Renal Safety of Intra-Arterial Treatment after Acute Ischemic Stroke with Multimodal CT Imaging selection

Zicheng Hu, MD,* Tingting Shang, MD,† Rongzhong Huang, MD,‡ Qi Li, MD,* Peng Zheng, MD,* Haiyang Wang, MD,§ and Peng Xie, MD*

Background: Multimodal computed tomography imaging is used to identify eligible patients for intra-arterial treatment. A concern with this method is the multiple use of iodinated contrast material which presents a possible risk of renal toxicity. We compared the safety of intra-arterial treatment versus intravenous treatment during acute ischemic stroke treatment with a focus on renal safety. *Methods*: Adult acute ischemic stroke patients who underwent a baseline Multimodal computed tomography, then intra-arterial treatment and/or intravenous treatment were identified. Primary outcomes were acute kidney injury and changes in serum creatinine at 24-72 hours (Δ serum creatinine). *Results*: A total of 184 patients received intra-arterial treatment, while 68 received intravenous treatment. There were no differences in mean serum creatinine in the 24-72-hour time period, 24-hour urine volume, or rates of acute kidney injury, dialysis, or mortality. Univariate regression analysis identified diabetes mellitus, operation duration and times of embolectomy as predictors of creatinine increase while the multiple regression model identified diabetes mellitus as the only significant predictor. *Conclusions*: There were no significant differences in renal safety between the intra-arterial treatment and intravenous treatment groups. Diabetes mellitus may be a predictor of acute kidney injury. The use of Multimodal computed tomography imaging in the selection of patients who could benefit from endovascular therapy is safe.

Key Words: Acute ischemic stroke—multimodal computed tomography—intra-arterial treatment—acute kidney injury—iodinated contrast material

Introduction

Recently, the therapeutic time window for the use of thrombectomy has been extended up to 24 hours in the American Heart Association 2018 stroke guidelines based on significant clinical benefits reported in the Triage of Wake-up and Late Presenting Strokes Undergoing Neurointervention With Trevo (DAWN) trial and Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3 (DEFUSE 3) trial.[1-3] The new clinical trial data and guidelines have led a large number of stroke centers to begin using advanced imaging with multimodal computed tomography (MCT) or magnetic resonance imaging (MRI) to evaluate patients who present with a possible large vessel occlusion in an extended time period. Imaging selection for patients in both DEFUSE 3 and DAWN required either MCT or MRI, with the majority selected by MCT. MCT can

From the *Department of Neurology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China; †Department of Ultrasound, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China; ‡Department of Geriatrics, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China; and §Institute of Neuroscience and The Collaborative Innovation Center for Brain Science, Chongqing Medical University, Chongqing, China.

Received January 26, 2019; revision received February 12, 2019; accepted February 23, 2019.

Funding: This work was supported by The National Natural Science Foundation of China (grant number:81801711).

Competing interests: None.

Ethics approval: This study was approved by the Ethical Committee of The First Affiliated Hospital of Chongqing Medical University.

Address correspondence to Peng Xie, MD, Department of Neurology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China. E-mail: Huzi0329@foxmail.com.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.02.027

provide quantitative estimates of the ischemic core and penumbra without user input and have excellent interobserver agreement. However, these techniques also have limitations, including apprehension concerning the use of radio-contrast material (CM) potentially inducing acute kidney injury (AKI). Contrast-associated AKI signifies a severe and usually reversible decline in kidney function that may develop within 72 hours after intravascular administration of iodinated CM. The condition is usually defined as an increase in the serum creatinine (SCr) level of more than .5 mg per deciliter (44 μmol per liter) or an increase of at least 25% in the level from baseline.[4]

Contrast-induced nephropathy (CIN) is a key trigger of acute renal failure and occurs within 72 hours after the use of iodinated radiographic CM.[5] In fact, the use of CM during imaging is the third most common trigger of iatrogenic AKI.[6] In previous reports, the use of CM has been associated with significant adverse events, such as renal failure, the need for dialysis treatment, stroke, myocardial infarction, and even death.[7] Previous studies have shown that MCT imaging does not affect the risk of AKI in stroke patients, even in those presenting preexisting kidney disease.[8] However, patients with acute ischemic stroke (AIS) receiving intra-arterial treatment (IAT) after baseline MCT imaging may receive multiple administrations of iodinated CM over a short time period. The incidence of AKI as well as the emergent need for dialysis in those who undergo intra-arterial acute ischemic stroke treatment after a baseline MCT imaging is largely unknown. We set up this study to investigate whether there was a difference between IAT and intravenous treatment (IVT) with respect to renal safety when performed after a baseline MCT for AIS treatment.

