

Cost Effectiveness of Drive and Retrieve System in Hokkaido for Acute Ischemic Stroke Patient Treatment Using Geographic Information System

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Background and Purpose: Although endovascular thrombectomy combined with recombinant tissue-type plasminogen activator is effective for treatment of acute ischemic stroke, regional disparities in implementation rates of those treatments have been reported. Drive and retrieve system, where a qualified neurointerventionist travels to another primary stroke center for endovascular thrombectomy, has been practiced in parts of Hokkaido, Japan. This study aims to simulate the cost effectiveness of the drive and retrieve system, which can be a method to enhance equality and cost effectiveness of treatments for acute ischemic stroke. *Materials and methods:* The number of patients who had acute ischemic stroke in 2015 is estimated. Those patients are generated according to the population distribution, and thereafter patient transport time is analyzed in the 3 scenarios (1) 60-minute drive scenario, (2) 90-minute drive scenario, in which the drive and retrieve system operates within 60-minute or 90-minute driving distance (3) without the system, using geographic information system. Incremental cost-effectiveness rate, quality-adjusted life years, and medical and nursing care costs are estimated from the analyzed transport time. *Findings:* The incremental cost-effectiveness rate by implementing the system was dominant. Cost reductions of \$213,190 in 60-minute drive scenario, and \$247,274 in the 90-minute scenario were expected, respectively. Such benefits are the most significant in Soya, Emmon, Rumoi, and Kamikawahokubu medical areas. *Conclusions:* The drive and retrieve system could enhance regional equality and cost effectiveness of ischemic stroke treatments in Hokkaido, which can be achieved using existing resources. Further studies are required to clarify its cost effectiveness from hospital perspective. **Key Words:** Cost effectiveness—geographic information system—ischemic stroke—endovascular thrombectomy—drive and retrieve system
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Introduction

Stroke is the fourth largest cause of death in Japan, and accounts for the largest proportion of patients with

nursing care needs.¹ Approximately 26.9% of patients with nursing care needs in Japan have had stroke.² In the aging society of Japan, where medical and nursing care

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costs have been increasing, the viewpoint of cost effectiveness of stroke treatments needs to be considered. The Japan Stroke Data Bank (2016) reported that ischemic stroke accounted for 68.7% of all types of strokes.³ Therefore, it is necessary to consider cost-effective management of ischemic stroke treatments.

Recombinant tissue-type plasminogen activator (rt-PA) and endovascular thrombectomy have been known as effective treatments of acute ischemic stroke (AIS).^{4,5} Several randomized controlled trials and meta-analysis have reported the effectiveness of these treatments.⁶⁻⁸ Despite the efficacy, disparity in implementation rates of the treatments between rural areas and urban areas have been reported due to their time limits.^{9,10} Furthermore, the later the reperfusion is performed, the worse the outcome will be.¹¹ Therefore, efforts should be made to shorten the processing time between symptom onset and treatment. Hokkaido, a prefecture in Japan, has the largest land area with lowest population density. Moreover, Hokkaido has the highest number of secondary medical areas among all the prefectures in Japan,¹² which are regional units that provide in-hospital medical services, including stroke care. Disparities in medical services¹³ and stroke treatments^{14,15} have been reported in Hokkaido. Although it is desirable that stroke care is provided equally in all medical areas, it is not always possible due to lacking medical resources such as computed tomography, magnetic resonance imaging, electrocardiogram, and qualified neurointerventionists for endovascular thrombectomy. Therefore, a system for medical cooperation that specializes in endovascular treatment for AIS is needed to ensure prompt initiation of treatment and to reduce the time from onset to reperfusion. Many such systems have been proposed till date. For example, some studies have evaluated the "drip and ship method,"¹⁶ whereas others have reported better results with centralized direct transport, or the "mothership" method, because of its reduced transportation time and potential reduction in mortality rate.¹⁷ Several studies have proposed the "drive and retrieve system," where neurointerventionists, who work at comprehensive stroke centers, travel to primary stroke centers to provide endovascular thrombectomy. By implementing the drive and retrieve system, more patients will be eligible for these treatments, and better outcomes can be expected due to earlier treatment initiation.¹⁸ To provide data to achieve equal and efficient treatments of patients with AIS, this study simulates the effect of the drive and retrieve system on accessibility to rt-PA and endovascular thrombectomy, and assesses the cost effectiveness of drive and retrieve system from the perspective of medical and nursing care expenditures.

Materials and Methods

Subjects and Outcomes

The subjects in this study are a virtual cohort of patients with AIS in Hokkaido in 2015 (for population

distribution and secondary medical areas in Hokkaido, refer to Fujiwara et al., 2017).¹⁵ The analysis period is 3 years from the patients' onsets. Solitary island areas are excluded in the analysis. Three scenarios, with (1) 60-minute and (2) 90-minute drive and retrieve systems (60-minute scenario and 90-minute scenario) where qualified neurointerventionists travel to primary stroke centers for endovascular thrombectomy within 60-minute or 90-minute drive distance (spoke hospitals) after patients' onsets, and (3) without the system (the current scenario) are compared and cost effectiveness achieved by implementing the drive and retrieve system is assessed. The primary outcome is incremental cost-effectiveness rate (ICER), which is calculated by dividing incremental costs with incremental quality-adjusted life years (QALY). ICER is the standard measurement for cost effectiveness at the National Institute of Health and Care Excellence in Britain,¹⁹ Japan,²⁰ and elsewhere. In this study, ICER is evaluated by the 5,000,000 JPY-per-QALY threshold (approximately 44,228\$), which is suggested by Ministry of Health, Labor, and Wealth for evaluating cost effectiveness in Japan.²¹ Cost gain (reduction) by the system is also analyzed. The costs include medical costs and nursing costs up to 3 years after symptom onset, and the gained QALYs are estimated for the same period. Per-time costs of the drive and retrieve system are also calculated for each secondary medical area by dividing the incremental cost by the number of patients whose transport time is shorten. R ver 3.5.1 a statistical software, was used for the analyses. Data on the 29 hospital where neurointerventionists are present (hub hospitals) and on 108 spoke hospitals (without neurointerventionists but equipped for the treatment) are obtained from the websites of The Japanese Society for Neuroendovascular Therapy²² and Hokkaido Medical Plan,¹³ respectively.

