

Safety following mechanical thrombectomy for acute ischemic stroke using iso-osmolar contrast media

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Abstract

Purpose

Mechanical thrombectomy (MT) in the treatment of acute ischemic stroke (AIS) is already recommended as the standard care according to international guidelines. However, symptomatic intracranial hemorrhage (SICH) is a major complication of MT. Several studies reported that use of iso-osmolar contrast media (IOCM) was associated with a lower incidence of cerebral hemorrhage than low-osmolar contrast media (LOCM) after MT. The objective of this study was to evaluate the safety of MT using IOCM compared with using LOCM.

Material and Methods

One hundred and thirty-nine consecutive patients (56 men, mean age 79.9 years) who underwent MT within 24 hours from onset of AIS between April 2020 and October 2024 (LOCM; n = 38, IOCM; n = 101) were retrospectively reviewed. The procedural success rate, incidence of SICH, proportion of patients with good prognosis, acute and delayed adverse reactions, and contrast-induced acute kidney injury (CI-AKI) were analyzed according to contrast media type.

Results

Successful recanalization was observed in 103 patients (74.1%). Overall, 5 patients (3.6%) developed SICH: 1 patient (1.0%) in the IOCM group and 4 patients (10.5%) in the LOCM group showing significant difference ($p = 0.007$). Overall, 53 patients (38.1%) had a good prognosis, and 5 patients (3.6%) had delayed adverse reactions from the contrast agent without differences. No acute adverse reactions or CI-AKI occurred in either group.

Conclusions

The incidence of SICH after MT was 1.0% using IOCM lower than using LOCM. The use of an IOCM may be a safe option in MT for AIS.

Introduction

A meta-analysis of randomized clinical trials¹⁾ has confirmed the viability of mechanical thrombectomy (MT) for acute ischemic stroke (AIS), appearing that the extent of patients with a mRS score of 0–2 at 90 days was higher within the intervention population than within the control population. However, mortality at 90 days did not differ between the populations. In particular, symptomatic intracranial hemorrhage (SICH) is such a potentially life-threatening complication as to cause poor outcomes and increase

mortality. Some studies have shown that 90-day mortality was higher in patients with SICH than in patients without SICH.^{2–4)}

Previous studies have reported that the use of contrast media in endovascular treatment was associated with intracranial hemorrhage (ICH).^{2–5)} Moser et al. reported that use of iso-osmolar contrast media (IOCM) was associated with a lower rate of hemorrhagic transformation than use of low-osmolar contrast media (LOCM) in patients with ischemic stroke.⁶⁾ A recent clinical study that assessed the correlations between contrast media type (IOCM or LOCM) and SICH after MT found a significantly lower frequency of SICH in the IOCM group than in the LOCM group among only successful recanalization cases.⁷⁾

The objective of this report was to evaluate the safety of MT using IOCM compared with those using LOCM.

Materials and Methods

This study protocol was approved by the ethics committee of our institution, and all patients provided written informed consent.

A total of 139 consecutive patients (56 men, mean age 79.9 years [31–98 years]) who underwent MT within 24 hours of onset of AIS due to occlusion of major arteries (38 patients of the ICA; internal carotid artery, 91 patients of the M1 or M2 portion of the MCA; middle cerebral artery, and 10 patients of the basilar artery) between April 2020 and October 2024 were retrospectively reviewed. A flow chart of patient selection is shown in Fig. 1. LOCM (n = 38) was used between April 2020 and September 2021, and IOCM (n = 101) was used between October 2021 and October 2024 (Fig. 1, Table 1). Dialysis patients were excluded. Sixty patients (59.4%) were cardiogenic, and 41 patients (40.6%) were atheromatous in origin. Systolic blood pressure (SBP) was controlled to within 100–139 mmHg during the initial 24 h post-MT in successful recanalization cases and to within 110–179 mmHg in unsuccessful recanalization cases.

Procedural success rate (recanalization rate; expanded treatment in cerebral infarction [eTICI] 2b-3), incidence of SICH, patients with good prognosis (mRS score 0–2), death within 90 days after MT, acute and delayed adverse reactions, and contrast-induced acute kidney injury (CI-AKI) were retrospectively reviewed⁹⁾, and the differences between contrast media type were evaluated.

Cone-beam CT was performed immediately after the procedure and non-contrast CT was performed whenever intracranial hemorrhage was suspected. All imaging examinations, including computed tomography and angiography, were reviewed by two experienced neuroradiologists the readers were not blinded to the clinical information, and clinical symptoms were prospectively recorded and adjudicated.

SICH was defined based on the Heidelberg criteria.¹⁰⁾ A diagnosis of SICH was based on any of the taking after conditions: 1) sudden increase in National Institutes of Health Stroke Scale (NIHSS) score by

≥4 after a previous slow decline; 2) increase in NIHSS score of ≥2 in any one category; or 3) deterioration in neurological status following intubation, hemicraniectomy, external ventricular drain placement, or other major restorative or surgical intervention.