Methods

Patients

This study was approved by the ethics committee of The First Affiliated Hospital of Chongqing Medical University. The investigators carried out a retrospective review as well as a chart review of adult patients with AIS who underwent IAT or IVT at our institution from December 2014 to May 2017. Patients aged >18 years with AIS were included in this review if they (1) had a baseline MCT evaluation, (2) received r-tPA IVT only, or r-tPA IVT plus IAT, or IAT only, and (3) had a prescan SCr result prior to MCT and as a minimum, one postscan (24-72 hours post-treatment) SCr result. Investigators excluded patients who (1) presented any preexisting renal dialysis requirements, (2) underwent partial or radical nephrectomy or received a kidney transplant, or (3) received IV or intra-arterial CM from any other test or procedure within 14 days. Investigators gathered demographic information, clinical characteristics, and laboratory data of each participant from chart reviews.

Imaging

Imaging was carried out according to our institution's acute stroke CT, CT angiography (CTA) and CT perfusion (CTP) protocols on Philips brand 256-slice CT scanners (Philips Brilliance iCT, Philips Healthcare, Cleveland). A total of 50 to 70 mL of CM (Iohexol, Omnipaque 350 mg I/mL; GE Healthcare) was administered at 5 mL/s with a 50 mL saline bolus chaser by means of a dual-head injector for CTA of the head and neck. A 50 mL bolus of CM was administered at 5 mL/s to attain fifty-five 4.5 seconds CTP images of 5-mm slices each. Philips Extended Brilliance Workspace (Philips Medical Systems Nederland BV) was used to process the CTA and CTP images. Measurements included cerebral blood volume, cerebral blood flow, mean transit time, delay time, an ischemic core, and penumbra maps.

IAT consisted of arterial catheterization with a microcatheter to the level of occlusion and delivery of a thrombolytic agent, mechanical thrombectomy, or both. The method of intra-arterial treatment was left to the discretion of the local interventionist.

The investigator was free to choose how IAT would be conducted. Up to 10 mg alteplase (5 mg if administered IV) or 1,000,000 IU (500,000 IU if IV) urokinase was allowed in this trial for intra-arterial thrombolysis. At least 1 investigator in each procedure must have completed a minimum of 5 full procedures with the corresponding device.

Measures of Safety

Safety outcomes comprised evidence of AKI, including Scrap as a marker of renal function. The investigators calculated the difference between the baseline (at the time of presentation) Scrap measurements and SCr measurements 24-72 hours after presentation (ΔCr). In this study, the definition of AKI was an increase in the highest observed SCr level of either (a) an absolute increase of more than .5 mg/dL (≥44 μmol/L), or (b) an increase of ≥25% within 3 days of CM use. No other etiology was done.

Statistical Analysis

Statistical analysis was performed using SPSS, version 22 (IBM Corp.) Included patients comprised of 2 groups: one group (IAT) received intra-arterial treatment (including intra-arterial treatment only and intravenous followed by intra-arterial treatment) after a baseline MCT imaging and the other group (IVT) received IVT after a baseline MCT imaging. A 2-sided, independent sample t test was used to compare all means. The Pearson χ^2 test was used for comparisons of categorical data, including sex, the existence of medical comorbidities, chronic kidney disease (CKD), the estimated glomerular filtration rate (eGFR) subgroups, AKI, dialysis, and death. Risk factors of contrast-

induced AKI in the IAT group were examined by univariate and multivariate logistic regression analyses. A P value less than .05 was considered as statistically significant.

Results

Patients who arrived at our institution with symptoms suggestive of AIS routinely underwent evaluation using the MCT imaging protocol, which consists of a noncontrast CT (NCCT) scan of the brain, CTA of the head and neck, and CTP of the head. If a favorable penumbral pattern was identified in conjunction with a proximal large vessel occlusion site that was amenable to endovascular intervention, patients were taken immediately to the interventional suite for possible intervention. If a proximal large vessel occlusion was not present, patients received r-tPA intravenously without thrombectomy. Therefore, at our institution, patients routinely received multiple administrations of iodinated CM over a relatively short time period.

