Endovascular Treatment in Acute Ischemic Stroke Adoption and Practice: A Single-Center Indonesian Experience

Taufik Mesiano a, Mohammad Kurniawan a, Kevin M. Saputri a, Rakhmad Hidayat a, Affan P. Permana b, Al Rasyid a, Salim Harris a

aDivision of Neurovascular and Neurosonology, Department of Neurology, Faculty of Medicine, University of Indonesia, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia; bDivision of Vascular, Department of Neurosurgery, Faculty of Medicine, University of Indonesia, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia

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Abstract
Indonesia is facing increasing stroke prevalence in the past 5 years. Ischemic stroke imposes economic and productivity burden if it is not addressed properly. Endovascular treatment studies are conducted in developed countries where facilities and cost do not count in therapy consideration if it is indicated. Developing countries like Indonesia should work hard to provide the best hyperacute stroke care with protocol deviation and limitation. This is the first review on endovascular treatment practice in a top single-center hospital in Indonesia. Further improvement is needed to catch up with state-of-the-art hyperacute ischemic stroke treatment.

Burden of Disease
Stroke is prevalent in both developed and developing countries and causes significant mortality and morbidity. This is a cardiovascular disease and is the main cause of death in Indonesia [1]. Its prevalence increased from 7% in 2013 to 10.9% in 2018 [1]. Two-thirds of stroke cases in Indonesia were ischemic stroke, where small vessel occlusion and large artery atherosclerosis were the main subtypes [2, 3].

Organization of Services/Care
Dr. Cipto Mangunkusumo Hospital is the top referral hospital in Jakarta, Indonesia. A “Code Stroke” team was developed to provide speeding hyperacute stroke service in our hospital [4]. Consultants and residents of the neurology, neurosurgery, radiology, and emergency departments; nurses; radiographers; and pharmacists worked together and simultaneously. The hospital marked its first intravenous thrombolysis (IVT) in 2014 and endovascular therapy (EVT) in 2017.
The inclusion criteria are adults aged at least 18 years, known onset within 6 h before admission, and no hyper-density on baseline noncontrast CT scan. The exclusion criteria are wake-up stroke, modified Rankin scale ≥2, major trauma within 3 months, and bleeding diathesis. Pre-procedural written informed consent, including granted data for research purpose statement, was obtained from spouses or family members. The dose of IVT (recombinant tissue plasminogen activator) used in our center is 0.6 mg/kgBW, of which 10% dose is given in bolus and the rest is given evenly within 1 h.

Mechanical thrombectomy is considered when patients present with National Institutes of Health Stroke Scale (NIHSS) ≥6 and Alberta Stroke Program Early CT Score (ASPECTS) ≥6. Advanced perfusion imaging, such as CT angiogram and CT perfusion, is not readily available; therefore, no baseline collateral and penumbra volume is known before reperfusion therapy. The procedures were performed by a trained neurointerventionalist team consisting of 2 neurologists and 1 neurosurgeon. The right femoral artery is chosen for arteriotomy access. The routine EVT technique performed in our center is

