Title
Analyzing Cost-Effectiveness of Allocating Neurointerventionist for Drive and Retrieve System for Patients with Acute Ischemic Stroke

Author(s)
Morii, Yasuhiro; Osanai, Toshiya; Fujiwara, Kensuke; Tanikawa, Takumi; Houkin, Kiyohiro; Gu, Songzi; Ogasawara, Katsuhiko

Citation
Journal of stroke and cerebrovascular diseases, 30(8), 105843
https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105843

Issue Date
2021-05-15

Doc URL
http://hdl.handle.net/2115/86422

Rights
© 2021. This manuscript version is made available under the CC-BY-NC-ND 4.0 license
https://creativecommons.org/licenses/by-nc-nd/4.0/

Type
article (author version)

File Information
revised manuscript without changes tracked_HUSCAP.pdf
Analyzing Cost-Effectiveness of Allocating Neurointerventionist for Drive and Retrieve System for Patients with Acute Ischemic Stroke

Abstract:

Objectives
There are regional disparities in implementation rates of endovascular thrombectomy due to time and resource constraints such as endovascular thrombectomy specialists. In Hokkaido, Japan, Drive and Retrieve System (DRS), where endovascular thrombectomy specialists perform early endovascular thrombectomies by traveling from the facilities where they normally work to facilities closer to the patient. This study analyzed the cost-effectiveness of allocating a neurointerventionist for DRS to treat stroke patients.

Materials and methods
The number of ischemic stroke patients expected to receive endovascular thrombectomy in Hokkaido in 2015 was estimated. It was assumed that an additional neurointerventionist was allocated for DRS. The analysis was performed from the government’s perspective, which includes medical and nursing-care costs, and the personnel cost for endovascular thrombectomy specialist. The analysis was conducted comparing the current scenario, where patients received endovascular thrombectomy in facilities where endovascular thrombectomy specialists normally work, with the scenario with DRS within 60-minute drive distance. Patient transport time was analyzed using geographic information system, and patient severity was estimated from the transport time. The primary outcome was incremental cost-effectiveness ratio (ICER) in each medical area which was calculated from the incremental costs and the incremental quality-adjusted life years (QALYs), estimated from patient severity using published literature. The entire process was repeated 100 times.
Results
DRS was most cost-effective in Kamikawachubu area, where the ICER was $14,173±16,802/QALY, significantly lower than the threshold that the Japanese guideline suggested.

Conclusions
Since DRS was cost-effective in Kamikawachubu area, the area should be prioritized when an endovascular thrombectomy specialist for DRS is allocated as a policy.

Key words: Cost-effectiveness Analysis, Geographic Information System, Drive and Retrieve System, Endovascular Thrombectomy, Ischemic Stroke

Introduction
The cost of stroke treatment accounts for approximately 6% of Japan's national medical expenditure (1), and stroke is the second most common condition, after dementia, that results in a requirement for long-term care. Thus, stroke has a significant impact on society (2). Cerebral infarction accounts for 60% or more of stroke cases (3). Systematic provision of highly equitable and efficient treatment for cerebral infarction is an important policy issue, such as the enactment of the Stroke and Cardiovascular Disease Control Act in December 2018 in Japan, as part of an effort to enhance provision of treatment for cerebral infarction (4).

Endovascular thrombectomy is a treatment that endeavors to improve the outcome for acute cerebral infarction patients by early recanalization of occluded arteries by the means of stents, etc., during the acute phase of cerebral infarction. The results of a series of randomized controlled trials were published from 2014 to 2015 (5-8), and meta-analysis of these reports found that
endovascular thrombectomy combined with medical treatment significantly improved the therapeutic effect, as compared to medical treatment alone, including intravenous alteplase therapy (recombinant tissue plasminogen activator: rt-PA) (9). Endovascular thrombectomy is thus an extremely important therapy to ensure that patients for whom rt-PA treatment is not feasible can also enjoy favorable outcomes (10).