Patient Generation

First, we estimate the number of stroke patients from the incidence data of Patient Survey from the Ministry of Health, Labor and Welfare, and the population (2014).²² Then the number of ischemic stroke patients is estimated using data from Japan Stroke Data Bank, a Japanese nationwide database of stroke patients in Japan.³ Thereafter, the number of patients is randomly allocated to each 1 km² mesh of the geographic information system (GIS), in accordance with its population. This allocation is repeated 10,000 times using R ver 3.5.1 and thereafter the average number for each mesh is used as the number of patients who are generated on ArcGIS Desktop10 (ESRI Inc.) using random point generation.

Transport Time Analysis

Transport time is analyzed using closest facility analysis of GIS. The sum of the time when an ambulance arrives at a patient location and the time of arrival from the patient

location to a hospital is defined as transport time. Ambulance locations are obtained from National Land Numerical Information (2015).²³ To assess the transport time in 60-minute and 90-minute scenarios, the 76 spoke hospitals which are within 60-minute driving distance from the 29 hospitals where neurointerventionists work (hub hospitals) are identified using “object identifier matrix” function of GIS. Likewise, the 84 spoke hospitals within 90-minute driving distance from the hub hospitals are identified. The transport time in each of the 3 scenarios is then analyzed. Patients are divided into 4 groups depending on the following time windows: (1) those transported within 1 hour (2) those transported between 1 and 2 hours (3) those transported between 2 and 3 hours, and (4) those transported more than 3 hours after symptom onset.

Patient Outcome Estimation

The drive and retrieve system aims to provide early rt-PA and endovascular thrombectomy for as many patients as possible. Our analysis attempts to study the outcomes that patients gain through earlier reperfusion, by using data from the Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke Trials (HERMES) collaboration study,²⁴ a meta-analysis of 5 randomized controlled trials.²⁵⁻²⁹ In the HERMES study, rt-PA was used for more than 83% of the patients treated with endovascular thrombectomy.²⁴ Furthermore, the guideline for using mechanical thrombectomy device in Japan (2015) stated that rt-PA should be given the first priority.⁵ These 2 treatments should be comprehensively considered. Therefore, it is assumed that endovascular thrombectomy is implemented after rt-PA treatment. In this study, rt-PA time window (4.5 hours) is used for patient severity estimate³⁰ Although the time limit is 4.5 hours after symptom onset, Spokoyny et al (2015) reported that onset time tended to be estimated around 30 minutes earlier than the actual onset time.³¹ In addition, the Japan Stroke Society (2015) recommends that rt-PA be administered within 1 hour after door time.⁴ Considering the uncertainty in onset time³¹ and the time until rt-PA administration,⁴ it is assumed that patients whose transport time is within 3 hours after symptom onset are eligible for rt-PA, and

subsequently endovascular thrombectomy. According to a report from Japan Stroke Association, it is assumed that rt-PA and endovascular thrombectomy implementation rates are 16.9% for those transported within 3 hours (Unpublished data: S Yamaguchi, The epidemiological trend of stroke observed from the Japanese Stroke Data bank. 2013. Tokyo. March 2013. Available at <http://att.ebm-library.jp/conferences/2013/stroke/08.html>[Accessed September 26, 2018] [in Japanese]). For severity estimation, modified Rankin Scale (mRS) at 90 days after symptom onset is used. The data on reperfusion time and mRS at 90 days are obtained from the HERMES study (Table 1).¹¹ According to the transport time groups, the patients are given the expected mRS stage distributions (Table 1). It is assumed that the patient severity distributions will not change during the study period.

Medical and Nursing Care Costs

Medical costs as well as nursing care costs are included in the cost analysis, since stroke patients are likely to suffer from poststroke disability.³² In Japan, official rates for medical costs and nursing care costs are applied throughout the country. In this study, these costs are estimated based on the expected mRS distribution. First, data for perpatient medical cost is obtained from Japan Stroke Data bank (Table 2).³ Nursing care services are insured based on patient care needs, which are assigned based on patients' severity. The care needs are divided into 7 categories (support levels 1 and 2, and care levels 1-5), with care level patients severer than support level patients. Higher levels mean that patients tend to have severer disability.³³ In this study, the care needs of the patients (Table 2) and nursing care costs are estimated from Statistics of Medical Care Activities in Public Health Insurance by the Ministry of Labor, Health, and Welfare,³⁴ in accordance with a previous research.³² The estimated per-year nursing care costs were \$3092 for Support Level 1, \$5285 for Support Level 2, \$11,311 for Care Level 1, \$15,288 for Care Level 2, \$22,389 for Care Level 3, \$26,689 for Care Level 4, and \$30,939 for Care Level 5. Hattori et al (2012) reported that patients at different mRS stages have different utilization rates of nursing care services,³⁵ that is,

Table 1. Expected mRS distribution at 3 months after onset¹¹

Eligibility for rt-PA and endovascular thrombectomy	Time window	Rates of patients at each mRS stage (%)						
		0	1	2	3	4	5	6
Eligible	Transported between 0 and 1 hour after onset	11.0	21.6	24.5	19.4	11.6	5.0	7.0
Eligible	Transported between 1 and 2 hours after onset	9.6	19.8	24.0	20.2	12.7	5.7	8.0
Eligible	Transported between 2 and 3 hours after onset	8.4	18.1	21.3	20.9	13.8	6.3	9.2
Not eligible		3.6	6.2	12.5	8.7	31.2	15.0	22.5

mRS, modified Rankin Scale; rt-PA, recombinant tissue-type plasminogen activator.