Acute adverse reaction was defined as occurring within 1 hour of contrast media injection, and delayed adverse reaction was defined as occurring from 1 hour to 1 week following contrast media injection.

CI-AKI was defined as increased serum creatinine [SCr] ≥ 0.3 mg/dL within 48 hours; or increased SCr ≥ 1.5 times baseline within the prior 7 days; or urine volume ≤ 0.5 mL/kg/h for 6 hours after intravascular administration of contrast media.

Statistical Analysis

Continuous variables were analyzed using the Mann–Whitney U test according to the normality of the distribution. Pearson's χ^2 test was used to compared frequencies for categorical variables between iso- or low-osmolar groups in univariate analyses.

Results

There were no differences in baseline characteristics between the IOCM and LOCM groups (Table 1). Overall, 124 patients (89.2%) were treated with a combination of a stent retriever and aspiration catheter, and 15 patients (10.8%) were treated with a direct aspiration first pass technique (ADAPT) alone.

Table 2 summarizes the results of MT for AIS. Successful recanalization (eTICI 2b-3) was observed in 103/139 (74.1%) and there was no difference between the two groups (IOCM, 75.2% vs. LOCM, 71.1%).

Overall, five patients (3.6%) developed SICH. In the IOCM group, 1 patient (1.0%) developed SICH. In contrast, 4 patients (10.5%) in the LOCM group developed SICH, significantly more than in the IOCM group ($p = 0.007$). All SICH were observed in successful procedure cases.

Overall, fifty-three (38.1%) patients had a good outcome (mRS score 0–2; IOCM, 38.6% vs. LOCM, 36.8%), the overall incidence of death within 90 days after MT was 12.2% (17/139; IOCM, 9.9% vs. LOCM, 18.4%), and there were no statistically significant differences between the types of contrast agent.

No acute adverse reactions occurred within 1 hour after administration of IOCM or LOCM during the MT procedure. There were 5 patients (3.6%) of delayed adverse reactions; 4 patients (4.0%) of urticaria of the limbs and trunk in the IOCM group and 1 patient (2.6%) of urticaria of the limbs in the LOCM group, as a side effect of contrast agent administration and all of which were mild. In all 5 patients, symptoms disappeared quickly with steroid administration or conservative observation, and there was no difference between the two groups. Mean contrast media volume for MT procedure was 127.3 (range 17–260) ml in IOCM group and 131.5 (range 68–250) ml in LOCM group (Table 1), including 5 chronic kidney disease patients (CKD3; glomerular filtration rate [GFR] 30–60 mL/min/1.73 m², 3 using IOCM and 2 using LOCM,

20–48 [average 30] ml of contrast media used). There were no cases of contrast-induced acute kidney injury (CI-AKI) and no cases of irreversible renal dysfunction or renal failure in both groups.

Discussion

In a meta-analysis of randomized clinical trials showing the efficacy of MT for AIS, the rate of successful reperfusion (TICI 2b or 3) after MT was 70.5%, and the proportion of patients with an mRS score 0–2 at 90 days was higher in the intervention population (46.0%) than in the control population (26.5%; $P < 0.0001$).¹⁾ In the present study, the successful recanalization rate (75.1%), the proportion with an mRS score 0–2 at 90 days (38.6%), and the mortality rate at 90 days (10%) were comparable to previous reports. Although Goyal et al.¹⁾ reported no significant differences between groups in mortality at 90 days (15.3% in the intervention population vs 18.3% in the control population), mortality rates at 90 days after MT remained high (15.3–26.3%).^{1–3)} Thus it remains important to understand which factors are related to mortality despite successful MT.

SICH after MT reportedly occurred in 4.4–16.0% of patients.^{1, 2)} SICH following MT seems to be associated with mortality. Hao et al. reported that the 90-day mortality rate was higher in patients with SICH (65.3%, 66/101) than in patients without SICH (18.8%, 100/531).²⁾ Efforts should therefore be made to minimize the risk of SICH to improve the mortality rate after MT. Moser et al. undertook a large, real-world analysis, finding an overall risk reduction in hemorrhagic transformation in patients undergoing MT who received IOCM compared with those who received LOCM, with an absolute risk reduction of 4.6% ($P = 0.028$),⁶⁾ although these data seemed to include any hemorrhagic transformation, not only symptomatic, but also asymptomatic. In addition, the study data were obtained from the Premier Healthcare Database, a large, all-payer data base containing records from hospitals around the United States, primarily nonprofit, nongovernmental, community, teaching hospitals, and health care systems from rural and urban areas, and therefore the procedural details were not shown. From the perspective of clinical daily practice, SICH is much more important than asymptomatic ICH. However, in the present study, the rate of SICH was only 1% using IOCM and 10.5% using LOCM (significant difference, $p = 0.007$). Therefore, IOCMs such as iodixanol should be considered in the treatment of patients with MT for AIS to reduce mortality after MT.