However, there are time constraints for the use of endovascular thrombectomy after cerebral infarction, and resource constraints in terms of facility standards and endovascular thrombectomy specialists who perform the treatment; therefore, there may be regional disparities in implementation rates (11). Hashi et al. have reported regional disparities in the use of rt-PA (12). Hokkaido, the largest prefecture in Japan, is characterized by regional disparities in lifestyle-related services and medical services (13). Fujiwara et al. also reported uneven regional distribution of stroke treatment resources for treatment of cerebral infarction in Hokkaido (14), and Morii et al. reported regional disparities in the geographical accessibility to endovascular thrombectomy treatment (11).

The Drive and Retrieve System (DRS) has been proposed in Hokkaido with the aim of eliminating regional disparities in cerebral infarction treatment (15). The DRS is a scheme whereby endovascular thrombectomy specialists perform early endovascular thrombectomies by traveling from the facilities where they normally work (hub facilities) to facilities closer to the patient, which have the equipment required to perform endovascular thrombectomy, such as angiography equipment, but which lack endovascular thrombectomy specialists (spoke facilities). The DRS is currently partially implemented in the suburbs of Sapporo, and it has been reported that the scheme has shortened the time until reperfusion in stroke patients (16).

Morii et al. used the geographic information system (GIS) to analyze the effect of the DRS in Hokkaido on accessibility to endovascular thrombectomy and on medical and long-term care
costs (11). The Japanese Guideline for Preparing Cost-Effectiveness Evaluation to the Central Social Insurance Medical Council stipulates that although medical and long-term care costs reflect the standard analytical perspectives, it is preferable to include other costs when such costs are expected to create a public burden (17). However, the study by Morii et al. does not consider the costs involved in implementing the DRS, including the labor costs of the doctors, despite the expected need for a sizeable policy intervention. It is also preferable to conduct analysis based on actual introduction of the system, such as analyzing into which specific regions the DRS should be introduced. In addition, the previous study by Morii et al. was a small study that used GIS to investigate the cost-effectiveness of the medical treatment delivery system, but the study was unable to consider the uncertainty of patient distribution, because the virtual patient generation trial was not repeated. Therefore, conducting a repeat trial is necessary to propose a methodology that is able to consider the uncertainty of patient distribution.

Thus, the present study simulated a cost-effectiveness of allocating a endovascular thrombectomy specialist for DRS, assuming the additional assignment of doctors based on the policy for the DRS, with a view to improve the system to provide highly equitable and cost-effective treatment for cerebral infarction.

Methods

Subjects and outcomes

The subjects were 1443 virtual patients with cardioembolic infarction in Hokkaido in 2015 who were potentially eligible for endovascular thrombectomy using DRS. The number of these virtual patients was calculated by multiplying the population of Hokkaido (approximately 5.4 million) obtained from the national census (18) by the incidence of cardioembolic infarction on a population basis (26.8/100000 population) as estimated by a previous study, assuming that those
patients are potentially eligible for endovascular thrombectomy (19). The regional unit for analysis was set to 21 secondary medical service areas in Hokkaido. Hokkaido Prefecture has a population of approximately 5.4 million people, and its largest city, Sapporo (within the Sapporo secondary medical service area shown in Figure 1), has a population of approximately 2 million people (18), followed by Asahikawa-shi (Kamikawachubu medical service area in Figure 1), with a population of approximately 350,000 people, and Hakodate-shi (Minamioshima medical service area in Figure 1), with a population of approximately 270,000 people. Secondary medical service areas are regional units that provide inpatient medical care within the Japanese healthcare system. The system for providing stroke treatment was considered for each secondary medical service area. During the analysis period, we analyzed the cost-effectiveness of providing DRS for patients with acute cerebral infarction over a 1-year period. The government perspective, which included costs that the government paid, was used as the cost-effectiveness analysis perspective. The analysis included the cost and therapeutic effect within 3 years from onset.

The implementation of DRS as a policy is expected to improve patient access to endovascular thrombectomy, but this requires the assignment of specialists to regions with superior cost-effectiveness from the perspective of publicly funded healthcare. Therefore, this study assumed that one endovascular thrombectomy specialist to operate the DRS would be additionally assigned to one hub facility, the labor costs of which the policy would prescribe public funding.