### Table 1. Subject characteristics based on therapy allocation (n = 29)

|                          | IVT and EVT (n = 14) | EVT only (n = 15) |
|--------------------------|----------------------|------------------|
| Demographic characteristics |                      |                  |
| Age, yr*                 | 56.50 (37.00–85.00)  | 55.00 (38.00–79.00) |
| Male†                    | 6 (42.9)             | 13 (86.7)        |
| Past medical history     |                      |                  |
| Hypertension†            | 9 (64.3)             | 8 (53.3)         |
| Diabetes†                | 3 (21.4)             | 5 (33.3)         |
| Dyslipidemia†            | 1 (7.1)              | 4 (26.7)         |
| Atrial fibrillation†     | 2 (14.3)             | 5 (33.3)         |
| CHF†                     | 5 (35.7)             | 7 (46.7)         |
| CAD†                     | 0 (0)                | 5 (33.3)         |
| Smoking†                 | 6 (42.9)             | 8 (53.3)         |
| Baseline clinical charac- |                      |                  |
| teristics               |                      |                  |
| NIHSS*                   | 13.00 (10.00–21.00)  | 13.00 (3.00–24.00) |
| Blood glucose, mg/dL*    | 133.00 (90.00–370.00)| 137.00 (86.00–483.00) |
| Imaging characteristics  |                      |                  |
| ASPECTS*                 | 8.00 (5.00–10.00)    | 9.00 (5.00–10.00) |
| MCA sign†                | 5 (35.7)             | 7 (46.7)         |
| Insular effacement†      | 9 (64.3)             | 10 (66.7)        |
| Occlusion location†      |                      |                  |
| Internal carotid artery  | 2 (14.3)             | 4 (26.7)         |
| MCA M segment            | 5 (35.7)             | 5 (33.3)         |
| MCA M2 segment           | 7 (50.0)             | 3 (20.0)         |
| Verteobasilar artery     | 0 (0)                | 3 (20.0)         |
| HT†                      | 11 (78.6)            | 7 (46.7)         |
| Treatment details        |                      |                  |
| Process time, min        |                      |                  |
| Onset*                   | 105.00 (30.00–210.00)| 180.00 (30.00–480.00) |
| <3 h†                    | 11 (78.6)            | 8 (53.3)         |
| 3–4.5 h†                 | 3 (21.4)             | 4 (26.7)         |
| >4.5 h†                  | 0 (0)                | 3 (33.3)         |
| Onset to puncture*       | 358.00 (193.00–683.00)| 360.00 (177.00–780.00) |
| Onset to recanalization* | 414.00 (214.00–755.00)| 454.00 (272.00–890.00) |
| mTICI 2b/3†              | 7 (50.0)             | 8 (53.3)         |
| Dead on discharge*       | 3 (21.4)             | 3 (20.0)         |

CAD, coronary artery disease; CHF, chronic heart failure; EVT, endovascular therapy; IVT, intravenous thrombolysis; MCA, middle cerebral artery; mTICI, modified TICI; HT, hemorrhagic transformation. * Data are median values with minimum-maximum values in parentheses. † Data are actual value with percentage in parentheses.
carried out using stent retriever with the Solitaire™ FR revascularization device (Micro Therapeutics Inc., Irvine, CA, USA). The recanalization rate is determined with modified TICI scores of 0, 1/2a, and 2b/3. Follow-up non-contrast CT scan is ordered within 24 h after performing EVT. Standard medical therapy in concordance to national guidelines is given to all patients. Expenses are covered by the Indonesian National Health Insurance Program.

Given these resource limitations and deviations as opposed to the strict criteria published in guidelines and studies conducted in developed countries, we conducted a review on our EVT with or without bridging IVT single hospital experience from May 2017 to January 2020. There were 19 men and 10 women included in this study. Patients who underwent EVT with and without bridging IVT were compared (Table 1). Men were twice more likely to undergo EVT only. Traditional risk factors were comparable between the 2 groups. Nevertheless, thrombectomy was chosen for all patients with known CAD, while combination therapy was more likely to be offered to those without prior CAD.
No AIS patient presenting with over 4.5 h of symptom onset was given bridging IVT, while a third patient who underwent EVT presented with a 4.5-to-6-h onset. Combination therapy was assigned to an earlier median stroke onset, but the onset to puncture time was similar within both groups. Furthermore, 11 of 18 patients having hemorrhagic transformation (HT) were assigned to combination therapy. Bridging IVT was observed with a higher trend of HT.

The incidence of HT was 62.1%, where 7 patients had parenchymal hematoma requiring surgical decompression and 11 patients had hemorrhagic infarction. Patients with no previous CAD were more likely to develop HT. In this kind of population, HT was experienced in 11 out of 14 patients (78.6%) who had prior thrombolysis and 60% who underwent EVT alone. Among 5 patients with known CAD, only 1 (20%) experienced HT.

