JoS JOURNAL OF STROKE

Journal of Stroke 2021;23(1):139-143
https://doi.org/10.5853/jos.2020.05043

Letter to the Editor

Health Economic Impact of First Pass Success: An Asia-Pacific Cost Analysis of the ARISE II Study

Leonard Yeo,[a,b] Osama O. Zaidat,[c] Jeffrey L. Saver,[d] Heinrich P. Mattle,[e] Stephanie Hsiao Yu Lee,[f] Emilie Kottenmeier,[g] Heather L. Cameron,[h] Rana A. Qadeer,[h] Tommy Andersson[i,j]

[a]Division of Neurology, National University Health System, Singapore
[b]Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[c]Department of Neuroscience, Mercy Health St. Vincent Mercy Hospital, Toledo, OH, USA
[d]Department of Neurology, University of California Los Angeles, Los Angeles, CA, USA
[e]Department of Neurology, Inselspital, University of Bern, Bern, Switzerland
[f]Johnson & Johnson Medical Asia Pacific, Singapore
[g]Cerenovus, Johnson & Johnson, Irvine, CA, USA
[h]EVERSANA, Burlington, ON, Canada
[i]Departments of Neuroradiology, Karolinska University Hospital and Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden
[j]Department of Medical Imaging, AZ Groeninge, Kortrijk, Belgium

Dear Sir:

The first pass effect (FPE) is an independent predictor of good functional outcomes (modified Rankin Scale [mRS] 0–2) and is associated with reduced 90-day mortality.[1] However, the economic impact of FPE has not been evaluated in the Asia-Pacific (APAC) region. This analysis assessed the procedural/hospitalization-related and long-term care economic impact of achieving FPE in patients with acute ischemic stroke in Australia, India, Japan, South Korea, Singapore, and Taiwan.

A detailed description of the methods can be found in Supplementary methods. Briefly, *post hoc* analyses were conducted using patient-level data from the 227 patients in the Analysis of Revascularization in Ischemic Stroke With EmboTrap (ARISE) II study, a prospective single-arm international multi-center clinical trial investigating the efficacy and safety of the EmboTrap device (Cerenovus, Irvine, CA, USA).[2] FPE was defined as restoring complete or near complete reperfusion (modified Thrombolysis in Cerebral Infarction [mTICI] 2c–3) in a single pass with the EmboTrap device. The target population comprised patients who achieved mTICI 2c–3 (n=172), stratified into two groups: FPE (mTICI 2c–3 after the first pass) and non-FPE (mTICI 2c–3 after multiple passes). Primary analyses were conducted in two steps. First, clinical and healthcare resource use data from the ARISE II study were evaluated for the FPE and non-FPE groups. Second, cost data from peer-reviewed literature or market research (Supplementary Table 1) were applied to healthcare resource use data from the ARISE II study to assess cost consequences in each group using two time-horizons to accommodate two different perspectives: (1) procedural/hospitalization-related (i.e., length of stay [LOS], standard bed days, intensive care unit [ICU] days, and procedural devices used) assessing costs from the healthcare provider perspective; and (2) long-term care costs based on 90-day mRS (*per annum* for Australia, Japan, and South Korea; 6 months for India) assessing costs from the payer perspective. All costs were reported as 2020 currencies or 2020 United States dollar (USD) except Singapore (2019 currencies) and were inflated using country-specific inflation indices. Sensitivity analyses, varying key input parameters (i.e., alternative definitions for FPE ["FPE, mTICI 3" and "FPE, mTICI 2b–3"], LOS, healthcare resource costs, and inclusion of costs for mRS 6), were conducted to test the robustness of the results.

Complete or near-complete reperfusion (mTICI 2c–3) was observed in 76% of the patients (n=172) in the ARISE II study. Among patients that achieved mTICI 2c–3, 53% (n=91) achieved FPE. Baseline characteristics were balanced between the FPE and non-FPE groups (Supplementary Table 2). Patients in the FPE group had better clinical outcomes (Supplementary Table 3). Furthermore, patients who achieved FPE required a

single EmboTrap device whereas 35% of patients in the non-FPE group required additional devices such as other stent retrievers and/or aspiration catheters. Patients in the FPE group had a significantly shorter mean LOS (6.10 days [interquartile range (IQR), 3.00 to 8.00] vs. 9.48 days [IQR, 3.00 to 11.00], $P<0.01$) and spent significantly fewer mean number of days in a standard bed (3.05 [IQR, 0.00 to 5.00] vs. 6.13 [IQR, 1.00 to 8.00], $P<0.01$). The mean number of days spent in the ICU (3.39