Two scenarios were selected: one in which DRS is not implemented (base scenario) and the other in which endovascular thrombectomy specialists travel to spoke hospitals within a 60-minute drive (DRS scenario). The incremental cost-effectiveness ratio (ICER) was calculated as the primary outcome by comparing the two scenarios. The most commonly used metric in cost-effectiveness analyses, the ICER is used by the National Institute for Health and Clinical Excellence in the UK, in Japan (17, 20), and elsewhere. The ICER is usually calculated by taking
the difference in therapeutic effect between two treatments as the denominator and the difference
in cost as the numerator to provide a ratio of the cost required to attain one unit of therapeutic
effect. The ICER calculation scheme used in this study is shown in Figure 2.

Quality-adjusted life years (QALYs), a commonly used therapeutic effect metric, was also used
in this study. The ICER was calculated for each secondary medical service area from where the
doctor traveled (the specialists’ working location), i.e. to which secondary medical service area
an additional specialist should be assigned for DRS was analyzed from a cost-effective
perspective.

The cost-effectiveness analysis perspective also included other public expenditures, such as
medical, long-term care, and specialist labor costs, for calculating the ICER, based on the
government perspective (Figure 2). The ICER evaluation standard was set as Japanese Yen (JPY)
5,000,000/QALY (approximately USD 48,146/QALY) based on the Japanese guidelines, and the
cost and QALY were discounted at an annual rate of 2%. The currency was converted from JPY
to USD using the exchange rate on December 4, 2020 (21). The series of processes used to
calculate the ICER from the next section onward was repeated 100 times by operating the GIS
using the programming language Python (version 5.7). The random generation of patients with
each repetition made it possible to conduct an analysis that considered the uncertainty of the
patient distribution.
Generating virtual patients and identifying target facilities

The generation of virtual patients was based on a previous study on DRS (11). We obtained 1-km² mesh data for the target region from the FY2015 national census (18) and determined the location of the estimated number of patients with cardioembolic infarction in Hokkaido as a whole using the statistical analysis R by The R Foundation (ver 3.5.2). The number of patients generated in each mesh was proportional to the population of each mesh. The number of patients for each determined mesh was generated on each GIS mesh using the GIS random point generation function. ArcGIS Desktop 10 (www.esri.com) was used for the geographical analysis in this study.

According to a previous study (11), the identification of target hub facilities and spoke facilities was based on a list of candidate facilities acquired from the Hokkaido branch of the Japanese Society for Neuroendovascular Therapy and the Hokkaido Medical Plan, respectively (13, 22). The criteria for spoke facilities were that they had the ability to perform: 1) blood tests and imaging tests (computed tomography, magnetic resonance imaging, ultrasound, etc.), 2) craniotomy (cerebral aneurysm clipping, removal of intracerebral hematoma, decompressive craniectomy), and 3) thrombolytic therapy with rt-PA. These spoke facilities were also equipped to perform angiography. Next, we searched for hospitals within a 60-minute drive from the 30 hub facilities where the specialists were stationed using the ArcGIS Network Analysis Origin-Destination Matrix function. As a result, 30 hub facilities and 74 spoke facilities were identified in Hokkaido. The DRS scenario was set up so that patients would be transported to both hub facilities and spoke facilities for endovascular thrombectomy. The distribution of hub and spoke facilities in Hokkaido are shown in Figure 1.

Transport time and doctor travel
Transport time was analyzed using the ArcGIS Search for Find Nearest Facility function based on a previous study (11). The time from the ambulance leaving the fire station to arriving at the patient location and the time from the ambulance leaving the patient location to arriving at the medical facility were analyzed, and the sum of the two times was defined as the transport time. The target patients were classified into time zones depending on the transport time: 0–1 hour, 1–2 hours, 2–3 hours, and 3 or more hours. The 1-hour coverage rate, which is the proportion of patients that could be transported within 1 hour, and similarly the 3-hour coverage rate were calculated as accessibility performance indicators. Additionally, information on the name and the distance to the nearest facility and the arrival facility was acquired from the ArcGIS Search for Find Nearest Facility function to estimate transportation costs and travel routes.

