# **SPECIAL ARTICLE**

# Evidence and Recommendations for Acute Stroke Rehabilitation from the Japan Stroke Society: Abridged Secondary Publication of the Japanese-language Version

Wataru Kakuda, MD, PhD <sup>a</sup> Makoto Nakajima, MD, PhD <sup>b</sup> Koichi Oki, MD, PhD <sup>c</sup> Tetsuo Koyama, MD, PhD <sup>d</sup> Naoki Oyama, MD, PhD <sup>e</sup> Masatoshi Koga, MD, PhD <sup>f</sup> Makoto Hayase, MD, PhD <sup>g</sup> Tsuyoshi Ohta, MD, PhD <sup>h</sup> Yasuyuki Iguchi, MD, PhD <sup>i</sup> Shigeru Fujimoto, MD, PhD <sup>j</sup> Tomohiro Omori, ST <sup>k</sup> Koichi Matsumoto, PT <sup>1</sup> Yoichiro Hashimoto, MD, PhD <sup>m</sup> Ryo Itabashi, MD, PhD <sup>n</sup> Masachika Niimi, MD, PhD <sup>o</sup> Hirokazu Ashiga, ST <sup>p</sup> Fumihiro Tajima, MD, PhD <sup>q</sup> and Kuniaki Ogasawara, MD, PhD <sup>r</sup>; the Japan Stroke Society's rehabilitation project team for equalizing and standardizing acute stroke rehabilitation

> **Objectives:** In Japan, acute stroke rehabilitation has been expanding more steadily than previously with the nationwide establishment of primary stroke centers. However, Japan previously had no established guidelines for the rehabilitation. Consequently, rehabilitation programs and the provision systems for acute stroke varied among the facilities. To equalize and standardize acute stroke rehabilitation in Japan, it is necessary to develop clinical recommendations for rehabilitation. Therefore, the rehabilitation project team of the Japan Stroke Society aimed to develop the first recommendations for acute stroke rehabilitation in Japan. Methods: The recommendations are based on the results of a survey on the current status of acute stroke rehabilitation at primary stroke centers in Japan, which was completed in 2022, and on a literature review conducted by the rehabilitation project team. Results: The recommendations consist of 19 clinical questions regarding the following topics of acute stroke rehabilitation: (1) head elevation and mobilization training, (2) acute complications, (3) training time and frequency for acute stroke rehabilitation, (4) dysphagia in the acute phase, and (5) acute rehabilitation during pandemics of novel and reemerging infections, particularly novel coronavirus disease 2019 (COVID-19). The team members agreed on all answers for these 19 clinical questions. Conclusions: These recommendations suggest broad principles of rehabilitative intervention in the acute phase of stroke. In the near future, it is expected that the dissemination of these recommendations will result in an increase in the quality of acute stroke rehabilitation in Japan.

Key Words: acute rehabilitation; COVID-19; dysphagia; mobilization; stroke

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- <sup>b</sup> Department of Neurology, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan
- <sup>c</sup> Department of Neurology, Stroke Center, Tokyo Saiseikai Central Hospital, Tokyo, Japan
- <sup>d</sup> Department of Rehabilitation Medicine, Nishinomiya Kyoritsu Neurosurgical Hospital, Nishinomiya, Japan
- <sup>e</sup> Department of Stroke Medicine, Kawasaki Medical School, Kurashiki, Japan
- <sup>f</sup> Department of Cerebrovascular Medicine, National Cerebral and Cardiovascular Center, Osaka, Japan
- <sup>g</sup> Department of Neurosurgery, National Hospital Organization Kyoto Medical Center, Kyoto, Japan
- <sup>h</sup> Department of Neurosurgery, Kobe City Medical Center General Hospital, Kobe, Japan
- <sup>i</sup> Department of Neurology, The Jikei University School of Medicine, Tokyo, Japan
- <sup>j</sup> Division of Neurology, Department of Medicine, Jichi Medical University, Tochigi, Japan
- <sup>k</sup> Division of Rehabilitation Medicine, International University of Health and Welfare Narita Hospital, Narita, Japan
- <sup>1</sup> Division of Rehabilitation Medicine, Tokyo General Hospital, Tokyo, Japan
- <sup>m</sup> Stroke Center, Saiseikai Kumamoto Hospital, Kumamoto, Japan