After applying exclusion criteria, 252 patients were included in our final analysis. A total of 184 patients received intra-arterial treatment after a baseline MCT imaging (IAT) and 68 patients received IVT after a baseline MCT imaging (IVT). Patients of the IAT group were generally younger (mean age, 64.4 versus 68.93 years; $P = .008$) than those who received IVT (Table 1).

Patients of the IAT group had higher rates of rheumatic heart disease (13% versus 2.9%; $P = .019$), and a higher NIH stroke scale score (16.56 versus 13.97, $P = .016$) than those of the IVT group (Table 1). Patients of the IAT group were administrated higher doses of iodinated CM (88.02 versus 38.42 g, iodine, $P < .001$). Patients of the IAT group also presented a higher renal function (eGFR, 87.45 versus 79.20 mL/min per 1.73 m^2; $P = .012$). They had lower rates of CKD (9.8% versus 20.6%), hypertension (36.4% versus 72.1%), and CAD/previous MI (24.5% versus 48.5%) than patients of the IVT group (Table 1). Patients of the IAT group were administered more fluids than the IVT group (3134 versus 2875 mL, $P < .001$). Otherwise the distribution of patients was similar in regard to sex, dyslipidemia, diabetes mellitus, atrial fibrillation, and 24 hours urine volume (Table 1).

The IAT group presented with lower baseline mean SCr measurements compared to the IVT (.845 mg/dL IAT, .958mg/dL IVT; $P = .008$) group (Table 2). Yet, at 24-72 hours after treatment no significant difference was reported between the group's mean SCr levels (.839 mg/dL IAT, .886mg/dL IVT; $P = .312$) although the IVT group had a lower ΔCr (−.006 IAT, −.072 IVT; $P = .039$) than the IAT group (Table 2). Sixteen patients in the IAT group (8.7%) developed AKI but no significant difference in those who developed AKI was found between the 2 groups (16 IAT versus 4 IVT; $P = .603$) (Table 2). Only 1 patient in the IAT group and no patients in the IVT group required hemodialysis due to deteriorative renal function ($P = 1.00$). There is no significant difference in the rate of death between the 2 groups (17 IAT versus 7 IVT; $P = .811$) (Table 2).

Table 1. *Patient demographics and baseline characteristics*

	IAT (n = 184)	IVT (n = 68)	P (95% CI)
Mean ± SD age, years	64.4 ± 12.54	68.93 ± 10.40	.008 (−7.885 to −1.175)
Male sex, n(%)	98 (53.3)	43 (63.2)	.157
Pre-existing comorbidities	-	-	-
Dyslipidemia, n(%)	61 (33.2)	26 (38.2)	.459
Hypertension, n(%)	117 (63.6)	49 (72.1)	.233
Diabetes mellitus, n(%)	48 (26.1)	25 (36.8)	.118
CAD/previous MI, n(%)	45 (24.5)	35 (51.5)	<.001
Rheumatic heart disease, n(%)	24 (13)	2 (2.9)	.019
Atrial fibrillation, n(%)	65 (35.3)	23 (33.8)	.882
Chronic kidney disease, n(%)	18 (9.8)	14 (20.6)	.032
Mean ± SD pre-MCT eGFR	87.45 ± 22.32	79.20 ± 24.19	.012 (1.868-14.634)
eGFR subgroups (mL/min)	-	-	-
≥90, n(%)	89 (48.4)	24 (35.3)	.086
60-89, n(%)	70 (38)	28 (41.2)	.665
30-59, n(%)	24 (13)	15 (22.1)	.115
<30, n(%)	1 (.5)	1 (1.5)	.468
Mean ± SD 24 h fluids administered after MCT, mL	3134 ± 662.00	2785 ± 696.42	<.001 (161.276-536.595)
Mean ± SD 24 h urine volume after MCT, mL	2173 ± 589.91	2064 ± 668.61	.21 (−61.790 to 280.324)
Mean ± SD presenting NIHSS	16.56 ± 6.78	13.97 ± 9.41	.016 (.489-4.690)
Mean ± SD dose of iodine, g	88.02 ± 1.28	38.42 ± .04	<.001 (45.575-53.629)

Abbreviations: CAD, coronary artery disease; CI, confidence interval; eGFR, evaluated glomerular filtration rate; IAT, intra-arterial treatment; IVT, intravenous treatments; MCT, multimodal computed tomography; MI, myocardial infarction; NIHSS, National Institutes of Health Stroke Scale.