It is preferable to perform DRS when an improvement in therapeutic effect can be expected, namely in areas where treatment can be commenced earlier by doctors traveling to the hospital. Therefore, in this study, it was decided that the doctors would travel when the transport time zone was shorter in the DRS scenario than in the base scenario (for example, if a patient’s transport time zone would be 1–2 hours in the current scenario but their transport time zone would be shortened to 0–1 h in the 60-minute DRS scenario, then the doctor would travel). In this instance, cases in which the travel time from the hub facilities to spoke facilities was less than 10 min were excluded from the analysis to avoid counting doctors traveling to neighboring hospitals because it was thought that the inclusion of these routes would have little substantial effect. The identified journeys were tabulated by the travel distance and the pair of hub and spoke facilities used for the analysis, while the number of journeys was tabulated by secondary medical service areas based on the original locations of the patient and the traveling doctor.

Estimating the severity of the patients’ conditions
The severity of the patients’ conditions was estimated in accordance with the previous study by Morii et al. (11) and based on the results of the HERMES trial, a meta-analysis of randomized controlled trials (RCTs) (13). The modified Rankin Scale (mRS) at 3 months after onset was used as the cerebral infarction severity index, as it is the most commonly used. The HERMES study, a meta-analysis of the main RCTs on the efficacy of endovascular thrombectomy, demonstrated that the percentage of patients whose prognosis was self-independent at 3 months after stroke significantly declined, and the proportion of patients with a severe condition increased with the delay in the treatment start time. Therefore, we attempted to reflect treatment that achieves better outcomes with an earlier start of treatment using the data on the relationship between the time from endovascular thrombectomy start and the mRS stage prognosis at 3 months after onset from the HERMES study to estimate the severity of the patients’ conditions (see Table 1 from the study by Morii et al. (11)). The results of the HERMES study showed that endovascular thrombectomy was significantly effective when reperfusion was achieved before approximately 7 hours. In this study, considering the time to rt-PA treatment and endovascular thrombectomy and time difference between onset time and uncertainty of onset time (23), it was assumed that the subjects transported within 3 hours were eligible for endovascular thrombectomy (11).

This simulation also assumed that the severity of the patients’ conditions did not change over the target period.

QALY analysis

QALYs were calculated by multiplying the time period by the quality of life (QOL) utility value, where death was 0 and perfect health was 1. QOL utility values were assumed to differ depending on the mRS-based severity and were allocated to each patient depending on the severity of their condition (15). The QOL utility values according to severity were acquired from a previous study.
of Japanese patients with stroke (Table 1) (24).

Cost analysis

The costs included the medical, long-term care, labor costs of doctors employed based on this policy, and the doctors’ transport costs, as mentioned earlier. The costs of the analysis are summarized in Table 2.

Medical costs were assumed to be dependent on the severity, and the total medical costs by severity, published from 2015 in the Stroke Databank, a database of Japanese cases, were used to calculate the medical costs (3). Furthermore, the cost of endovascular thrombectomy is automatically incurred when doctors travel; thus, the cost of one endovascular thrombectomy, set as USD3,192 (FY2018 Medical Service Fee K-178-4) was included in the calculation (25). The fee includes a fee for the angiography inspection. In Japan, the cost of these services does not differ, as official prices are set for all medical and long-term care services.

To calculate the long-term care cost, we first converted the severity of the patient’s condition estimated based on mRS to the nursing care level used to allocate long-term care services in Japan, based on a previous study (11). Under the Japanese long-term care insurance system, patients who require support to avoid long-term care are classified as Support Level 1 or Support Level 2.

Patients who require long-term care services are classified into long-term care levels 1–5. The larger the number, the greater the need for long-term care. The cost of long-term care was based on the converted level of long-term care needed, while the costs were allocated to each patient according to the level of long-term care needed in accordance with the method proposed by Yamaga and Ikeda (Table 1) (26).