Most of the patients with HT presented within 3 h of symptom onset but required longer time to recanalization. Although the difference was statistically not significant, the proportion of concurrent IVT and unsuccessful recanalization rate were higher in the HT group (Table 2). Both M1 and M2 MCA segments were the most common occluded locations, where M1 segment was more prevalent in the HT group and M2 segment accounted for more than half in the non-HT group.

Endovascular treatment challenges faced in developing countries are limited number of neurointerventionalists, high cost, weaknesses in the referral system, and challenges in managing hospital facilities [5]. Major studies highlight the importance of perfusion imaging to delineate salvageable penumbra tissue. Yet, adoption and application of perfusion imaging in developing countries like Indonesia is limited by its added cost and small availability. Health-care appliances, including endovascular device, are more expensive here due to the added import “luxury” tax.

Time-delay origins can be multifactorial. First, earlier onset time imposes less pressure on the team and produces minute delay from drug order until administration. A shorter residual window period raises a more “urgent feeling” for treating physicians. It should be warranted that all patients receive similar teamwork speed regardless of their symptom onset time. Second, informed consent was obtained twice for IVT and EVT. Arterial catheter insertion was interpreted as “more invasive.” Final consent was often huddled up by kinship and mutual family consideration [6]. Third, there is still no dedicated thrombectomy suite in our hospital. Thrombectomy is often held up by ongoing cardiac procedure.

Future Directions

To the best of our knowledge, this was the first retrospective review of EVT practice based on the Indonesian population. Our sample size was small and it was based in a single top referral center, which limited its generalizability. Our findings advocate further efficiency to limit intra-hospital delay. Government advocacy and the Indonesian Neurological Association support are warranted to improve hyperacute ischemic stroke treatment in the future. Endovascular treatment inclusion criteria and workflow should be adjusted to available local facility. It is also imperative to collaborate data with other Indonesian hospitals with larger sample size.

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Statement of Ethics

Informed consent was not needed because data were collected from medical records. Ethical approval was obtained from Faculty of Medicine, University of Indonesia, Ethical Committee Number 20-09-1013.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Taufik Mesiano: main idea, data collection, data analysis, data interpretation, and composing the text. Mohammad Kurniawan: data collection, data analysis, data interpretation, and composing the text. Kevin Mulya Saputri: data collection, data analysis, data interpretation, and composing the text. Rakhmad Hidayat: data analysis, data interpretation, and composing the text. Affan P. Permana: data interpretation and composing the text. Al Rasyid: data interpretation and composing the text. Salim Harris: data analysis, data interpretation, and composing the text.
References

1. Kementerian Kesehatan Badan Penelitian dan Pengembangan Kesehatan. Hasil utama Riskesdas 2018 [Internet]. Kementerian Kesehatan RI; 2018 [cited 2020 Jul 20]. Available from: https://www.kemkes.go.id/resources/download/info-terkini/hasil-riskesdas-2018.pdf.

2. Kim BJ, Kim JS. Ischemic stroke subtype classification: an asian viewpoint. J Stroke. 2014;16(1):8.

3. Harris S, Kurniawan M, Rasyid A, Mesiano T, Hidayat R. Cerebral small vessel disease in Indonesia: lacunar infarction study from Indonesian stroke registry 2012–2014. Sage Open Med. 2018 Jun 20;6:2050312118784312.

4. Hidayat R, Fattah Yasfi H, Diafiri D, Eddy Yunos R, Ade Wijaya Ramlan A, Mesiano T, et al. Membangun sistem code stroke pada dua rumah sakit pendidikan di Indonesia. Neurona. 2020.

5. Tsang ACO, Yang I-H, Orru E, Nguyen Q-A, Pamatmat RV, Medhi G, et al. Overview of endovascular thrombectomy accessibility gap for acute ischemic stroke in Asia: a multi-national survey. Int J Stroke. 2020 Jul;15(5):516–20.

6. Chai E, Li C, Jiang L. Factors affecting in-hospital delay of intravenous thrombolysis for acute ischemic stroke: a retrospective cohort study. Medicine. 2019 May;98(19):e15422.