	Australia (2020 AUD)	India (2020 INR)	Japan (2020 ¥)	South Korea (2020 ₩)	Singapore (2019 SGD)*	Taiwan (2020 TWD)
Difference, LOS (original currencies)	-AUD 5,987	-INR 11,404	-¥118,695	-₩1,274,291	-SGD 3,367	-TWD 17,299
Difference, devices/methods (original currencies)	-AUD 2,634	-INR 56,314	-¥120,797	-₩729,856	-SGD 2,177	-TWD 24,612
Difference, total (original currencies)	-AUD 8,621	-INR 67,718	-¥239,493	-₩2,004,146	-SGD 5,544	-TWD 41,911
Difference, total (2020 USD)†	-$5,951	-$894	-$2,241	-$1,655	-$3,981	-$1,416
Percent cost savings for the FPE group	32%	27%	30%	31%	31%	29%

Figure 1. Estimated per-patient procedural and hospitalization-related healthcare use cost savings for the first pass effect (FPE) and non-FPE groups. Negative values represent cost savings for patients in the FPE group as compared with the non-FPE group. Numbers may not sum due to rounding. AUD, Australian dollar; INR, Indian rupee; SGD, Singapore dollar; TWD, Taiwan dollar; LOS, length of stay; USD, United States dollar. *Reported as charges; †Reported as 2019 USD for Singapore. Exchange rates reported for June 22, 2020 16:00 Coordinated Universal Time (UTC) were used for all countries. The exchange rates were as follows: 1.00 AUD:0.69 USD; 1.00 INR:0.01 USD; 1.00 JPY:0.01 USD; 1.00 ₩:0.001 USD; 1.00 SGD:0.72 USD; and 1.00 TWD:0.03 USD.

https://doi.org/10.5853//jos.2020.05043

	% Achieving mRS score		Average long-term care costs/mRS score by country			
	FPE (n=91)	Non-FPE (n=81)	Australia (annual) (2020 AUD)	India (6-mo) (2020 INR)	Japan (annual) (2020 ¥)	South Korea (annual) (2020 ₩)
mRS						
0	41.38%	19.48%	AUD 11,846	INR 74,030	¥775,354	₩14,416,468
1	21.84%	27.27%	AUD 14,927	INR 85,482	¥1,661,827	₩16,928,191
2	17.24%	14.29%	AUD 17,988	INR 115,907	¥3,292,456	₩28,055,626
3	9.20%	7.79%	AUD 19,790	INR 105,956	¥4,011,676	₩48,953,557
4	2.30%	11.69%	AUD 23,436	INR 119,387	¥4,339,415	₩78,744,490
5	2.30%	5.19%	AUD 27,269	INR 184,308	¥4,831,394	₩86,834,243
6	5.75%	14.29%	AUD 0	INR 0*	¥0	₩0†
Results by country						
FPE (n=91)			AUD 14,248	INR 86,010	¥1,831,141	₩22,807,458
Non-FPE (n=81)			AUD 14,646	INR 86,078	¥2,145,403	₩28,962,463
Difference (original currencies)			-AUD 398	-INR 68	-¥314,262	-₩6,155,006
Difference (2020 USD)†			-$275	-$1	-$2,941	-$5,084
Percent cost savings for the FPE group			3%	0.1%	15%	21%

Figure 2. Estimated per-patient long-time care cost savings, based on 90-day modified Rankin Scale (mRS), for the first pass effect (FPE) and non-FPE groups. Negative values represent cost savings for patients in the FPE group as compared with the non-FPE group. Numbers may not sum due to rounding. AUD, Australian dollar; INR, Indian rupee; USD, United States dollar. *Reported for India and South Korea but not used for analyses to ensure consistency with other countries that did not report a cost for death (i.e., mRS 6); †Exchange rates reported for June 22, 2020 16:00 Coordinated Universal Time (UTC) were used for all countries. The exchange rates were as follows: 1.00 AUD:0.69 USD; 1.00 INR:0.01 USD; 1.00 JPY:0.01 USD; and 1.00 ₩:0.001 USD.