This table shows the expected mRS distributions used in the simulation, which is quote from.¹¹ It is assumed that patient severity varies with patient transport time and eligibility for rt-PA and subsequent endovascular thrombectomy.

Table 2. Data on costs, care need level, and nursing care utilization rate, and QALY for each mRS stage used in the simulation

	mRS stage						
	0	1	2	3	4	5	6
Total medical costs (\$US) ³	7626	10,286	14,632	16,848	20,218	28,642	24,031
Care-need level ³³	No care	Support Level 1	Support Level 2	Care Level 1	Care Level 2 or 3*	Care Level 4 or 5*	No care
The rate at which nursing care services are utilized (%) ³⁶	0	26.1	91.8	98.5	100	100	0
QALYs ³⁶	0.89	0.797	0.65	0.588	0.363	0.092	0

Table 2 shows the data on total medical costs,³ care-need levels,³³ the rates at which nursing care services,³⁵ and quality-adjusted life years (QALYs) for patients at each mRS stage³⁵ used in the simulation. It is assumed that those parameters vary with patient mRS stages.

severe patients are likely to utilize nursing care services. It is assumed that patients utilize nursing care services at the rates shown in Table 2. This process of estimating medical costs and nursing care costs is applied to patients for each transport time window, and perpatient cost expectations are calculated for each of the transport time windows in each scenario. The expected medical costs and nursing care costs are converted to US dollars at the currency exchange rate as of November 21, 2018 and are discounted at 2% per year.²⁰

QALY

As mentioned above, QALY is used as a measurement of patient outcome. QALY is a standard measurement for health technology assessment. The Ministry of Labor, Health, and Welfare (2016) recommends QALY for evaluating cost effectiveness of medical treatments or services.²¹ In this study, QALY data are assigned to patients based on the results of Hattori et al (Table 2).³⁵ The expected QALYs are discounted at 2% per year.²⁰

Results

Patient Accessibility

The estimated number of AIS patients was 8528, excluding 16 patients in the solitary island areas. Figure 1 shows the rates for patients transported to hospitals with endovascular thrombectomy within 3 hours (covered rate), and the detailed results (eg, the number of patients in each time window, the covered rates) are shown in Table 3. Covered rates were 98.5% (8397) for the current scenario, 99.0% (8442) for the 60-minute scenario, and 99.1% (8448) for the 90-minute scenario. The transport time of 178 and 248 patients would be shortened by the 60-minute and 90-minute scenario, respectively (these figures are obtained by summing the number of patients whose transport time was shortened at each medical area [Table 3]). In 14 of the 21 secondary medical areas, covered rate was 100% in the current scenario. Currently, approximately 7.6% of the patients are transported to hub hospitals within 1 hour in the Kamikawahokubu medical

area. The rate can increase to 85% with the drive and retrieve system. In Emmon, Kitaoshimahiyama, and Kamikawahokubu areas, the cover rates would be 100% in the 60-minute scenario. In Rumoi area, the covered rate was 87% in the current scenario. The number increases to 93% in the 60-minute scenario, and 100% in the 90-minute scenario. Soya has the lowest covered rate in the current scenario (1%). Although the rate would increase to 25% and 26% in the 60-minute and 90-minute scenarios, respectively, rt-PA and endovascular thrombectomy would still not be accessible to a large number of patients. In Hidaka and Nemuro, 5% and 2% of patients would currently not be transported to hub hospitals within 3 hours, and the rate would not change even in the 90-minute scenario, respectively.

Perpatient Medical and Nursing Care Costs

When calculated considering treatment eligibility and the transfer time windows, the perpatient medical and nursing care costs for patients treated with rt-PA and endovascular thrombectomy were \$36,323 in the 0- to 1-hour window, \$38,139 in the 1- to 2-hour window, \$39,774 in the 2- to 3-hour window, and \$55,506 without these treatments. After adjusting these costs with the implementation rate of these treatments, the expected perpatient costs at each transport time window were \$51,852 in the 0- to 1-hour window, \$52,159 in the 1- to 2-hour window, \$52,436 in the 2- to 3-hour window, and \$55,506 in the over 3-hour window.