Matusevicius et al.¹¹⁾ reported that $SBP \geq 160$ mmHg was associated with a greater frequency of SICH (OR 6.82, 95%CI 1.53–38.09) compared with the reference range of 100–119 mmHg with successful recanalization after MT and was associated with more SICH (OR 6.62, 95% CI 1.07–51.05) than the reference SBP of 120 to 139 mmHg with unsuccessful recanalization after MT. In contrast, Mazighi et al.¹²⁾ reported that an intensive SBP target of 100–129 mmHg after successful MT did not reduce radiographic intraparenchymal hemorrhage rates at 24–36 h compared with a standard-care SBP target of 130–185 mmHg. In the present study, SBP was controlled to within 100–139 mmHg during the initial 24 h after MT in successful recanalization cases and controlled to within 120–179 mmHg in unsuccessful recanalization cases. However, SICH still occurred in 5 (1 in IOCM, 4 in LOCM) successful

recanalization cases and did not occur in unsuccessful recanalization cases. Blood pressure control alone may not be enough to prevent SICH.

Another factor appeared to be the osmolality of contrast media. The reason why the osmolality of contrast media was associated with ICH was already reported in an animal study.⁶⁾ The effect could be due to its larger molecular size or a reduced hydrodynamic effect of its more viscous macromolecular properties, resulting in less leakage across the blood-brain barrier. LOCM with an osmolality between 600 and 800 mOsm/kg water are the most commonly used contrast agents in clinical practice. IOCM or third-generation contrast agents have similar osmolality to that of serum.¹⁵⁾ Becker et al.²⁸⁾ reported that on coronary CT angiography, IOCM produced less coronary arterial enhancement due to reduced opacification than LOCM. However, contrast media were injected with unequal iodine delivery rates. Marisa et al.²⁹⁾ reported that IOCM or third-generation contrast agents have similar osmolality to that of serum and opacification is not inferior to that of LOCM if injected at comparable iodine delivery rates. In this present study, although each contrast medium was injected manually, opacification of IOCM was similar to LOCM. It was speculated opacification may be associated with the quality of the angiography system in our angiosuite.

Morales et al. showed a significant reduction in cortical intracranial hemorrhage with the IOCM compared with the low-osmolar LOCM using a reperfusion rat model; and the presence of HT may represent a direct/indirect effect of radiographic CM in the brain parenchyma, with less impact of the IOCM compared with the LOCM^{13, 14)} In the present clinical study, the rate of SICH was only 1% using IOCM and 10.5% using LOCM. Therefore, IOCMs such as iodixanol may be considered in the treatment of patients with MT for AIS to reduce mortality by SICH after MT.

In a previous study reviewing successful recanalization cases after MT, overall incidence of SICH was 5.5%.⁷⁾ And Hao et al.²⁾ reported 612 patients treated with MT for AIS, that there was no difference in the incidence of SICH between patients with successful and failed reperfusion (5.3% vs. 4.5%, $p = 0.71$). Another report on risk factors of ICH after MT of anterior circulation AIS ($n = 612$), SICH with complete reperfusion (eTICI 3, 2.7%) were attributable to lower than SICH with subtotal recanalization (eTICI 2b and 2c, 7.0%), and there was no SICH in unsuccessful recanalization cases.²⁷⁾ In this study, including both successful and unsuccessful reperfusion cases, all SICH occurred in reperfusion patients (5/139, 3.6%). This may be attributed to the small number of cases. It is important to note, however, that SICH can occur regardless of whether recanalization is achieved.

In the report about the outcomes of AKI, the rate of death with no evidence of CI-AKI after contrast administration was 0.5%, whereas the mortality in those with CI-AKI was significantly higher (9.7%, $P < 0.001$).¹⁸⁾ In patients with normal renal function, the incidence of CI-AKI is estimated to be between 1% and 2%, and in patients with CKD, its incidence can be as high as 25%.^{19, 20)} Several clinical studies and meta-analyses have demonstrated lower incidences of adverse renal and cardiovascular outcomes associated with the use of IOCM than LOCM in patients undergoing intra-arterial interventional

procedures.^{21–25)} Prasad et al.²⁵⁾ reported that, in patients at high risk of AKI, the incidence of major adverse renal events (including AKI, development of end-stage kidney disease, and death from renal causes) was lower with the use of IOCM (ARR = 1.4%, $P = 0.0072$). In the present study, there were no CI-AKI in either contrast media group, and no cases of irreversible renal dysfunction or renal failure were observed. Although this may be attributed to the small number of cases, the use of IOCM for high-risk patients undergoing MT might be useful to prevent CI-AKI.