Table 2. *Laboratory and clinical outcome*

	IAT	IVT	*P* (95% CI)
Mean ± SD Creatinine on arrival, mg/dL	.845 ± .26	.958 ± .38	.008 (−.196 to −.030)
Mean ± SD Creatinine at 24-72 h, mg/dL	.839 ± .32	.886 ± .35	.312 (−.139 to −.045)
Mean ± SD Delta creatinine, mg/dL	−.006 ± .24	−.072 ± .15	.039 (−.003 to −.128)
Acute kidney injury, n(%)	16 (8.7)	4 (5.9)	.603
Dialysis within 30 d, n(%)	1 (.5)	0 (0)	1.00
Death within 30 d, n(%)	17 (9.2)	7 (10.3)	.811

Abbreviations: CI, confidence interval; IAT, intra-arterial treatment; IVT, intravenous treatments.

The diagnosis of AKI is mainly based on the increase in serum creatinine concentration.[4] Therefore, we wanted to see if we could identify any predictors of creatinine increase. We performed both univariate and logistic regression analyses using multiple demographic and clinical factors as independent variables. We performed these analyses on patients with or without AKI in the IAT group. The demographic variables included age and sex, while the clinical variables included, but were not limited to, dyslipidemia, hypertension, diabetes mellitus, procedure duration, and the number of times an embolectomy was performed (Table 3). In univariate regression analyses, diabetes mellitus, operation duration, and the number of times of embolectomy were significant predictors of creatinine increase. There was no significant difference in dose of iodinated CM between the AKI (+) and AKI(−)groups. AKI may be associated with a high mortality and poor functional outcome (Table 3). However, in multivariate logistic analysis, only diabetes mellitus remained an independent predictor of creatinine increase (OR = 5.134, 95% CI (1.650-15.970), *P* = .005) (Table 4).

Table 3. *Univariate analysis of the demographic and clinical between AKI (+) and AKI (−) in the IAT group*

	AKI (+) (n = 16)	AKI (−) (n = 168)	*P* (95% CI)
Mean ± SD age,years	66.37 ± 13.40	64.21 ± 12.48	.511 (−4.317 to 8.651)
Male sex, n(%)	7 (43.8)	91(54.2)	.445
Pre-existing comorbidities	-	-	-
Dyslipidemia, n(%)	5 (31.3)	58 (34.5)	1.00
Hypertension, n(%)	11 (68.8)	106 (63.1)	.789
Diabetes mellitus, n(%)	9 (56.3)	39 (43.8)	.007
CAD/previous MI, n(%)	4 (25)	41 (24.4)	1.00
Rheumatic heart disease, n(%)	1 (6.3)	23 (13.7)	.699
Atrial fibrillation, n(%)	8 (50)	57 (33.9)	.273
Chronic kidney disease, n(%)	3 (18.8)	15 (8.9)	.195
Mean±SD Pre-MCT eGFR	88.30 ± 17.21	87.37 ± 22.79	.873 (−10.619 to 12.491)
eGFR subgroups (mL/min)	-	-	-
≥90, n(%)	7 (43.8)	82 (48.8)	.796
60-89, n(%)	8 (50)	62 (36.9)	.419
30-59, n(%)	1 (6.3)	23 (13.7)	.699
<30, n(%)	0 (0)	1 (.6)	1.00
Mean ± SD 24 h fluids administered after MCT, mL	3208.19 ± 683.87	3126.88 ± 661.54	.640 (423.78-456.49)
Mean ± SD 24 h urine volume after MCT, ml	2058.44 ± 780.25	2184.32 ± 570.32	.416 (178.93-296.86)
Mean ± SD presenting NIHSS	18.19 ± 4.22	16.40 ± 6.87	.310 (−1.669 to 5.235)
Mean ± SD operation duration	207.81 ± 89.56	164.49 ± 72.62	.027 (5.035-81.602)
Mean ± SD times of embolectomy	2.69 ± 1.66	1.60 ± 1.30	.002 (.400-1.773)
Mean±SD Dose of iodine, g	98.59±3.99	87.01±1.28	.352 (−20.129 to −3.029)
Mean ± SD creatinine on arrival, mg/dL	.78 ± .24	.85 ± .26	.285 (−.209 to .062)
Mean±SD creatinine at 24-72 h, mg/dL	1.28 ± .61	.80 ± .25	<.001 (.327-.630)
Mean ± SD delta creatinine, mg/dL	.50 ± .42	−.05 ± .15	<.001 (.454-.649)
mRS ≤ 2, n(%)	3 (18.8)	96 (57.1)	.004
Mortality, n(%)	7 (43.8)	10 (6)	<.001