Cost Effectiveness of the Drive and Retrieve System

ICER after implementing the drive and retrieve system was calculated from the results of patient transport time, perpatient costs, and QALYs for each transport time window. The ICER was dominant, both in the 60-minute and 90-minute scenarios. QALY gain was 7.0 in the 60-minute scenario, and 8.13 in the 90-minute scenario. The results showed cost reduction of \$213,190 in the 60-minute scenario (Fig 2) and \$247,272 in the 90-minute scenario (Fig 3). Figure 2 shows the cost reduction in each secondary medical area achieved in the 60-minute scenario. Cost

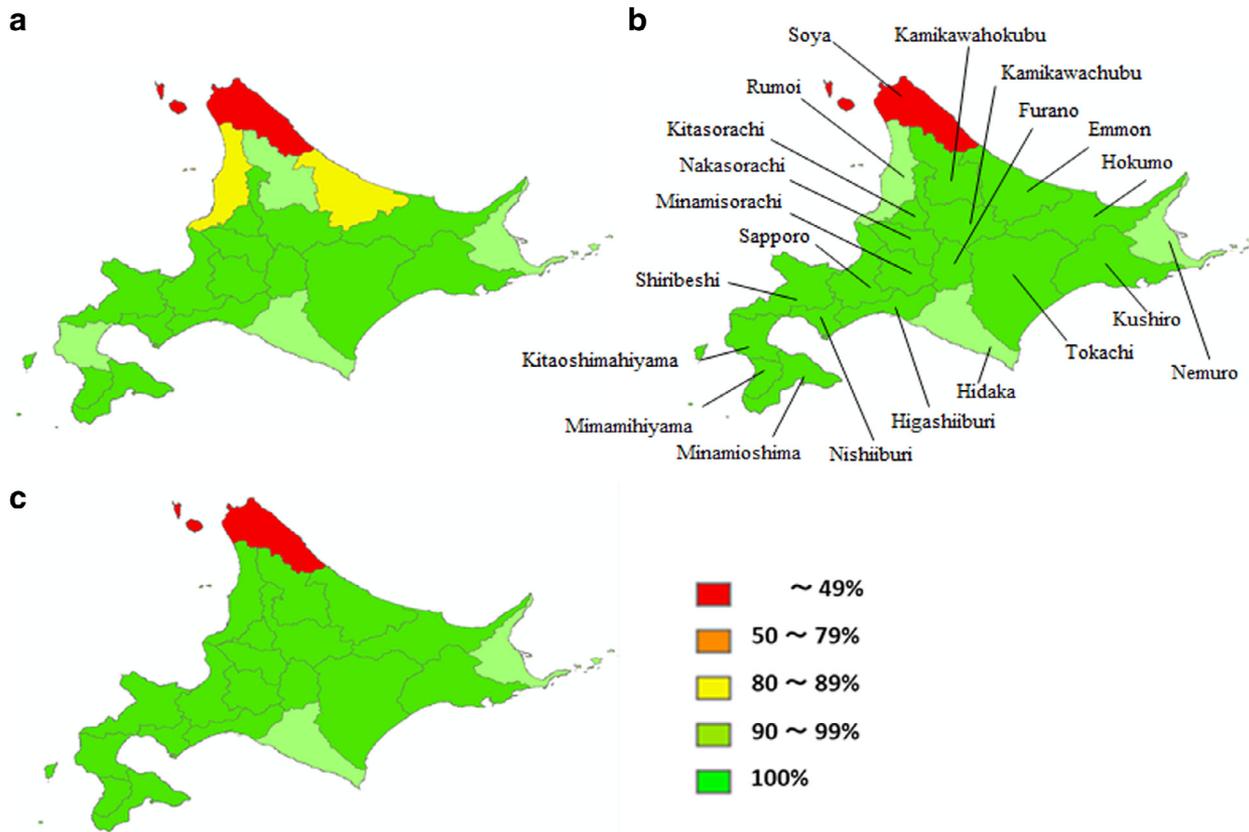


Figure 1. Covered rate in each scenario. The rates of patients whose transport time are within 3 hours (cover rate) in each scenario ((a) the current scenario, (b) the 60-minute scenario, and (c) the 90-minute scenario) are visualized. The results showed that 100% cover rate was achieved in 14 of 21 areas in the current scenario. The 100% cover rate would be achieved in the 60-minute drive scenario in Emmon, Kitahitamaoshima, Kamikawahokubu medical areas, in the 90-minute drive scenario in Rumoi area. In Hidaka and Nemuro medical areas, the cover rates would not change even by implementing the drive and retrieve system. In Soya area, the cover rate would still be 26% even with the drive and retrieve system.

reduction is the highest in Soya (\$70,433), followed by Emmon (\$46,425), Kamikawahokubu (\$34,232), and Rumoi (\$18,067) in the 60-minute scenario. The reduction for these medical areas accounted for approximately 79% of the reduction in the whole Hokkaido. Figure 3 shows the cost reduction for each secondary medical area achieved in the 90-minute scenario. In 15 of the 21 medical areas, no change was observed between the results in 60-minute and 90-minute scenarios. In the 90-minute scenario, Soya area has the largest cost reduction (\$75,149), followed by Emmon (\$52,489), Rumoi (\$35,033), and Kamikawahokubu medical areas (\$34,232). Figure 4 shows the perpatient cost reduction. Expected perpatient cost reduction was the highest when the drive and retrieve system was applied to patients in Soya (\$3062 per case), followed by Emmon (\$1934 per case), Rumoi (\$1807 per case), and Kitaoshimahiyama (\$1296 per case).