Labor was set as a fixed cost. Information on the doctors’ general wages was obtained from the Basic Survey on Wage Structure conducted by the Ministry of Health, Labour, and Welfare (27).
Employment, welfare pension, social, and disaster insurance premiums estimated from the original amount were included in labor costs (28-31). Transport costs were assumed to depend on the distance traveled. Labor and transport costs were subject to a sensitivity analysis, and the ICER was also calculated in the event that there was a 50% increase or a 33% decrease.

**Results**

**One- and 3-hour coverage rates**

Figure 3a shows the results for each scenario for the 1-hour coverage rate based on patient location, while Figure 3b shows the 3-hour coverage rate. The 1-hour coverage rate was around 90% throughout Hokkaido, but the rates were low in medical service areas in Minami Hiyama, Kitaoshimahiyama District, Hidaka, Rumoi, Soya, and Nemuro. In the DRS scenario, the 1-hour coverage rate increased mainly in the medical service areas in Kamikawahokubu, Hokumo, Kitaoshimahiyama, Shiribeshi, and Rumoi. The 3-hour coverage rate was 99% throughout Hokkaido. In the DRS scenario, the 3-hour coverage rate increased mainly in the medical service areas in Rumoi, Soya, and Nemuro, but it remained at around 30% in the Soya medical service area.

**Number of DRS journeys**

Figure 4a shows the number of doctors’ journeys by patient location in secondary medical service areas. Patients in the Hokumo medical service area had the highest number of doctors’
journeys, at 13.9 per year, followed by the Kamikawahokubu medical service area (11.7 journeys/year), Rumoi medical service area (4.6 journeys/year), Shiribeshi medical service area (4.5 journeys/year), and Soya medical service area (4.2 journeys/year).

Figure 4b shows the number of doctors’ journeys based on the travel starting point. Figure 4 shows only the secondary medical service areas with hub facilities. The highest number of journeys were in the Kamikawahokubu medical service area (20.7 journeys/year), followed by Hokumo (15.4 journeys/year), and Nishiiburi (4.9 journeys/year).

Figure 4. Number of drive and retrieve systems expected in each medical area (a) by patient location and (b) specialist location

**Facilities that performed DRS**

This analysis obtained information on the numbers of doctors’ journeys and facilities sending doctors. The facilities that sent a comparatively large number of doctors are shown in Figure 5. Figure 5a shows that the largest number of journeys were from the Kamikawahokubu medical service area, but it also shows that the treatment routes for patients in the Kamikawahokubu, Soya, Rumoi, and Emmon medical service areas, with doctors traveling from Kamikawahokubu to hospitals in the Kamikawahokubu medical service area (Figure 5a). The treatment routes for patients were identified in the Hokumo medical service area with doctors traveling to Abashiri city, which is within the same medical service area, or traveling within the same medical service area and from the Nemuro medical service area (Figure 5b). Figure 5c shows that the DRS was used for several patients in the Shiribeshi medical service area, and treatment routes for patients
in the Shiribeshi medical service area were identified as doctors traveling from hospitals in the Sapporo medical service area to hospitals in the Shiribeshi medical service area (Figure 5c), while treatment routes for patients in the medical service areas in Shiribeshi and Kitaoshimahiyama were identified as doctors traveling from Muroran city in Nishiiburi medical service area to Date city (Figure 5d).

Figure 5. Identified drive and retrieve system routes that are expected to be used frequently

QALY and cost

The mean value of 100 trials of QALY increments obtained from the DRS is shown in Figure 6a, while the mean reduction in medical and long-term care costs based on the departure point is shown in Figure 6b. Doctors traveling from the Kamikawachubu medical service area had the highest gain in QALY gain (4.33 QALYs), followed by Hokumo medical service area (1.58 QALYs). The reduction in medical costs and long-term care costs based on the departure point were largest in the Kamikawachubu medical service area (USD 115,015), followed by the Hokumo medical service area (USD 39,005).