[IQR, 2.00 to 4.00] vs. 3.58 [IQR, 2.00 to 4.00], *P*=0.70) was similar between groups. Achieving FPE led to estimated per-patient procedural/hospitalization-related cost savings in every country studied (8,621 Australian dollar [AUD] or $5,951 USD for Australia, 67,718 Indian rupee [INR] or $894 USD for India, ¥239,493 or $2,241 USD for Japan, ₩2,004,146 or $1,655 USD for South Korea, 5,544 Singapore dollar [SGD] or $3,981 USD for Singapore, and 41,911 Taiwan dollar [TWD] or $1,416 USD for Taiwan) (Figure 1). Similarly, achieving FPE led to estimated per-patient long-term care cost savings in every country studied (398 AUD or $275 USD for Australia, 68 INR or $1 USD for India, ¥314,262 or $2,941 USD for Japan, and ₩6,155,006 or $5,084 USD for South Korea) (Figure 2). Results from the sensitivity analyses were consistent with the primary analyses; notably, inclusion of costs for mRS 6 resulted in long-term care cost savings of 13,353 INR for India and ₩8,359,695 for South Korea (Supplementary Table 4).

This study demonstrated that achieving FPE led to potential per-patient procedural/hospitalization-related cost savings, which is especially meaningful for healthcare systems that pay hospitals on the basis of diagnosis-related groups or related payment models. These potential cost savings were largely driven by improvements in clinical outcomes; research has shown that increases in mean LOS are directly correlated with mRS evaluated 90 days after a stroke.[3] The potential long-term care cost savings from improvements in functional outcomes are linked to reduced healthcare resource use and decreased costs for patients surviving stroke.[4] Our findings are aligned with a cost-effectiveness analysis that showed that achieving expanded Thrombolysis in Cerebral Infarction (eTICI) 3 resulted in more quality-adjusted life years, as well as healthcare and societal cost savings compared with achieving eTICI 2b among patients with large vessel occlusions.[5]

There are several factors related to the treating physician (e.g., training), setting (e.g., available equipment), and patient (e.g., clot composition) that may impact the ability to achieve FPE; however, techniques involving the combined use of stent retrievers and other devices (e.g., intermediate catheters) may improve recanalization rates and the rate of FPE.[6,7] As such, it may be beneficial to use techniques involving multiple devices immediately rather than beginning with a single device approach and gradually combining additional devices to achieve reperfusion after initial failure.

This study had some limitations. First, healthcare resource use collected from clinical trials may not reflect the real-world setting. It is plausible that costs calculated from ARISE II resource utilization may be different in Asia due to variations in clinical practice or population-specific factors. Although sensitivity analyses assessing differences by ethnic groups/regions were considered, such analyses were not feasible due to small sample sizes. Second, the ARISE II study did not report cost data; as such, costs were obtained from peer-reviewed literature or market research, limiting validity. However, this study used the best available estimates, which were validated by clinical experts in interviews.

In conclusion, achieving FPE led to potential procedural/hospitalization-related and long-term care cost savings in the APAC region in addition to clinical benefits. As such, achieving reperfusion with a single pass is a relevant goal for endovascular treatment of acute ischemic stroke with holistic benefits.

Supplementary materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2020.05043.

References

1. Zaidat OO, Castonguay AC, Linfante I, Gupta R, Martin CO, Holloway WE, et al. First pass effect: a new measure for stroke thrombectomy devices. *Stroke* 2018;49:660-666.
2. Zaidat OO, Bozorgchami H, Ribó M, Saver JL, Mattle HP, Chapot R, et al. Primary results of the multicenter ARISE II study (Analysis of Revascularization in Ischemic Stroke With EmboTrap). *Stroke* 2018;49:1107-1115.
3. Dawson J, Lees JS, Chang TP, Walters MR, Ali M, Davis SM, et al. Association between disability measures and healthcare costs after initial treatment for acute stroke. *Stroke* 2007;38:1893-1898.
4. Lobotesis K, Veltkamp R, Carpenter IH, Claxton LM, Saver JL, Hodgson R. Cost-effectiveness of stent-retriever thrombectomy in combination with IV t-PA compared with IV t-PA alone for acute ischemic stroke in the UK. *J Med Econ* 2016;19:785-794.
5. Kunz WG, Almekhlafi MA, Menon BK, Saver JL, Hunink MG, Dippel DWJ, et al. Public health and cost benefits of successful reperfusion after thrombectomy for stroke. *Stroke* 2020;51:899-907.
6. Maegerlein C, Berndt MT, Mönch S, Kreiser K, Boeckh-Behrens T, Lehm M, et al. Further development of combined techniques using stent retrievers, aspiration catheters and BGC: The PROTECTPLUS Technique. *Clin Neuroradiol* 2020;30:59-65.
7. Delgado Almandoz JE, Kayan Y, Young ML, Fease JL, Scholz JM, Milner AM, et al. Comparison of clinical outcomes in patients with acute ischemic strokes treated with mechanical

thrombectomy using either Solumbra or ADAPT techniques. *J Neurointerv Surg* 2016;8:1123-1128.