Discussion

The patients in this study were generated based on the incidence and the actual population distribution in each 1 km² mesh in Hokkaido. Therefore, this distribution is

likely to reflect the actual patient distribution. The covered rate was 98.5% in the current system, which indicates that a large number of patients can be eligible for rt-PA and endovascular thrombectomy, especially in the urban areas such as Sapporo, Kamikawachubu, and Minamihiyama, even in the current scenario. Soya had the lowest rate (1%), followed by Rumoi (86%), and the other 5 areas (Table 3). These medical areas do not have spoke hospitals. The results indicate that regional disparity exists in accessibility of patients to these treatments, which supports previous studies,¹⁷ and corporation for AIS treatments among secondary medical areas is of importance to deliver more equal and efficient treatments. By implementing a 60-minute drive and retrieve system, the covered rate in Hokkaido would increase to 99.0%. A total of 178 and 248 patients would benefit from the system by being transported in a shorter time window (Table 3). Therefore, the drive and retrieve system can increase equality in access to treatment for ischemic stroke patients, which can be achieved using existing medical resources. The cover rate would increase from 1% to 25% in Soya, 89% to 100% in Emmon, 87% to 93% in Rumoi, and 96% to 100% in Kitaoshimahiyama. The results

Table 3. The number of patients transported in each time window in each medical area

Secondary medical area	Scenario	Transport time window					Cover rate (%)
		Total	0-1 hour	1-2 hours	2-3 hours	Over 3 hours	
All Hokkaido	Current	8528	7085	8037	8397	131	98.5
All Hokkaido	60-minute	8528	7270	8104	8442	86	99.0
All Hokkaido	90-minute	8528	7270	8163	8448	80	99.1
Minamioshima	Current	615	555	608	615	0	100
Minamioshima	60-minute	615	561	608	615	0	100
Minamioshima	90-minute	615	561	615	615	0	100
Minamihiyama	Current	26	0	26	26	0	100
Minamihiyama	60-minute	26	0	26	26	0	100
Minamihiyama	90-minute	26	0	26	26	0	100
Kitaoshimahiyama	Current	55	0	30	53	2	96
Kitaoshimahiyama	60-minute	55	0	36	55	0	100
Kitaoshimahiyama	90-minute	55	0	52	55	0	100
Sapporo	Current	3781	3772	3781	3781	0	100
Sapporo	60-minute	3781	3779	3781	3781	0	100
Sapporo	90-minute	3781	3779	3781	3781	0	100
Shiribashi	Current	335	200	322	335	0	100
Shiribashi	60-minute	335	229	331	335	0	100
Shiribashi	90-minute	335	229	331	335	0	100
Minamisorachi	Current	263	241	263	263	0	100
Minamisorachi	60-minute	263	242	263	263	0	100
Minamisorachi	90-minute	263	242	263	263	0	100
Nakasorachi	Current	178	173	178	178	0	100
Nakasorachi	60-minute	178	173	178	178	0	100
Nakasorachi	90-minute	178	173	178	178	0	100
Kitasorachi	Current	53	39	53	53	0	100
Kitasorachi	60-minute	53	48	53	53	0	100
Kitasorachi	90-minute	53	48	53	53	0	100
Nishiiburi	Current	286	278	286	286	0	100
Nishiiburi	60-minute	286	283	286	286	0	100
Nishiiburi	90-minute	286	283	286	286	0	100
Higashiiburi	Current	338	332	338	338	0	100
Higashiiburi	60-minute	338	333	338	338	0	100
Higashiiburi	90-minute	338	333	338	338	0	100
Hidaka	Current	118	0	32	112	6	95
Hidaka	60-minute	118	0	32	112	6	95
Hidaka	90-minute	118	0	32	112	6	95
Kamikawachubu	Current	624	610	623	624	0	100
Kamikawachubu	60-minute	624	614	624	624	0	100
Kamikawachubu	90-minute	624	614	624	624	0	100
Kamikawahokubu	Current	105	8	91	103	2	98
Kamikawahokubu	60-minute	105	89	103	105	0	100
Kamikawahokubu	90-minute	105	89	103	105	0	100
Furano	Current	74	10	73	74	0	100
Furano	60-minute	74	10	73	74	0	100
Furano	90-minute	74	10	74	74	0	100
Rumoi	Current	76	0	51	66	10	87
Rumoi	60-minute	76	0	61	71	5	93
Rumoi	90-minute	76	0	67	76	0	100
Soya	Current	97	0	0	1	96	1
Soya	60-minute	97	0	0	24	73	25
Soya	90-minute	97	0	6	25	72	26
Hokumo	Current	354	112	352	354	0	100
Hokumo	60-minute	354	132	354	354	0	100
Hokumo	90-minute	354	132	354	354	0	100

(Continued)

Table 3 (Continued)

Secondary medical area	Scenario	Transport time window					Cover rate (%)
		Total	0-1 hour	1-2 hours	2-3 hours	Over 3 hours	
Emmon	Current	119	0	27	106	13	89
Emmon	60-minute	119	0	51	119	0	100
Emmon	90-minute	119	0	73	119	0	100
Tokachi	Current	531	440	527	531	0	100
Tokachi	60-minute	531	457	529	531	0	100
Tokachi	90-minute	531	457	530	531	0	100
Kushiro	Current	378	315	371	378	0	100
Kushiro	60-minute	378	320	372	378	0	100
Kushiro	90-minute	378	320	372	378	0	100
Nemuro	Current	122	0	5	120	2	98
Nemuro	60-minute	122	0	5	120	2	98
Nemuro	90-minute	122	0	5	120	2	98

This table shows the patient transport time, and the number of patients transported in each time window, and cover rate (the rate of patients who are transported within 3 hours) in the 3 scenarios in each secondary medical area in Hokkaido, and in overall Hokkaido.