Figure 6. Gained quality-adjusted life years (a) and medical and reduced nursing care costs (b) in each medical area (based on departure point)
The base scenario is being trialed in the Minamioshima, Higashiiburi, and Nakasorachi medical service areas in the 100 trials, which made it impossible to calculate the mean ICER. The ICER for employing a full-time doctor in the Sapporo medical service area is USD 969,766 ± 816,293/QALY, USD1,634,635 ± 819,612 in Nakasorachi medical service area, USD 567,511 ± 544,292/QALY in the Nishiiburi medical service area, USD 12,572 ± 16,518/QALY in Kamikawachubu Medical Service Area, USD 89,899 ± 51,416/QALY in the Hokumo medical service area, USD 1,078,899 ± 721,417/QALY in the Tokachi medical service area, and USD 1,438,215 ± 1,062,089/QALY in the Kushiro medical service area, which means that employing specialists in Kamikawachubu medical service area is the most cost-effective (Table 3). The mean ICERs were calculated excluding trials in which incremental QALY were zero in Minamioshima, Higashiiburi, and Nakasorachi medical service areas (Table 3). The mean ICER in the Kamikawachubu medical service area was significantly lower than the USD 48,146, the evaluation standard based on Japanese guidelines (21). Similar trends were observed in the sensitivity analysis (Figure 7).

Discussion

This study conducted a cost-effectiveness analysis by simulation, assuming policy-based introduction of the DRS with the aim of constructing a system to provide highly equitable and cost-effective cerebral infarction treatments. This analysis was added to that of a previous study.
mainly in that we attempted to conduct a more specific cost-effectiveness analysis by including the costs of the endovascular thrombectomy specialist, transportation, and endovascular thrombectomy, and its geographical analysis was more complete for DRS implementation by acquiring analyzed information on facilities at the departure and destination points rather than by analyzing cost-effectiveness only. The results will be of great importance in considering where an endovascular thrombectomy specialist for DRS should be allocated, where the endovascular thrombectomy specialist should travel, and the cost-effectiveness of the system.

Concerning the number of virtual patients, this study used the number of patients with cardioembolic infarction who were potentially eligible for endovascular treatment, while a previous study used the overall number of patients with stroke. We tried to estimate how many patients would benefit from DRS in each medical service area. Furthermore, the entire analytical process was repeated to decrease the extent of uncertainty in the randomly generated patient distributions. Some of the results of geographic accessibility were similar to those of previous research (11), and the results of this study should more comprehensively consider the uncertainty.

Although the 3-hour coverage rate was high in almost all medical service areas, it was less than 30% in the Soya medical service area, even with the DRS scenario, which is consistent with the trends reported by Morii et al. and Fujiwara et al., indicating regional disparities in accessibility to cerebral infarction treatment in Hokkaido (11,14).

The highest number of endovascular thrombectomies performed by traveling doctors was in the Kamikawahokubu medical service area, followed by the Hokumo, Rumoi, Shiribeshi, and Soya medical service areas. Except for the Hokumo medical service area, these medical service areas are characterized by a lack of hub facilities. DRS has been shown to increase accessibility to endovascular thrombectomy in medical service areas without hub facilities (11). The Hokumo medical service area is relatively large. Although there is a hub hospital in Kitami-city, there are
none in Abashiri City (Figure 5b). Therefore, even within the same secondary medical service area, there are patients who can be transported within 1 hour, while other patients require 2 or more hours for transportation. Given that the DRS increased the 1-hour coverage rate in the Kitami medical service area, sending specialists from Kitami to hospitals in Abashiri should shorten treatment start times.

There are no spoke facilities within a 60-minute drive of hub facilities in the Soya and Rumoi medical service areas. In addition, there are currently patients for whom transport to medical facilities within 3 hours would be difficult. The Stroke and Cardiovascular Disease Control Act and Cardiovascular Disease stipulates that it is important for different regions to collaborate to build a medical provision system when the provision of medical services is difficult within one region (4). DRS is considered an effective scheme for improving regional disparities in regions where accessibility to treatment is not guaranteed, such as the Soya, Emmon, Kamikawahokubu, and Rumoi medical service areas (11). This study set the area for travel to 60 minutes, but it may be possible to investigate a more detailed medical provision system, better suited to the actual situation in the region, by conducting the same analysis using a 90-minute scenario given the geographical characteristics of Hokkaido, which has a large land area. Furthermore, based on the low 3-hour coverage rate in the Soya medical service area, it may be necessary to conduct a comprehensive investigation, including the use of medical helicopters, in addition to the DRS explored here.