- <sup>o</sup> Department of Rehabilitation Medicine, Nihon University School of Medicine, Tokyo, Japan
- <sup>p</sup> Department of Speech and Hearing Sciences, School of Health Sciences at Narita, International University of Health and Welfare, Narita, Japan
- <sup>q</sup> Chuzan Hospital, Okinawa City, Japan
- r Department of Neurosurgery, Iwate Medical University School of Medicine, Morioka, Japan

<sup>&</sup>lt;sup>a</sup> Department of Rehabilitation Medicine, International University of Health and Welfare School of Medicine, Narita, Japan

<sup>&</sup>lt;sup>n</sup> Stroke Center, Division of Neurology and Gerontology, Department of Internal Medicine, Iwate Medical University School of Medicine, Morioka, Japan

Correspondence: Wataru Kakuda, MD, PhD, 852 Hatakeda, Narita, Chiba 286-8520, Japan, E-mail: wkakuda@iuhw.ac.jp

# INTRODUCTION

Acute stroke rehabilitation has been expanding more steadily than previously in Japan with the nationwide establishment of primary stroke centers. However, Japan previously had no established guidelines for acute stroke rehabilitation, which therefore varied widely among facilities. Consequently, the rehabilitation project team of the Japan Stroke Society developed the first recommendations for acute stroke rehabilitation with the aim of equalizing and standardizing acute stroke rehabilitation in Japan. The Japanese Association of Rehabilitation Medicine and the Japanese Association of Acute Medicine and Rehabilitation cooperated for the development of the recommendations. The Japan Stroke Society project team made the Japanese-language version of the recommendations publicly available on the society website in June 2023. Subsequently, the Japanese-language version was published in the Japanese Journal of Stroke on January 25, 2024.<sup>1)</sup> The recommendations were developed based on the results of a survey on the current status of acute stroke rehabilitation at primary stroke centers in Japan and on a literature review conducted by the rehabilitation project team. During the 1-year period from April 2022 to March 2023, work on the development of the recommendations was supported by a Health, Labour, and Welfare Policy Research Grant (Special Research). Now the team has abridged the original Japanese-language version of the recommendations and developed an English-language version of the recommendations. Therefore, this English-language version of the recommendations is an abridged secondary publication of the original Japanese-language version.

The recommendations are based on the answers to 19 clinical questions on the following five topics: (1) head elevation and mobilization training, (2) acute complications, (3) training time and frequency for acute stroke rehabilitation, (4) dysphagia in the acute phase, and (5) acute rehabilitation during pandemics of novel and re-emerging infections, particularly novel coronavirus disease 2019 (COVID-19). We sincerely hope that the dissemination of these recommendations will result in an increase in the quality of acute stroke rehabilitation, not only in Japan, but globally.

Abbreviations used in Commentary sections: mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; AHA, American Heart Association; ASA, American Stroke Association; ROM, range of motion; BI, Barthel Index; AVERT, A Very Early Rehabilitation Trial; ADL, activities of daily living; DVT, deep venous thrombosis; rt-PA, recombinant tissue plasminogen activator; SLHT, speech-language-hearing therapist; VF, videofluorography; VE, videoendoscopy.

#### **CLINICAL QUESTIONS**

# **1 Head Elevation and Mobilization Training** *Clinical Question 1-1*

• What is the appropriate time to start head elevation in acute stroke (mainly ischemic stroke)?

#### Answer 1-1

• The appropriate time to start head elevation is still unknown. However, uniformly keeping the head elevated for 24 h immediately after admission does not affect outcome in stroke patients.

■ Although caution is required for some patients, such as those with large-vessel occlusion, there is little need to uniformly maintain acute stroke patients in a lying-flat position on the bed.