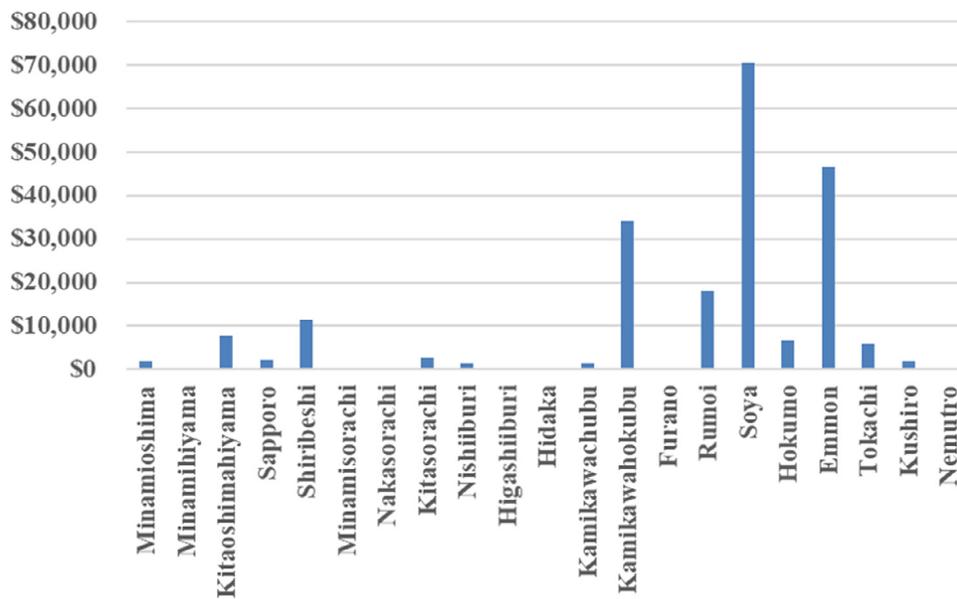


Figure 2. The cost reduction in each secondary medical area in 60-minute scenario (\$US). This figure shows the cost reduction in each of the secondary medical areas achieved by implementing the 60-minute drive scenario. The result showed that the total cost reduction was \$213,190. Cost reduction is the highest in Soya (\$70,433), followed by Emmon (\$46,425), Kamikawahokubu (\$34,232), and Rumoi (\$18,067).

indicate that the drive and retrieve system within 60-minute drive distance is effective in these medical areas. In Kamikawahokubu, the rate of patients transported in the 0- to 1-hour time window would increase from 7.6% to 85%. Patients in this medical area can benefit from an early start of treatment. In Rumoi, the covered rates were 87%, 93%, and 100% under the 3 scenarios. The 90-minute scenario would help in providing more equal treatment in Rumoi area.

Perpatient expected costs were cheaper, and perpatient expected QALYs were higher with shorter time windows. This is attributed to better outcomes due to an early start of treatment, which results in less medical and nursing

care costs. The amount of QALY gained was not substantial because in Hokkaido, a large part of population can be transported within 3 hours even in the current scenario. However, since the ICER from implementing the drive and retrieve system was dominant, the system can be a solution to enhance equality and cost effectiveness of treatments for patients with AIS.

There were cost reduction effects of the drive and retrieve system. The analysis revealed that cost reduction was high in Soya, Emmon, Rumoi, and Kamikawahokubu. As mentioned above, patients in these medical areas can expect better outcomes through transportation in a shorter time window, and the increase in cover rates.

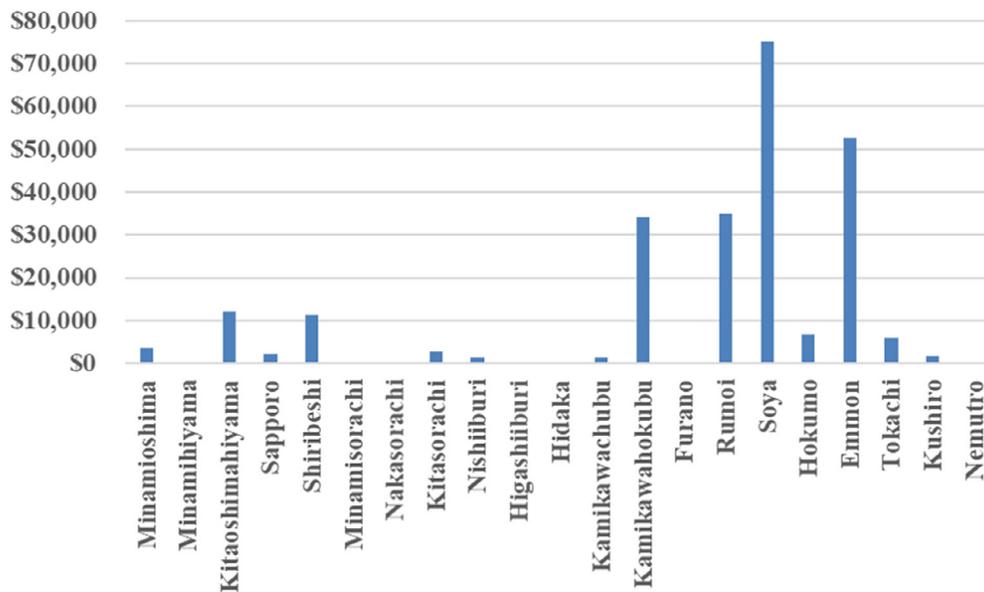


Figure 3. The cost reduction in each secondary medical area in 90-minute scenario (\$US). This figure shows the cost reduction in each of the secondary medical areas achieved in the 90-minute scenario. The result showed that the total cost reduction was \$247,272. Soya area has the largest cost reduction (\$75,149), followed by Emmon (\$52,489), Rumoi (\$35,033), and Kamikawahokubu medical areas (\$34,232).