Correspondence: Leonard Yeo
National University Hospital, Kent Ridge Wing, Level 4, 5 Lower Kent Ridge Road, 119074, Singapore
Tel: +65-6779-5555
Fax: +65-6872-4101
E-mail: leonard_ll_yeo@nuhs.edu.sg
https://orcid.org/0000-0002-4249-0402

Received: December 17, 2020
Revised: December 17, 2020
Accepted: December 29, 2020

This study was funded by Cerenovus, a subsidiary of Johnson and Johnson.

Leonard Yeo is a consultant for Stryker and See-mode. Leonard Yeo has equity in Cereflo; Osama O. Zaidat is a consultant for Neuravi, Stryker, Penumbra, and Medtronic; Jeffrey L. Saver is an employee of the University of California, which holds a patent on retriever devices for stroke. The University of California, Regents receives funding for Jeffrey L. Saver's services as a scientific consultant regarding trial design and conduct to Covidien/Medtronic and Stryker. Jeffrey L. Saver serves as a consultant (modest) for Abbott, Medtronic, Stryker, and Neuravi/Cerenovus. Jeffrey L. Saver also has contracted stock options (modest) for Rapid Medical; Heinrich P. Mattle reports personal fees from Covidien/Medtronic, personal fees from Neuravi/Cerenovus, personal fees from Servier, and personal fees from Bayer outside the submitted work; served on the steering committees of the SWIFT PRIME and ARISE studies; Stephanie Hsiao Yu Lee and Emilie Kottenmeier are employees of Johnson and Johnson; Heather L. Cameron and Rana A. Qadeer are paid consultants for Cerenovus; Tommy Andersson is a consultant for Neuravi/Cerenovus, Anaconda, Amnis Therapeutics, and Rapid Medical; served on the steering committees of the ARISE studies.

Supplementary methods

Primary data source

Post hoc analyses were conducted using patient-level data from the 227 patients in the Analysis of Revascularization in Ischemic Stroke With EmboTrap (ARISE) II study, a prospective single-arm international multi-center clinical trial investigating the efficacy and safety of the EmboTrap device (Cerenovus, Irvine, CA, USA).[1]

Target population

In accordance with the ARISE II study,[1] first pass effect (FPE) was defined as complete or near complete reperfusion (modified Thrombolysis in Cerebral Infarction [mTICI] 2c–3) after the first pass of the EmboTrap device; alternative definitions for FPE were explored in sensitivity analyses. The target population comprised of patients who achieved mTICI 2c–3 (n=172) and patients who did not achieve mTICI 2c–3 (n=55) were excluded from the primary analyses to avoid potential biases. The target population was then stratified into two groups: FPE group (achieved mTICI 2c–3 after the first pass) and non-FPE group (achieved mTICI 2c–3 after multiple passes). The two groups were defined based on the mTICI score measured after the first pass and the subsequent total number of passes after the first pass did not impact categorization.

Primary analyses

Primary analyses were conducted in two steps. First, clinical and healthcare resource use data from the ARISE II study (i.e., baseline characteristics, clinical outcomes, and healthcare resource used) were evaluated for the FPE and non-FPE groups. Second, cost data from peer-reviewed literature or market research were applied to data from the ARISE II study to assess cost consequences among the two groups.

Baseline characteristics

Baseline characteristics (i.e., patient demographics, vascular risk factors, clinical presentation, occlusion location, and procedural factors) were compared between the FPE and non-FPE groups to examine potential bias.

Clinical outcomes

The clinical outcomes included mTICI score after each pass and the procedure, 90-day modified Rankin Scale (mRS; categorized into good [mRS 0–2] and excellent [mRS 0–1] functional outcomes), 90-day mortality, occurrence of symptomatic intracranial hemorrhage within 24 hours post-procedure based on the Heidelberg Bleeding Classification, and embolization into new territory assessed at 7-day post-procedure.

Healthcare resource use

Procedural/hospitalization-related healthcare resources, associated with the initial stroke event, included total length of stay (LOS), days in the intensive care unit, standard bed days, and procedural device use (stent retrievers and aspiration devices).

