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Letter to the Editor: Assessing the Effect of Thrombectomy up to 24h After Onset of Stroke Requires Large, Prospective, International Studies

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► See the article “Improving the Prognosis of Patients With Acute Ischemic Stroke Treated in the Late Time Window After the Introduction of Advanced Imaging Software: Benefits From Thrombectomy in the Extended Time Window” in volume 37, number 50, e358.

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To the Editor

We read with interest the article by Ok et al.¹ about a retrospective, observational, single centre study on the effect of mechanical thrombectomy (MT) carried out up to 24 hours after clinical onset of ischemic stroke (n = 24, EMT group), with patients eligible for MT but receiving only standard medical treatment (n = 27, SMT group), and with patients undergoing MT within 6 hours after onset of stroke (n = 61, MTW6 group). It was found that EMT patients had a better prognosis than SMT patients but that the prognosis and outcome were similar between the EMT and MTW6 patients.¹ The study is appealing but carries limitations that raise concerns and should be discussed.

The main limitation of the study is its retrospective design. A retrospective design has the disadvantage that missing data can no longer be collected, that not all patients undergo the same diagnostic and therapeutic procedures according to a predefined protocol, and that patients are not available for re-investigation and re-evaluation.

A second limitation of the study is that group sizes in the SMT and the EMT group were very small.¹ These small group sizes significantly reduce the significance of the study. Comparing only 27 patients from the SMT group with 24 patients from the EMT group does not allow reliable conclusions regarding the outcome and prognosis.

A third limitation of the study is that prognosis and outcome of MT may not only depend on the applied technique, the expertise of the interventional radiologist, the latency between onset of the clinical manifestations and recanalization, but also on the occluded vessel and the distance between artery stem and location of occlusion. Therefore, the different number of patients in several subgroups (e.g. tandem stenosis [SMT n = 8] and EMT [n = 2]) limits the significance considerably.

A fourth limitation of the study is that the diagnosis was based on computed tomography (CT) evaluation but not on magnetic resonance imaging (MRI). Although we agree with the statement that performing an emergency MRI examination is challenging in many healthcare institutions,¹ MRI-based diagnosis of acute ischemic stroke is feasible and provides better results in some studies regarding diagnosis and outcome as compared with CT studies.

Surprisingly, no patients with an acute occlusion of the vertebral arteries were included. We should know whether and for what reason patients with vertebral artery occlusion were excluded from the evaluation or whether truly no occlusion of the vertebral arteries occurred during the observational period.

We also should know why only 9 patients of the 27 patients in the SMA group underwent thrombolysis with rtPA. All patients of this group reached the hospital within 12 hours after onset of neurological deficits. Did those not undergoing thrombolysis arrive too late to be eligible for thrombolysis? It would be also interesting to know in how many of the nine patients undergoing thrombolysis, recanalization could be achieved.

The number of patients with unknown onset of stroke is high in each group (SMT [n = 13], EMT [n = 21], MTW6 [n = 6]).¹ Did all these patients experience wake-up strokes or did that many strokes go unwitnessed?

Overall, the interesting study has limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could improve the study. To assess the effect of MT up to 24 hours after stroke onset, prospective, international, multi-centre studies with bigger group sizes are warranted.

Authors' Response to the Letter

Dear Editor:

Authors' Response to the Letter We appreciate your interest and helpful suggestions in our study.¹ As you mentioned, our study has limitations that are difficult to overcome due to its retrospective design and small number of subjects, which were already described in the discussion. If we were able to collect study subjects from multiple institutions and analyzed them, additional statistical analysis could be used to obtain more reliable results. However, it was difficult to enroll study subjects externally because few institutions were adopting the expanded indications for mechanical thrombectomy (MT) using advanced imaging software in South Korea.

There are many factors that can affect the prognosis of patients who have undergone MT, such as the experience of the operator, the location of the occluded cerebral artery, and the time taken from symptom onset to recanalization. In our hospital, stent-retriever and balloon guiding catheter were used as first line for MT. There was no change in this procedure policy during the study period, and the operators were the same. Since this study compared the standard medical treatment (SMT) group without MT and the extended MT (EMT) group, the time from symptom onset to recanalization was not appropriate to use as an independent variable to compare the prognosis between the two groups. It has been reported that more than 50% of patients with ischemic stroke who underwent MT with tandem occlusion had a

good prognosis.² This is similar to the result of other MT study.³ Therefore, it is highly likely that the results would not have been different even though the ratio of tandem occlusion was higher in the EMT group in this study.

According to a study conducted by the Korean Society of Interventional Neuroradiology, 69% of tertiary hospitals in South Korea operate a CT-based protocol to select patients for MT.⁴ Since there are no research results concluding any difference between MRI and CT-based protocols, each medical institution is operating a practically applicable protocol. Patients with vertebral artery occlusion were not excluded from our study. If there was only one vertebral artery occlusion with patent basilar artery blood flow through the contralateral vertebral artery, it might not be an indication for MT. Patients with basilar artery occlusion may be accompanied by vertebral artery occlusion, and it has been reported that 20–25% of patients with basilar artery occlusion are accompanied by vertebral artery occlusion.^{5,6} In our study, there were patients who had vertebral artery occlusion along with basilar artery occlusion, but these were not classified separately. In other MT studies targeting patients with basilar artery occlusion, they also classified the patients as vertebrobasilar artery occlusion without separating the patients with vertebral artery occlusion.⁷

Intravenous tissue plasminogen activator (tPA) can be administered within 4.5 hours of the onset of the neurological deficit.⁸ Nine out of 27 patients in the SMT group met the tPA time indication, and 18 patients visited the hospital outside the time window. There were patients with thrombus migration after tPA treatment, but none with complete recanalization. A wake-up stroke is defined as an absence of symptoms prior to falling asleep, followed by awakening with stroke symptoms. In our study, 7 out of 13 patients from the SMT group, 11 out of 21 patients from the EMT group, and 2 out of 6 patients from the MT within 6 hours (MTW6) group corresponded to wake-up stroke, without any statistically significant difference.

Although we cited the results of real-world studies on the prognosis of MT with extended indications,^{9,10} not much related research has been reported yet. Therefore, as suggested by Dr. Finsterer, it is expected that better research results can be obtained by collecting and analyzing the data from multiple institutions in the future.

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