Abbreviations: AKI, acute kidney injury; CAD, coronary artery disease; CI, confidence interval; eGFR, evaluated glomerular filtration rate; IAT, intra-arterial treatment; MCT, Multimodal computed tomography; MI, myocardial infarction; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

Table 4. *Multivariate logistic regression analysis of AKI risk factors*

	OR	95% CI	*P* value
Operation duration	.997	.988-1.005	.436
Times of embolectomy	.681	.440-1.056	.086
Diabetes mellitus	5.134	1.650-15.970	.005

Abbreviations: AKI, acute kidney injury; CI, confidence interval; OR, odds ratio.

Discussion

The DAWN and DEFUSE 3 trials demonstrated the benefit of delayed (>6 hours from onset) mechanical thrombectomy in patients with large penumbra and small infarct core. DAWN enrolled patients who could be treated between 6 and 24 hours,[2] and DEFUSE 3 enrolled patients who could be treated between 6 and 16 hours after last known well.[3] At 90-day follow-up, both trials reported improved functional outcomes in the treated group. Multimodal imaging was used to select patients in both DAWN and DEFUSE 3 required either CTP or MRI, with the majority being selected by CTP. In response, CTA and CTP are increasingly used in the triage of AIS patients. The American Heart Association and American Stroke Association strongly recommend the use of CTP, DWI-MRI, or MRI perfusion for selecting eligible patients for mechanical thrombectomy.[1] While increased usage of advanced imaging techniques has aided the triage needs of patients with AIS and their outcomes, these modes of imaging continue to depend upon the use of IV iodinated contrast, with well-known risks, especially contrast-induced AKI.

The pathophysiology of CIN is not fully understood and may be caused by both direct tubular toxicity and renal ischemic injury.[9] Risk factors of CIN include cardiovascular disease, diabetes, collagen vascular disease, NSAIDs use, dehydration, paraproteinemia, aminoglycoside antibiotics, and advanced age.[10,11] Diabetics and those patients with an underlying kidney dysfunction present the highest risk of CIN[12,13] and likely overlap with patients most likely to present with stoke. Our study has important clinical implications because patients who present with renal dysfunction when admitted to the hospital for stroke are more likely to experience poor outcomes.[14] At the immediate stroke triage, the medical histories of patients are often unknown and rarely do patients have the ability to convey this history. Therefore, it is unlikely that providers will be privy to the CIN risk factors of a patient in this early and important stage. Many institutions require, per protocol, evaluation of serum creatinine levels in patients with AIS, upon arrival to the emergency department before performing MCT. Waiting to make clinical decisions based on the return of these results, especially when it is known that deferrals in the onset-to-perfusion time can diminish the efficacy of therapy, can be impractical.[15,16]

Previous research of CIN inferred the administration of an iodinated CM to be the causal factor in AKI from the short time period between their use and the onset of renal function changes. Several studies evaluated the safety and efficacy of CT imaging studies in AIS patients.[17,18] In a study of 289 patients, Ehrlich et al[19] found that CTA was safe from a renal function perspective in acute ischemic stroke. In another study of 53 consecutive patients undergoing the CT protocol (NCCT, CTA, CTP) for suspected clinical stroke or transient ischemic attack, Smith et al[20] reported that no renal injury were observed. Josephson et al[21] further studied this topic by retrospectively reviewing the data of 1075 patients receiving routine CTA and CTP at a single institution. The authors reported that 52 of 1075 patients (4.8%) included in the analysis had an increase in creatinine levels over >.5 mg/dL. In 4 of these patients the cause of renal injury was considered to be the contrast administration. Adnan et al[22] evaluated the incidence of AKI after CTSS and DSA within a 48 hour period. This study provides preliminary evidence of the safety and feasibility of obtaining CTSS with additional DSA imaging. Sharma et al[23] also found a relatively low rate of contrast-induced nephropathy (CIN) of 1.5% in patients undergoing vascular imaging and endovascular procedures. However, both studies had an extended interval between the MCT and DSA, and there was no intergroup control. These studies evaluated the risk of kidney injury associated with noninvasive stroke imaging (eg CTA and CTP) or additional DSA imaging after a long interval. While the incidence of contrast-induced AKI has decreased over the last 10 years,[24] however, previous studies reported that the incidence of AKI is substantially higher following intra-arterial CM administration compared to intravenous administration,[25] and the dose-dependent risk was commonly presumed.[26,27] Therefore, the risk for patients in urgent need of IAT who have received multiple administrations of iodinated CM within a short time frame is still unknown. With a greater number of patients expected to be triaged to IAT, we aimed to investigate whether the addition of IAT performed in the acute period portends an increased risk of contrast-induced nephropathy.