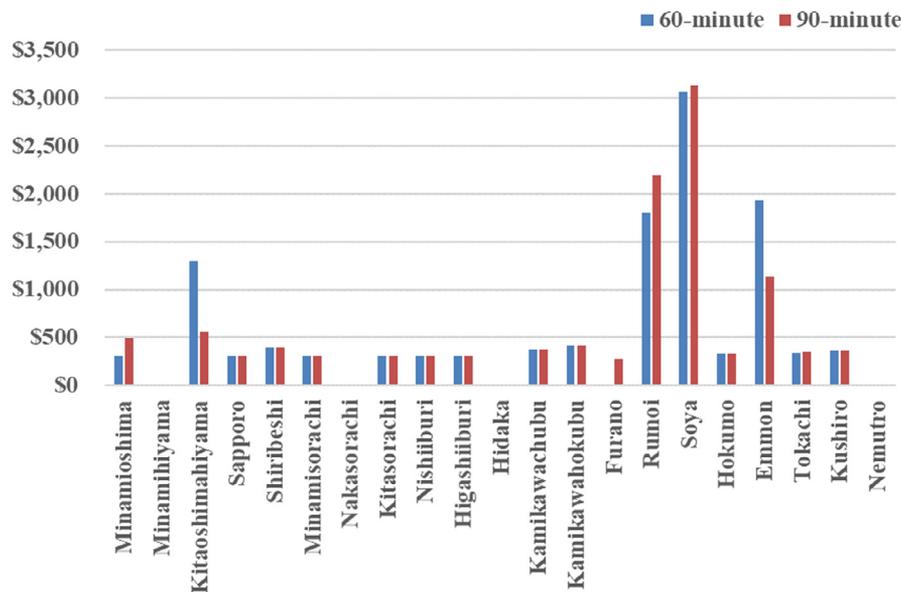


Figure 4. The cost reduction gained per 60-minute drive and retrieve system (\$US). This figure shows the results of perpatient cost reduction in each secondary medical area, which is calculated by deriving the total cost reduction by the number of patients whose transport time are shorten by 60-minute drive scenario. Perpatient cost reduction was largest in Soya area (\$3062 per case), followed by Emmon area (\$1934), Rumoi (\$1807), and Kitaohiyama (\$1296).

Since the number of neurointerventionists is limited, it is necessary to prioritize the allocation of new human resources in these medical areas.

Perpatient cost reduction is the highest in Soya, followed by Emmon, Rumoi, and Kitaoshimahiyama. More and more patients became eligible for rt-PA and endovascular thrombectomy with this system in these areas. Since high effectiveness of rt-PA and endovascular thrombectomy have been reported,^{4,5} it is desirable that these treatments

are given to as many patients as possible. Even though the increase in the number of patients covered by the system is not substantial, it would be of great importance in providing more equal and cost-effective treatment for patients with ischemic stroke in Hokkaido. Further cost analysis is required from the hospital perspective.

However, this study has several limitations. First, the period of QALY and cost analyses is 3 years due to lack of data. Poststroke disability is likely to last for a lifetime.³²

Therefore, lifetime analyses with detailed data will give a better assessment of the effects of the drive and retrieve system. Second, due to lack of data, the implementation rate of rt-PA and endovascular thrombectomy is constantly set at 16.9%. In a clinical condition, it is possible that the rate varies with transport time, and the implementation rate can improve and change over time. Third, although the results of this study revealed the possible cost reduction brought by implementing the drive and retrieve system, our analysis did not contain public costs to maintain the system that may arise if the system is implemented as a policy (eg, subsidy for hospitals that manage the system). Lastly, further research is required to apply the drive and retrieve system in a wider area, after considering the availability of the neurointerventionists.

Conclusions

In this study, the effects of the drive and retrieve system in Hokkaido on patient accessibility to rt-PA and endovascular thrombectomy were analyzed using GIS; and the cost effectiveness of the system was assessed with ICER from the public perspective as a primary outcome, in order to provide data for effective management of ischemic stroke treatments. The results indicated that there were regional disparities in patient accessibility to these treatments. It is possible to reduce disparities using the drive and retrieve system. The cost-effectiveness analysis revealed that the ICER was dominant after implementing this system, and cost reduction would be expected. Therefore, this system can be a solution to achieve more equal and cost-effective treatments. Additionally, the results showed that cost reductions were high in Soya, Emmon, Rumoi, and Kamikawahokubu medical areas. Further analysis from hospital perspective is required to clarify whether the system is cost effective for involved hospitals.

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Conflicts of Interest

The authors declare that they have no conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found in the online version at [doi:10.1016/j.jstrokecerebrovasdis.2019.05.020](https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.05.020).

