compared with 87 patients with AIS undergoing CTA alone.[11] As expected, there were significant differences in baseline characteristics between both groups. Patients receiving CTA and MT had a significantly higher NIHSS at admission (14 versus 3, *P*<0.001) and more often a history of heart failure and atrial fibrillation. AKI occurred in 7 (7.4%) of the 94 patients receiving both CTA and MT, and in 2 (2.3%) of 87 patients with CTA alone (*P*=0.172). The volumes of contrast agent used for CTA (mean 94.0±7.5 mL) and MT (mean 93.4±15.7 mL) were in the range of those used in our study. No usage of additional CTP was reported.

We used a standardized postprocedural hydration protocol with physiological Ringer solution at an infusion rate of 80 mL/h for at least 48 hours after repeated contrast agent administration in patients with AIS. A large-scaled, cluster-randomized, multiple-crossover, open trial recently showed that the use of physiological-balanced isotonic solutions (lactated Ringer solution or Plasma-Lyte A [Baxter Healthcare Corporation]) resulted in a lower rate of the composite outcome of death from any cause, new renal replacement therapy, or persistent renal dysfunction compared with the use of 0.9% sodium chloride saline among 15 802 critically ill patients (15.4% versus 14.3%; OR, 0.91 [95% CI, 0.84–0.99]).[16] The incidence of new renal replacement therapy or persistent renal dysfunction alone did not differ statistically between patients with balanced crystalloids and saline.

To date, no studies have systematically investigated the effect of pre-existing CKD on AKI incidence in patients with AIS undergoing MT. With more than 1000 included patients with AIS, our study was adequately powered to perform multivariable regression analysis. Ten percent of our patients with AIS had known CKD at baseline, and these patients had both a significantly higher incidence of post-contrast AKI and in-hospital mortality, and only patients with known CKD needed transient hemodialysis. As a consequence, patients with AIS with known CKD should be closely monitored for development of AKI after receiving intravenous contrast agent for diagnostic brain imaging followed by therapeutic intra-arterial contrast media during the MT procedure. However,

known CKD was not an independent predictor for AKI in multivariable regression analysis.

Patients with post-contrast AKI showed a nonsignificant worse short-term clinical outcome at discharge and had significantly higher in-hospital mortality. AKI was also an independent predictor of in-hospital death in multivariable regression analysis in our study. Several previous studies showed that an episode of AKI was a marker for increased short- and long-term morbidity and mortality, while systematic reviews and meta-analysis reported inconclusive results in other patient populations, mainly patients receiving iodinated contrast agent for coronary angiography.[2,3,17–19] A systematic review and meta-analysis investigating contrast-induced AKI after coronary angiography in 139 603 patients reported an increased risk of death in those patients with post-contrast AKI in 33 of 34 studies published until June 2011, although the effect size varied between studies.[2] In contrast, another systematic review and meta-analysis that included 13 nonrandomized studies with 25 950 patients following intravenous contrast medium administration published through September 2011 did not find an increased risk of death in patients who received contrast medium.[19]

Post-contrast AKI might increase mortality in patients with AIS by different pathophysiological means, ie, lack of volume regulation, enhancement of cerebral edema, electrolyte disturbances such as hypernatremia or hyponatremia, coagulation abnormalities, distant organ injury with increased cytokines, and vasoconstriction. However, three quarters of the patients with post-contrast AKI in our study mostly likely died as a result of malignant brain infarction itself either caused by missing collaterals in case of tandem vessel occlusions, long-lasting MT procedures with several thrombectomy maneuvers and futile/incomplete recanalization, or severe SICH, and not direct or indirect effects of the AKI itself. The NIHSS at 24 hours had not improved in any of these severely affected patients with AIS and did not secondarily deteriorate as a result of developing AKI. Worsening of kidney function in patients with AIS with severe brain damage might also occur in the natural disease course and result in persistent confounding despite adjustment for the most relevant covariables in our multivariable regression analyses. In line with this hypothesis, all 3 deaths in patients with AKI in the study by Loh and coworkers[9] were also judged to be related to the stroke itself and not to AKI, as return to baseline creatinine levels occurred before death.

We did not observe a higher AKI incidence in patients with AIS with additional CTP use in combination with CTA and MT, nor in those receiving intra-arterial contrast agent volumes of ≥150 mL during MT. Furthermore, additional use of CTP or the total amount of iodinated contrast agent volume applied for CTA/CTP and MT were not independent predictors for AKI, and should therefore not be delayed for awaiting kidney

values nor omitted in patients with AIS who are possible candidates for MT by using enhanced CT imaging, as "time is brain."[20] In contrast, a higher total amount of contrast agent volume, which was mostly caused by a higher volume of intra-arterial contrast agent for longer MT procedures in patients who needed several thrombectomy maneuvers, was an independent predictor for in-hospital death. A recent pooled analysis from 7 prospective interventional US databases also showed that longer MT procedures exceeding 60 minutes or 3 MT passes resulted in lower rates of functional independence and higher rates of SICH and complications.[21]

Study Limitations

There are several limitations of our study. First, assessment of NIHSS at discharge or in-hospital mortality rate was not performed at fixed time points. Second, data on long-term functional outcome or possible adverse events of our standardized hydration protocol cannot be provided because of the retrospective nature of our study and lack of systematic follow-up. Third, the subgroups of patients with known CKD and additional CTP use each comprised only about 100 patients, despite a large overall patient number with more than 1000 patients in our study. With the expected increasing use of CTP in patients with AIS in the near future, further studies should be performed to scrutinize our finding. Because of the relatively small number of patients with known CKD in our study, we did not investigate the effect of CKD stage on incidence of AKI or in-hospital mortality. Fourth, we were not able to assess a possible relationship of baseline proteinuria on AKI as a result of missing information. Patients who developed AKI after percutaneous coronary intervention had significantly higher levels of baseline proteinuria compared with those who did not.[22] Fifth, serum creatinine measurement was not performed at a predefined time point after the MT procedure and most of the patients had their measurement performed at 24 hours. Previous studies have shown that creatinine levels typically peak at 3 to 5 days after contrast administration, which might result in a higher incidence of AKI.[23] The higher observed incidence of AKI in patients with stroke with known CKD in our study might be partially related to an increased sensitivity of the older AKI definition used (including a serum creatinine rise of ≥0.5 mg/dL from baseline as one criterion) in patients with CKD who had higher absolute serum creatinine changes. Use of point-of-care whole blood creatinine measurement, performed in one referring hospital at baseline, might have led to overestimation of renal function in severe kidney failure.[24] Finally, we did not investigate a potentially protective role of statin treatment on AKI incidence in our study.[25]

Conclusions

Post–contrast AKI is rare in patients with AIS who received combined intravenous and intra‐arterial contrast agent for CTA/CTP and MT along with a standardized postprocedural hydration protocol with Ringer solution. Only 0.4% of all patients needed intermittent hemodialysis, all of whom had pre‐existing CKD. Thus, kidney values in patients with AIS with known CKD treated with MT after CTA should be closely monitored in the first several days. Use of additional CTP did not increase the incidence of post–contrast AKI. Our study results show that fear of post–contrast AKI should not result in delay or omission of diagnostic CTA/CTP or the endovascular procedure itself in patients with AIS with possible large vessel occlusion, as "neurons are *still* over nephrons."[4]

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Disclosures

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