This study calculated the cost-effectiveness of assigning specialists individually to each secondary medical service area with a hub facility. In this study, the ICER in the Kamikawahubu medical service area was significantly lower than the evaluation criteria of JPY 5,000,000/QALY, and the results were lower than the evaluation criteria after the sensitivity analysis, considering the uncertainty of the doctors’ wages. In the previous study, only medical costs (except those for
endovascular thrombectomy and one endovascular thrombectomy specialist was employed from the public budget. This result suggests that it is cost-effective to assign an additional specialist who is able to perform endovascular thrombectomy for traveling from Kamikawachubu to the Kamikawahokubu medical service area (Fig 5a). One of the reasons for the superior cost-effectiveness is that the labor costs (the annual wage) of the doctors’ travels were recorded as a fixed cost, and recouping fixed costs over a number of journeys is thought possible. Profitability may not be ensured if specialists are assigned to hospitals with only a small number of journeys.

As mentioned earlier, another reason may be that doctors traveling from Asahikawa would be expected to travel to the Rumoi, Soya, Enmon, and northern Kamikawa medical service areas. At the present time, it takes 3 or more hours for some patients in the Rumoi, Soya, and Enmon medical service areas to travel to medical facilities in Kamikawachubu; thus, implementing DRS in these areas would increase the possibility of endovascular thrombectomy for indicated patients who previously would not have expected a significant therapeutic effect from this procedure, which would in turn be expected to improve the therapeutic effect. Thus, the Kamikawachubu medical service area is a central base for treating patients in northern Hokkaido, making it desirable to enhance the system for endovascular thrombectomy in this region.

These results have shown the effect of DRS on improving accessibility and demonstrated that deploying the DRS in the Kamikawachubu medical service area has superior cost-effectiveness. This shows that the Kamikawachubu medical service area is a high priority area for DRS implementation. This study clarified how many travels were expected in each area by DRS and how cost-effective it is to assign an endovascular thrombectomy specialist in each area, including the related costs; therefore, its findings will be of great importance in DRS implementations. Conducting further analyses based on the number of specialists and facility capacity rather than
on accessibility alone may provide additional useful information for policy formulations.

Although the study found that assigning additional specialists to the Sapporo and Nishiiburi medical service areas was not cost-effective, it demonstrated that there was a certain need for doctors to travel from these secondary medical service areas (Figure 5c and 5d). This result will provide political insight into DRS route implementation. Although it was not cost-effective to assign an additional specialist to these secondary medical service areas, there are a large number of hub facilities and specialists in the Sapporo medical service area (Figure 1). It is preferable to consider the possibility of building a DRS using existing specialists to facilitate equitable treatment accessibility.

This study analyzed a sample of Hokkaido, a region in Japan with geographical disparities in accessibility to medical treatment. However, the methodology of using GIS and the existing secondary data implemented in this study could also be applicable to other regions in Japan as well as to other countries. This analysis may be helpful for examining the transportation system for patients with cerebral infarction and formulating policies, including the additional assignment of doctors. This study is one of the few that considers the geographic accessibility and cost-effectiveness of the healthcare provision system. Its methodology considers the accessibility and cost-effectiveness of other situations in which transport time is a determinant of patient outcomes, such as myocardial infarction.

Nevertheless, this study has a number of limitations. First, the cost and QALY analysis period was fixed at 3 years due to limited data availability. Alleviating stroke using endovascular thrombectomy would reduce the cost of long-term care over an individual’s lifetime; hence, analyzing the effect over a person’s lifetime may enable the estimation of a greater number of QALY. Setting a fixed QALY did not allow for consideration of changed circumstances, such as an individual’s death, but this type of effect is thought to be equal with or without availability of
DRS-type offerings; therefore, it is unlikely that this process would significantly affect the trend of incremental QALY.

Second, this analysis followed the standards set out in the Japanese Guideline for Preparing Cost-Effectiveness Evaluation, and the cost analysis was conducted from the government perspective (17). Yamaga et al. calculated the cost of illness due to stroke, including loss of opportunity, given the marked loss of opportunity due to stroke sequelae (26). Further analyses conducted from a social perspective, including loss of opportunity, may provide findings that are more useful for policy decision-making.