References

1. The Ministry of Health Labour and Welfare. Comprehensive survey of living conditions: 2013. Available at: <https://www.mhlw.go.jp/toukei/list/20-21.html> (Accessed September 27, 2018)
2. The Ministry of Health Labour and Welfare. Survey of long-term care benefit expenditures, 2017. Available at: <https://www.mhlw.go.jp/toukei/list/45-1.html> (Accessed September 27, 2018)
3. Kobayashi S. The Japanese Stroke Data bank 2015. Tokyo: Nakayama Shoten; 2016.
4. Minematsu K, Toyoda K, Hirano T, et al. Guidelines for the intravenous application of recombinant tissue-type plasminogen activator (alteplase), the second edition, partly revised in October 2016, a guideline from the Japan Stroke Society. *Jpn J Stroke* 2017;39:43-86. (In Japanese).
5. Minematsu K, Iihara K, Ogasawara K, et al. Guideline for the proper use of mechanical thrombectomy device, the second edition: a guideline from the Japan Stroke Society, the Japan Neurosurgical Society and the Japanese Society for Neuroendovascular Therapy. *Jpn J Stroke* 2015;37:259-279. (In Japanese).
6. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995;333:1581-1588.
7. Yamaguchi T, Mori E, Minematsu K, et al. Alteplase at 0.6 mg/kg for acute ischemic stroke within 3 hours of onset: Japan Alteplase Clinical Trial (J-ACT). *Stroke* 2006;37:1810-1815.
8. Toyoda K, Koga M, Naganuma M, et al. Routine use of intravenous low-dose rt-PA in Japanese patients: general outcomes and prognostic factors from the SAMURAI register. *Stroke* 2009;40:3591-3595.
9. Kleindorfer D, Xu Y, Moomaw CJ, et al. US geographic distribution of rt-PA utilization by hospital for acute ischemic stroke. *Stroke* 2009;40:3580-3584.
10. Okada Y, Minematsu K, Ogawa A. Nation-wide survey of intravenous rt-PA (alteplase) therapy during the first four years after approval – for overcoming regional gaps. *Jpn J Stroke* 2010;32:365-372. (In Japanese).
11. Saver JL, Goyal M, van der Lugt A, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA* 2016;316:1279-1288.
12. Geospatial Information Authority of Japan. Statistical reports on the land area by prefectures and municipalities in Japan, 2017. Available at: <http://www.gsi.go.jp/KOKUJYOHO/MENCHO201710-index.html> (Accessed September 26, 2018) (In Japanese)
13. The prefectural office of Hokkaido. Hokkaido Healthcare Plan [revised edition]; 2013. Available at: <http://www.pref.hokkaido.lg.jp/hf/cis/iryokeikaku/00hokkaidouiryokeikaku.htm>. (Accessed September 26, 2018) (In Japanese)
14. Hashi K. Present status of intravenous rt-PA therapy and regional difference in its availability in Japan. *Jpn J Stroke* 2010;32:770-772. (In Japanese).
15. Fujiwara K, Osanai T, Kobayashi E, et al. Accessibility to tertiary stroke centers in Hokkaido, Japan: use of novel metrics to assess acute stroke care quality. *J Stroke Cerebrovasc Dis* 2018;27:177-184.
16. Sheth KN, Smith EE, Grau-Sepulveda MV, et al. Drip and ship thrombolytic therapy for acute ischemic stroke use, temporal trends, and outcomes. *Stroke* 2015;46:732-739.
17. Milne MS, Jessalyn HK, Hill MD, et al. Drip 'n ship versus mothership for endovascular treatment: modeling the best transportation options for optimal outcomes. *Stroke* 2017;48:791-794.
18. Osanai T, Ito Y, Ushikoshi S, et al. Efficacy of "Drive and Retrieve" as a cooperative method for the prompt endovascular treatment for acute ischemic stroke. *J Neurointerv Surg* 2019;0:1-5.

19. Central Social Medical Insurance Council. Establishment of a threshold in health technology assessment 2018. Available at: <https://www.mhlw.go.jp/file/05-Shingikai-12404000-Hokenkyoku-Iryouka/0000211609.pdf> (Accessed October 17, 2018) (In Japanese)
20. National Institute of Health and Care Excellence. The guideline manual, 7 Assessing cost effectiveness. Available at: <https://www.nice.org.uk/process/pmg6/chapter/assessing-cost-effectiveness> (Accessed October 17, 2018) (In Japanese)
21. Fukuda T, Shirowa T, Ikeda S, et al. Guideline for economic evaluation of healthcare technologies in Japan. *J Natl Inst Public Health* 2013;62:625-640. (In Japanese).
22. Hokkaido Division of the Japanese Society for Neuro Endovascular Therapy, Specialists in Hokkaido. Available at: <http://jsnet.hkdo.jp/>. (Accessed June 5, 2017) (In Japanese)
23. Ministry of Land, Infrastructure, Transport, and Tourism. National land numeral information download service 2018. Available at: <http://nlftp.mlit.go.jp/ksj/gmlold/> (Accessed September 26, 2018) (In Japanese)
24. Goyal M, Menon BK, van Zwam WH. Endovascular thrombectomy after large-vessel ischaemic stroke. *Lancet* 2016;387:1723-1731.
25. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med* 2015;372:11-20.
26. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med* 2015;372:1019-1030.
27. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med* 2015;372:2285-2295.
28. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med* 2015;372:1009-1018.
29. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med* 2015;372:2296-2306.
30. Hacke W, Donnan G, Fieschi C, et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet* 2004;363:768-774.
31. Spokoyny I, Raman R, Ernstrom K, et al. Accuracy of first recorded "last known normal" times of stroke code patients. *J Stroke Cerebrovasc Dis* 2015;24:2467-2473.
32. Yamaga M, Ikeda S. Cost of illness after stroke. *J Int Univ Health Welfare* 2016;21:82-92. (In Japanese).
33. Health and Welfare Bureau for the Elderly, Ministry of Health, Labour and welfare. Long-term care insurance system of Japan, 2016. Available at: https://www.mhlw.go.jp/english/policy/care-welfare/care-welfare-elderly/dl/ltcisj_e.pdf (Accessed October 17, 2018)
34. Ministry of Health, Labour and Welfare. Statistics of medical care activities in public health insurance 2014. Available at: <https://www.mhlw.go.jp/toukei/list/45-1.html> (Accessed September 27, 2018)
35. Hattori N, Hirayama T, Katayama Y. Medical Care for Chronic-Phase Stroke in Japan. *Neurol Med Chir* 2012;52:175-180.