Economic outcomes

Cost analyses included comparison of cost consequences between the FPE and non-FPE groups from the perspective of six countries (Australia, India, Japan, South Korea, Singapore, and Taiwan) in the Asia-Pacific (APAC) region. These analyses used two time-horizons and perspectives: (1) procedural/hospitalization-related costs were compared from the healthcare provider perspective and (2) long-term care costs after the initial stroke event were compared from the payer perspective. All costs were reported as 2020 currencies or 2020 United States dollar (USD) except Singapore (reported as 2019 currencies) and were inflated using country specific inflation indices if required. Exchange rates were used to convert original currencies to USD for all countries.

The procedural/hospitalization-related economic impact was assessed in four steps. First, the procedural/hospitalization-related healthcare use (i.e., total LOS and procedural devices used) data were obtained for the FPE and non-FPE groups from the ARISE II study. Second, country-specific costs from a provider perspective were obtained from peer-reviewed literature or market research reports.[2-9] The LOS costs were based on resources used during the hospitalization period (i.e., direct medical costs such as salaries and wages, medical supplies, pharmaceuticals, examinations, and imaging) (Supplementary Table 1). Third, the country-specific costs were applied to the procedural/hospitalization-related healthcare use data to obtain per-patient procedural/hospitalization-related costs for the FPE and non-FPE groups. Fourth, per-patient incremental differences between the FPE and non-FPE groups were calculated.

Long-term care economic impact, based on the 90-day mRS, was also calculated in four steps. First, the proportions of patients achieving each level of mRS score (i.e., mRS 0 to 6) at 90 days, stratified by FPE status, were obtained from the ARISE II study. Second, country-specific costs for long-term care from a payer perspective, based on 90-day mRS scores, were obtained from the published literature.[5,10-12] The resources captured in the long-term care costs generally included direct medical costs (e.g., rehabilitation, aged/long-term care facilities, general practice visits, and special consultations); however, the long-

term care costs for India also included direct non-medical (e.g., relocation expenses, and costs of making changes to one's diet, house, car, or related items) and indirect (e.g., production value lost to society due to absence from work) costs. Additionally, while the long-term care costs for Australia, Japan, and South Korea were on a *per annum* basis, the costs for India were for 6 months. Notably, in the base case, costs for mRS 6 were excluded from the analyses for India and South Korea to ensure consistency with other countries that did not report costs for death (i.e., mRS 6). Long-term care costs were not found for Singapore and Taiwan. Third, country-specific costs were applied to the proportions of patients achieving each level of mRS score to obtain per-patient long-term care costs for the FPE and non-FPE groups. Fourth, per-patient incremental differences between the FPE and non-FPE groups were calculated.

Sensitivity analyses

Deterministic sensitivity analyses, varying key input parameters, were conducted to test the robustness of the results. These analyses included two alternative definitions for FPE: (1) "FPE (mTICI 3)," defined as achieving mTICI 3 after the first pass and (2) "FPE (mTICI 2b–3)," defined as achieving mTICI 2b–3 after the first pass. When these alternative definitions were assessed, the target population was modified accordingly (e.g., patients in whom mTICI 2b–3 was not achieved were excluded from the analyses when the definition of FPE was changed to FPE [mTICI 2b–3]). Additional sensitivity analyses included variations in total LOS around its interquartile range (IQR), variations in healthcare resource costs by 20% (i.e., increased and decreased by 20%), and inclusion of costs for mRS 6 in long-term care costs for India and South Korea (only countries that reported these costs). Other sensitivity analyses assessing differences by ethnic groups/regions and occlusion locations (i.e., anterior vs. posterior) were considered but were not feasible due to small sample sizes.

Statistical analyses

Categorical variables were described using the number of observations and relevant proportions, while continuous variables were described using the mean or median and standard deviation (SD) or IQR, respectively. Statistical differences between the FPE and non-FPE groups were determined using t-tests or Wilcoxon rank-sum (Mann-Whitney) tests for continuous data and chi-square or Fisher's exact test for categorical data. Differences between groups were considered statistically significantly different when *P*-values were less than 0.05. All statistical analyses of the ARISE II data were performed using Stata version 15 (StataCorp., College Station, TX, USA).