In this retrospective study, the investigators evaluated the risk of AKI in AIS patients who had undergone a baseline MCT selection and IAT within a 4-hour period. Compared to IVT group, patients of the IAT group were administrated higher doses of CM (88.02 versus 38.42 g, iodine, $P < .001$), the investigators found that early IAT based on MCT was not associated with impairment of renal functions within 24-72 hours. Even while over 9.8% of included patients had CKD at baseline, no difference was found in the relative or absolute creatinine measurements between the AKI (+) and AKI (−) groups within the

first 72 hours. Adjustment for a variety of reported risk factors for creatinine increase did not change the results. The present study showed that using MCT imaging to triage patients who may benefit from endovascular therapy was safe in regard to renal function. We defined AKI as either an increase of .5 mg/dL or an increase of at least 25% from the baseline creatinine level. In this way, we aimed to address new renal injury regardless of baseline function. Of the 16 patients who experienced AKI according to this criterion, only 3 had baseline CKD. We also studied the change in creatinine level as a means to control for any baseline renal dysfunction and found a significantly greater change in patients who developed AKI compared with those who did not. As we know, patients presenting with AIS often have underlying medical comorbidities that may predispose them to the development of renal failure/renal injury. Univariate regression analysis showed diabetes mellitus, operation duration, and times of embolectomy predicted the increase of serum creatinine. Logistic regression analysis reported that only diabetes mellitus ($P = .005$) significantly predicted AKI. The current study shows that AIS patients with history of diabetes mellitus, have a high risk of AKI after treatment with IAT after MCT estimation. Our findings suggest that caution must be taken while treating these patients, including timely monitoring and adjusting the total dose of CM while performing IAT. Appropriate precautions such as consuming more fluids within 24 hours after the CM is administered may promote excretion of the CM, reduce serum creatinine, and thereby reduce the risk of AKI. There is an independent association between AKI and the risks of mortality after IAT. AKI predicts both mortality and poorer outcome after AIS.

There are several limitations in this retrospective study. First, this is not randomized study and patients may have disparity in baseline creatinine values, eGFR, and the rates of CKD and NIH stroke scale. Second, selection bias is a heavy burden in retrospectively designed studies. The operator in this study had full discretion to make the decision to obtain an IAT for each patient. A constraint of available data occurred because creatinine values were documented only at 24-48 hours even while AKI may take time to develop. Third, our study is based on the data and protocol of a single center and may not be generalizable to other facilities. Future studies with adequately sized samples are needed to identify the best imaging technology to triage patients for endovascular therapy.

Author Contributions

ZH and PX were responsible for the study concept and design. ZH, TS, HW, and PZ contributed to acquisition of the data. ZH, TS and RH contributed to analysis and interpretation of the data. All authors contributed to drafting of the manuscript. ZH, TS, QL and PX contributed to critical revision of the manuscript for important intellectual content. PX contributed to study supervision. ZH and TS contributed equally to this work. PX is corresponding author of this paper.

Supplementary Materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2019.02.027.