Third, it did not consider uncertainties associated with the time of day in which the cerebral infarction occurred or the weather. In addition, this analysis does not consider lengthening the time windows for endovascular thrombectomy [32,33]. Therefore, our analysis could have underestimated the benefits of endovascular thrombectomy and DRS, but it did not overestimate them. Further analyses that consider these points may enable a more precise simulation.

Conclusion

This study analyzed the cost-effectiveness of assigning an additional specialist who is able to perform endovascular thrombectomies for the DRS in Hokkaido and in the secondary medical service areas of Hokkaido using a GIS, with a view to support the construction of a treatment provision system for acute cerebral infarction patients with superior accessibility and cost-effectiveness in Hokkaido. The results of the study demonstrated that Kamikawachubu medical service area is likely to involve a large number of doctor’s journeys and would therefore facilitate the greatest cost reduction effect for medical care and long-term care and attain desirable QALY. It was expected that doctors would travel from Kamikawachubu medical service area to the Soya, Rumoi, Enmon, and Kamikawahokubu medical service areas. The ICER fell below the evaluation
criteria of USD48,146/QALY only when additional specialists were assigned to the central
Kamikawa medical service area (USD 14,173 ± 16,802/QALY), demonstrating the cost-
effectiveness of assignment of additional specialists able to perform endovascular thrombectomy
by traveling to Kamikawahokubu medical service area. These results suggest that the central
Kamikawa medical service area is a region where the introduction of the DRS should be
prioritized.

Acknowledgement

We would like to thank Editage (www.editage.jp) for English language editing.

Declaration of interest

None

References

1. The Ministry of Health Labour and Welfare. Survey on the Trend of Medical Care
(Accessed on November 18, 2019) (In Japanese)

on September 27, 2018) (In Japanese)


available at


15. Hokkaido University Department of Neurosurgery, Graduate School of Medicine, Hokkaido University. Clinical Research Available at https://neurosurgery-hokudai.jp/research/clinical/ (Accessed on


25. ELSEVIER. Today’s clinical support. Available at https://clinicalsup.jp/contentlist/shinryo/ika_2_10_1_3_1/k178-4.html (Accessed on December 4, 2020) (In Japanese)


**Figures and figure legends**
Figure 1. the number of Hub hospitals and Spoke hospitals in each medical area

Figure 1 shows the hub Hub hospitals and Spoke hospitals in each medical area identified by “Origin-Destination Matrix” of GIS.

---

**Figure 2: Scheme of calculating ICER**

\[
\text{ICER} = \frac{\text{Difference of costs between DRS scenario and in base scenario}}{\text{Difference of gained QALYs between DRS scenario and base scenario (severity-dependent)}}
\]

---

Costs consist of medical costs, nursing care costs, neurointerventionist fee, and transportation cost.
Figure 3: 1-hour cover rate and 3-hour cover rate

Figure 3 shows the rate of patients transferred to Hub hospitals or Spoke hospitals within 1 and 3 hours in the 2 scenarios.

Figure 4: The number of DRS expected in each medical area

Figure 4 shows the number of DRS expected in each medical area in one year. Figure 4-a is based on patients-location, while Figure 4-b is based on endovascular thrombectomy specialists’ location.
Figure 5: Identified DRS routes which are expected to be used frequently.

Figure 5 shows the DRS routes identified by the GIS analysis which are expected to be used frequently.
Figure 6: Gained QALYs (a) and medical and reduced nursing-care costs in each medical area (specialist-location-based)

Figure 6 shows gained QALYs (a) and medical and reduced nursing-care costs in each medical area (specialist-location-based), which indicate how much costs will be reduced by allocating an endovascular thrombectomy specialist for DRS in each area.

Figure 7: Result of sensitivity analysis on specialist personnel and transportation cost

Figure 7 shows the result of sensitivity analysis of specialist personnel and transportation cost. The red bar shows the higher case, and the blue bar shows the lower case.