The correlation between the volume of contrast media administered and the risk of CI-AKI has been recognized, there was a 10-fold increase in volumes exceeding the Maximal Allowable Contrast Dose (MACD) compared with those who did not exceed the MACD (21% vs. 2%, $P < 0.001$).²⁶⁾ In the present study, the mean volume of contrast media was 127.3 mL (range 17–260 mL, Table 1), including 5 CKD patients, which did not exceed the MACD, and there were no cases of CI-AKI. The use of contrast media with the lowest possible dose of contrast medium might be useful to prevent CI-AKI.

Some limitations of the present study must be addressed when interpreting the results. The study used a retrospective design and included a relatively small number of cases. In the statistical analysis, propensity score–based adjustment could not be performed due to the limited number of cases and events. Prospective studies with a large number of patients to investigate the benefit of IOCM for patients undergoing MT are needed.

Conclusions

The use of IOCM was associated with an incidence of SICH after MT of only 1%, which is lower than that using LOCM, and adverse events were also fewer. These findings suggest that IOCM may be a safe option in MT for AIS.

Abbreviations

ADAPT

a direct aspiration first pass technique

ARR

absolute risk reduction

AIS

acute ischemic stroke

CI-AKI

contrast-induced acute kidney injury

CKD

chronic kidney disease

eTICI

expanded treatment in cerebral infarction

GFR

glomerular filtration rate
ICH
intracranial hemorrhage
IOCM
iso-osmolar contrast media
LOCM
low-osmolar contrast media
MACD
Maximal Allowable Contrast Dose
MT
mechanical thrombectomy
NIHSS
National Institutes of Health Stroke Scale
SCr
serum creatinine
SICH
symptomatic intracranial hemorrhage
SBP
Systolic blood pressure

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Tables

Tables 1 and 2 are available in the Supplementary Files section.

Figures

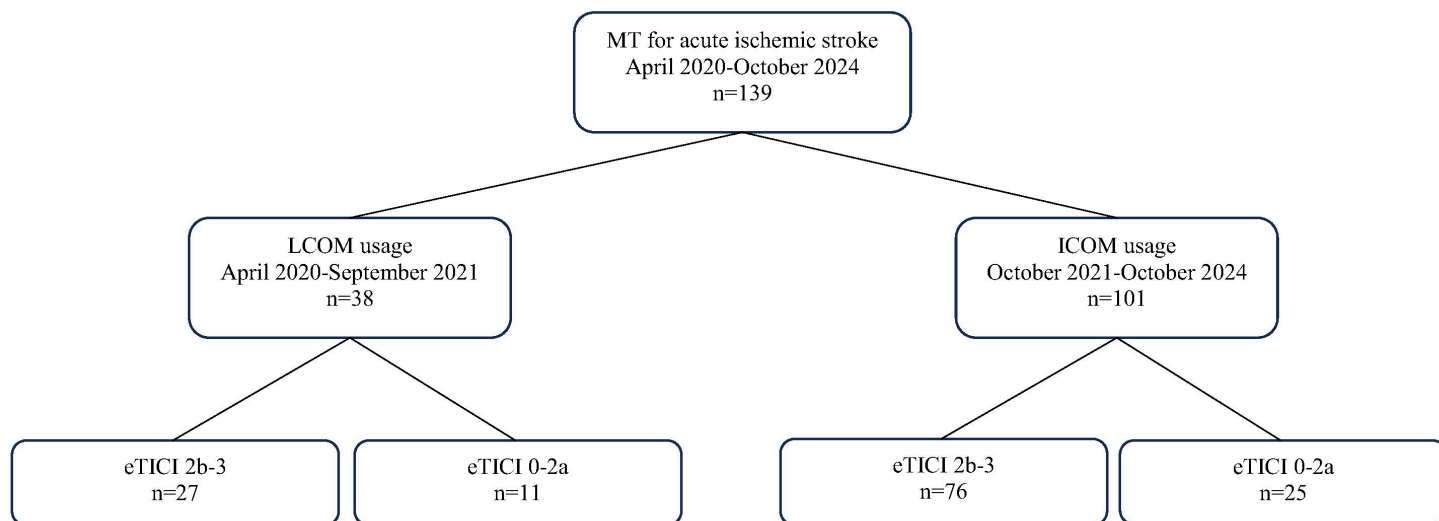


Figure 1

Flow chart for patients underwent MT for acute ischemic stroke. eTICI: expanded thrombolysis in cerebral infarction; ICOM: iso-osmolar contrast media; LCOM: low-osmolar contrast media; MT, mechanical thrombectomy

Supplementary Files

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- [Table.xlsx](#)