References

1. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2018;49:e46-e110.
2. Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. N Engl J Med 2018;378(1):11-21.
3. Albers GW, Marks MP, Kemp S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. N Engl J Med 2018;378(8):708-718.
4. Rosner MH. Prevention of contrast-associated acute kidney injury. N Engl J Med 2018;378:671-672.
5. Demel SL, Grossman AW, Khoury JC, et al. Association between acute kidney disease and intravenous dye administration in patients with acute stroke: a population-based study. Stroke 2017;48:835-839.
6. Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. Am J Kidney Dis 2002;39(5):930-936.
7. Mitchell AM, Kline JA, Jones AE, et al. Major adverse events one year after acute kidney injury after contrast-enhanced computed tomography. Ann Emerg Med 2015;66(3):267-274. e4.
8. Brinjikji W, Demchuk AM, Murad MH, et al. Neurons over nephrons: systematic review and meta-analysis of contrast-induced nephropathy in patients with acute stroke. Stroke 2017;48:1862-1868.
9. Fähling M, Seeliger E, Patzak A, et al. Understanding and preventing contrast-induced acute kidney injury. Nat Rev Nephrol 2017;13:169-180.
10. Gleeson TG, Bulugahapitiya S. Contrast-induced nephropathy. Am J Roentgenol 2004;183(6):1673-1689.
11. Singh J, Daftary A. Iodinated contrast media and their adverse reactions. J Nucl Med Technol 2008;36:69-74. quiz 76-7.
12. Morcos SK. Contrast media-induced nephrotoxicity—questions and answers. Br J Radiol 1998;71:357-365.
13. Morcos SK, Thomsen HS, Webb JA. Contrast-media-induced nephrotoxicity: a consensus report. Contrast Media Safety Committee, European Society of Urogenital Radiology (ESUR). Eur Radiol 1999;9:1602-1613.
14. Rowat A, Graham C, Dennis M. Renal dysfunction in stroke patients: a hospital-based cohort study and systematic review. Int J Stroke 2014;9(5):633-639.
15. Marler JR, Tilley BC, Lu M, et al. Early stroke treatment associated with better outcome: the NINDS rt-PA stroke study. Neurology 2000;55:1649-1655.
16. Ang TE, Bivard A, Levi C, et al. Multi-modal CT in acute stroke: wait for a serum creatinine before giving intravenous contrast? Int J Stroke 2015;10:1014-1017.
17. Hopyan JJ, Gladstone DJ, Mallia G, et al. Renal safety of CT angiography and perfusion imaging in the emergency evaluation of acute stroke. Am J Neuroradiol 2008;29:1826-1830.

18. Aulicky P, Mikulík R, Goldemund D, et al. Safety of performing CT angiography in stroke patients treated with intravenous thrombolysis. J Neurol Neurosurg Psychiatry 2010;81:783-787.
19. Ehrlich ME, Turner HL, Currie LJ, et al. Safety of computed tomographic angiography in the evaluation of patients with acute stroke: a single-center experience. Stroke 2016;47:2045-2050.
20. Smith WS, Roberts HC, Chuang NA, et al. Safety and feasibility of a CT protocol for acute stroke: combined CT, CT angiography, and CT perfusion imaging in 53 consecutive patients. Am J Neuroradiol 2003;24:688-690.
21. Josephson SA, Dillon WP, Smith WS. Incidence of contrast nephropathy from cerebral CT angiography and CT perfusion imaging. Neurology 2005;64:1805-1806.
22. Hall SL, Munich SA, Cress MC, et al. Risk of acute kidney injury associated with neuroimaging obtained during triage and treatment of patients with acute ischemic stroke symptoms. J Neurointerv Surg 2016;8(12):1231-1234.
23. Sharma J, Nanda A, Jung RS, et al. Risk of contrast-induced nephropathy in patients undergoing endovascular treatment of acute ischemic stroke. J Neurointerv Surg 2013;5:543-545.
24. McCullough PA, Choi JP, Feghali GA, et al. Contrast-induced acute kidney injury. J Am Coll Cardiol 2016;68:1465-1473.
25. Solomon R. Contrast-induced acute kidney injury: is there a risk after intravenous contrast. Clin J Am Soc Nephrol 2008;3:1242-1243.
26. Sherwin PF, Cambron R, Johnson JA, et al. Contrast dose-to-creatinine clearance ratio as a potential indicator of risk for radiocontrast-induced nephropathy: correlation of D/CrCL with area under the contrast concentration-time curve using iodixanol. Invest Radiol 2005;40:598-603.
27. Laskey WK, Jenkins C, Selzer F, et al. Volume-to-creatinine clearance ratio: a pharmacokinetically based risk factor for prediction of early creatinine increase after percutaneous coronary intervention. J Am Coll Cardiol 2007;50:584-590.