https://doi.org/10.5853//jos.2020.05043

Supplementary Table 1. Sources used to obtain costs for analyses

Study	Country	Currency	Components included in costs	Cost (original currency)	Cost (2020 currency)
LOS cost per day					
Cadilhac et al. (2019)[4]	Australia	2010 AUD	Clinical costing data from hospitals (e.g., salaries and wages, medical supplies, pharmaceuticals, pathology equipment, imaging, hotel expenses, and indirect costs such as administration, research, and training)	AUD 1,192.15	AUD 1,771.34
Kwatra et al. (2013)[5]	India	2013 INR	Direct medical costs for inpatient care (hospitalization expenses including investigations)	INR 2,388.15	INR 3,373.93
Yoneda et al. (2005)[6]	Japan	2002 ¥	Direct medical costs for beds, staffs, examinations, medications including surgical procedures, rehabilitation, and other minor miscellaneous expenses such as commissions	¥33,075.00	¥35,116.98
Jeong et al. (2017)[7]	South Korea	2017 ₩	Acute care costs for room, neurological/physical examination, medication/injection, bed-side rehabilitation, laboratory test, and imaging studies	₩367,109.20	₩377,009.06
Chow et al. (2010)[8]	Singapore	2007–2008 SGD	Direct costs incurred during each hospitalization, including cost of resources utilized and services received (i.e., ward charges, radiology investigations, laboratory investigations, expert medical care, cost of services rendered such as ward procedures, emergency services, implant fees and rehabilitation, medication cost, and miscellaneous)	SGD 769.00	SGD 996.11 (2019 SGD)
Liu et al. (2016)[9]	Taiwan	2009 TWD	Direct medical cost of acute stroke care from the time of admission to discharge, including the expense for the personnel, imaging studies, laboratory examinations, medications, and any interventional management in the emergency department, intensive care unit, and neurology ward	TWD 4,661.52	TWD 5,118.04
Cost per mRS score(s)					
Arora et al. (2018)[10]	Australia	2016 AUD	Range of costs, in particular further rehabilitation, aged-care facilities, general practice visits, and special consultations	mRS 0: AUD 10,499.00 mRS 1: AUD 13,230.00 mRS 2: AUD 15,943.00 mRS 3: AUD 17,540.00 mRS 4: AUD 20,772.00 mRS 5: AUD 24,169.00	mRS 0: AUD 11,845.68 mRS 1: AUD 14,926.97 mRS 2: AUD 17,987.96 mRS 3: AUD 19,789.80 mRS 4: AUD 23,436.36 mRS 5: AUD 27,269.08
Kwatra et al. (2013)[5]	India	2013 INR	Direct medical costs (i.e., hospitalization, laboratory, radiology and cardiology-related investigations, drugs, nursing charges, consultant fees, rehabilitation services, and interdepartmental consultations), direct nonmedical costs (i.e., transportation costs to healthcare providers, relocation expenses, and costs of making changes to one's diet, house, car, or related items), and indirect costs (i.e., production value lost to society due to absence from work, disability and death)	mRS 0: INR 52,400.00 mRS 1: INR 60,506.00 mRS 2: INR 82,042.00 mRS 3: INR 74,998.00 mRS 4: INR 84,505.00 mRS 5: INR 130,458.00 mRS 6: INR 110,133.00	mRS 0: INR 74,029.58 mRS 1: INR 85,481.56 mRS 2: INR 115,907.15 mRS 3: INR 105,955.54 mRS 4: INR 119,386.82 mRS 5: INR 184,308.22 mRS 6: INR 155,593.50
Hattori et al. (2012)[11]	Japan	2011 ¥	Direct medical costs (i.e., admission to general hospitals, rehabilitation clinics, and long-term care institutions)	mRS 0: ¥738,432.00 mRS 1: ¥1,582,692.00 mRS 2: ¥3,135,672.00 mRS 3: ¥3,820,644.00 mRS 4: ¥4,132,776.00 mRS 5: ¥4,601,328.00	mRS 0: ¥775,353.60 mRS 1: ¥1,661,826.60 mRS 2: ¥3,292,455.60 mRS 3: ¥4,011,676.20 mRS 4: ¥4,339,414.80 mRS 5: ¥4,831,394.40
Kim et al. (2020)[12]	South Korea	2015 ₩	Four categories of costs: inpatient care, outpatient care, prescribed medication, and long-term care	mRS 0: ₩14,037,907 mRS 1: ₩16,483,675 mRS 2: ₩27,318,915 mRS 3: ₩47,668,088 mRS 4: ₩76,676,743 mRS 5: ₩84,554,067 mRS 6: ₩25,142,286	mRS 0: ₩14,416,468 mRS 1: ₩16,928,191 mRS 2: ₩28,055,626 mRS 3: ₩48,953,557 mRS 4: ₩78,744,490 mRS 5: ₩86,834,243 mRS 6: ₩25,820,300

LOS, length of stay; AUD, Australian dollar; INR, Indian rupee; SGD, Singapore dollar; TWD, Taiwan dollar; mRS, modified Rankin Scale.

Supplementary Table 2. Baseline characteristics for the FPE and non-FPE groups

Variable	FPE (n=91)	Non-FPE (n=81)	*P**
Demographic			
Age	68.4±11.9	67.7±14.3	0.70
Male sex	43 (47.3)	33 (40.7)	0.39
Vascular risk factors			
Hypertension	66 (72.5)	57 (70.4)	0.75
Atrial fibrillation	32 (35.2)	38 (46.9)	0.12
Diabetes mellitus	16 (17.6)	17 (21.0)	0.57
Dyslipidemia	38 (41.8)	37 (45.7)	0.61
Smoking	19 (20.9)	21 (25.9)	0.43
Previous MI/CAD	23 (25.3)	11 (13.6)	0.06
Previous stroke	16 (17.6)	13 (16.1)	0.79
Clinical presentation			
Baseline NIHSS score	16 (11–19)	16 (13–20)	0.40
Baseline systolic BP (mm Hg)†	144 (130–158)	148 (134–158)	0.31
Baseline diastolic BP (mm Hg)†	80 (70–91)	81 (72–93)	0.29
Occlusion location			
Internal carotid artery	14 (15.4)	13 (16.1)	0.90
M1 middle cerebral artery	48 (52.8)	46 (56.8)	0.60
M2 middle cerebral artery	22 (24.2)	20 (24.7)	0.94
Posterior	7 (7.7)	2 (2.5)	0.17
Procedural factors			
Time from onset to puncture (min)	214 (161–263)	220 (153–270)	0.54
General anesthesia	33 (36.3)	25 (30.9)	0.46
IV tPA use	59 (64.8)	56 (69.1)	0.55
Balloon guide catheter use	71 (78.0)	60 (74.1)	0.54
Intermediate catheter use	20 (22.0)	41 (50.6)	<0.01

Values are presented as mean±standard deviation, number (%), or median (interquartile range).
FPE, first pass effect; MI, myocardial infarction; CAD, coronary artery disease; NIHSS, National Institutes of Health Stroke Scale; BP, blood pressure; IV, intravenous; tPA, tissue plasminogen activator.
**P*-values presented for t-test besides means, Wilcoxon rank sum (Mann-Whitney) test besides medians, and chi-square or Fisher's exact tests besides proportions; †Four patients missing data for systolic and diastolic BP.

https://doi.org/10.5853//jos.2020.05043

Supplementary Table 3. Clinical outcomes for the FPE and non-FPE groups

Outcome	FPE (n=91)	Non-FPE (n=81)	*P**
90-Day mRS (categorized into good and excellent functional outcomes)†			
90-Day mRS, good outcomes (mRS 0–2)	70 (80.46)	47 (61.04)	<0.01
90-Day mRS, excellent outcomes (mRS 0–1)	55 (63.22)	36 (46.75)	0.03
90-Day mortality‡	5 (5.68)	11 (13.75)	0.08
sICH within 24 hours	2 (2.20)	4 (4.94)	0.42
ENT	2 (2.20)	9 (11.11)	0.03

Values are presented as number (%).
FPE, first pass effect; mRS, modified Rankin Scale; sICH, symptomatic intracranial hemorrhage; ENT, embolization into new territory.
**P*-values presented for chi-square or Fisher's exact tests; †Eight patients missing data for 90-day mRS; ‡Four patients missing data for 90-day mortality.

Supplementary Table 4. Estimated cost differences from sensitivity analyses comparing average per-patient procedural/hospitalization-related and long-term care costs for the FPE and non-FPE groups

Country	Australia (2020 AUD)	India (2020 INR)	Japan (2020 ¥)	South Korea (2020 ₩)	Singapore (2019 SGD)*	Taiwan (2020 TWD)
Procedural/hospitalization-related cost differences						
Base case	AUD 8,621	INR 67,718	¥239,493	₩2,004,146	SGD 5,544	TWD 41,911
FPE (mTICI 3)	AUD 8,824	INR 73,091	¥248,278	₩2,055,116	SGD 5,725	TWD 44,203
FPE (mTICI 2b–3)	AUD 7,229	INR 51,509	¥192,473	₩1,657,149	SGD 4,576	TWD 33,430
LOS (first quartile)†	AUD 2,634	INR 56,314	¥120,797	₩729,856	SGD 2,177	TWD 24,612
LOS (third quartile)†	AUD 7,948	INR 66,436	¥226,148	₩1,860,883	SGD 5,165	TWD 39,966
Costs increased by 20%	AUD 10,345	INR 81,262	¥287,391	₩2,404,976	SGD 6,652	TWD 50,293
Costs decreased by 20%	AUD 6,897	INR 54,174	¥191,594	₩1,603,317	SGD 4,435	TWD 33,529
Long-term care cost differences						
Base case	AUD 398	INR 68	¥314,262	₩6,155,006	NA‡	NA‡
FPE (mTICI 3)	AUD 361	INR 500	¥196,260	₩5,277,829	NA‡	NA‡
FPE (mTICI 2b–3)	AUD 651	INR 1,725	¥400,368	₩8,620,940	NA‡	NA‡
Costs increased by 20%	AUD 477	INR 81	¥377,114	₩7,386,007	NA‡	NA‡
Costs decreased by 20%	AUD 318	INR 54	¥251,409	₩4,924,004	NA‡	NA‡
Costs for mRS 6 included in analyses	NA§	INR 13,353	NA§	₩8,359,695	NA‡	NA‡

All values represent cost savings for patients in the FPE group as compared with the non-FPE group.
FPE, first pass effect; AUD, Australian dollar; INR, Indian rupee; SGD, Singapore dollar; TWD, Taiwan dollar; NA, not applicable; mTICI, modified Thrombolysis in Cerebral Infarction; LOS, length of stay; mRS, modified Rankin Scale.
*Reported as charges; †Variations in LOS did not impact long-term care cost differences; ‡Long-term care costs, based on 90-day mRS, were not found for Singapore and Taiwan; §Costs for 90-day mRS 6 not reported for Australia and Japan.

Supplementary references

1. Zaidat OO, Bozorgchami H, Ribó M, Saver JL, Mattle HP, Chapot R, et al. Primary results of the multicenter ARISE II study (Analysis of Revascularization in Ischemic Stroke With EmboTrap). *Stroke* 2018;49:1107-1115.
2. Iyer S. Neurovascular Devices-Market Insights-Asia Pacific (Supplemental). Decision Resources Group (DRG). https://decisionresourcesgroup.com/report/m360nv0006-medtech-neurovascular-devices-market-insights-asia/. 2019. Accessed Deceember 30, 2020.
3. Yadav V. Neurovascular Devices-Market Insights-Japan. Decision Resources Group (DRG). https://decisionresourcesgroup.com/report/m360nv0013-medtech-neurovascular-devices-market-insights-japan/. 2020. Accessed Deceember 30, 2020.
4. Cadilhac DA, Dewey HM, Denisenko S, Bladin CF, Meretoja A. Changes in acute hospital costs after employing clinical facilitators to improve stroke care in Victoria, Australia. *BMC Health Serv Res* 2019;19:41.
5. Kwatra G, Kaur P, Toor G, Badyal DK, Kaur R, Singh Y, et al. Cost of stroke from a tertiary center in northwest India. *Neurol India* 2013;61:627-632.
6. Yoneda Y, Okuda S, Hamada R, Toyota A, Gotoh J, Watanabe M, et al. Hospital cost of ischemic stroke and intracerebral hemorrhage in Japanese stroke centers. *Health Policy* 2005;73:202-211.
7. Jeong HS, Shin JW, Kwon HJ, Koh HS, Nam HS, Yu HS, et al. Cost benefits of rapid recanalization using intraarterial thrombectomy. *Brain Behav* 2017;7:e00830.
8. Chow WL, Tin AS, Meyyappan A. Factors influencing costs of inpatient ischaemic stroke care in Singapore. *Proc Singap Healthc* 2010;19:283-291.
9. Liu CH, Wei YC, Lin JR, Chang CH, Chang TY, Huang KL, et al. Initial blood pressure is associated with stroke severity and is predictive of admission cost and one-year outcome in different stroke subtypes: a SRICHS registry study. *BMC Neurol* 2016;16:27.
10. Arora N, Makino K, Tilden D, Lobotesis K, Mitchell P, Gillespie J. Cost-effectiveness of mechanical thrombectomy for acute ischemic stroke: an Australian payer perspective. *J Med Econ* 2018;21:799-809.
11. Hattori N, Hirayama T, Katayama Y. Medical care for chronic-phase stroke in Japan. *Neurol Med Chir (Tokyo)* 2012;52:175-180.
12. Kim SE, Lee H, Kim JY, Lee KJ, Kang J, Kim BJ, et al. Three-month modified Rankin Scale as a determinant of 5-year cumulative costs after ischemic stroke: an analysis of 11,136 patients in Korea. *Neurology* 2020;94:e978-e991.

https://doi.org/10.5853//jos.2020.05043