#### Commentary

A study of 57 patients with acute ischemic stroke from four observational studies published in 2014 reported that keeping the head position close to flat increased cerebral blood flow velocity as determined by transcranial Doppler ultrasonography.<sup>2)</sup> A combined analysis of these findings with the addition of data from the HeadPoST (Head Positioning in Acute Stroke Trial) pilot study<sup>3)</sup> showed a significant association between head elevation and cerebral blood flow.<sup>4</sup>) In 2020, a systematic review and meta-analysis of 21 studies was reported. In 17 of these 21 studies, patient head position was significantly associated with cerebral blood flow. However, there was high degree of inter-study variability among the studies with respect to factors such as the degree and duration of head elevation and the methods used to evaluate cerebral blood flow.<sup>5)</sup> In a cluster-randomized study conducted at several centers as a pilot study of HeadPoST, head elevation starting at several hours (mean, 5 h) after onset was compared with lying flat on the bed in 94 patients with mild-moderate acute ischemic stroke involving anterior cerebral circulation. Although cerebral blood flow velocity by transcranial Doppler ultrasonography was significantly increased in patients lying flat, no relationship between the velocity increase and neurological outcome could be demonstrated.<sup>3)</sup> The HeadPoST study was an international, multicenter, collaborative study published in 2017. The study was conducted at 116 centers in nine countries. The subjects were 11,093 acute stroke patients (85% of the strokes were

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ischemic). They were randomly assigned to a group who were maintained with their head in a flat-lying position for 24 h after admission or a group who were placed in a sitting-up position for the same period with the head elevated to at least 30 degrees. The median interval between stroke onset and the initiation of intervention was 14 h, which was somewhat longer than in the previously mentioned pilot study. There was no difference between the groups in the distribution of mRS scores at 90 days after onset (P=0.84), which was the primary outcome, or the mortality rate (7.3% vs. 7.4%, P=0.83). Moreover, the results for these outcomes were similar in patients with ischemic stroke and in those with intracerebral hemorrhage. There was also no difference in adverse events including pneumonia.<sup>6)</sup> Criticisms of this pivotal randomized trial include the large number of patients who had a mild symptom (median NIHSS score of 4), the lack of information about vascular lesions that could affect cerebral blood flow, the late timing of intervention when compared with the pilot study, the large number of dropouts, and the prospective, randomized, open-label, blindedendpoint (PROBE) method.<sup>4,7)</sup>

However, a subanalysis of the HeadPoST study for patients with moderate-to-severe stroke also showed no association between head elevation and outcome.<sup>8)</sup> In contrast, an observational study published after the HeadPoST study compared head-elevation position (+30 degrees) with head-down position (-15 degrees) in 209 patients with supratento-rial large-vessel occlusion; the investigators found that the NIHSS scores 48 h after onset were lower in the head-down group than in the head-elevation group.<sup>9)</sup>

The AHA/ASA guidelines published in 2019 indicated that the benefit of lying flat on the bed early after hospitalization is uncertain (recommendation class IIb, evidence level B-R).<sup>10)</sup> A systematic review by the National Institute for Health and Care Excellence (NICE) in the United Kingdom, published in 2019,<sup>11)</sup> evaluated the quality of the evidence from the HeadPoST study and its pilot study, but did not provide any specific recommendation on positioning. The report concluded that the position of acute stroke patients should be determined after evaluating the patient's condition and personal preferences.<sup>11)</sup> In other words, acute stroke patients should be assessed to establish the optimum position that is individually suited to each patient.

A questionnaire survey of 959 primary stroke centers in Japan in 2022 showed that in ischemic stroke and intracerebral hemorrhage (nonoperative patients), more than half of the facilities started head elevation of at least 30 degrees on the day of admission and that nearly all started elevation by the second day of hospitalization.<sup>12)</sup> Moreover, there was a tendency for such elevation to start earlier in lacunar infarction, branch atheromatous disease, atherothrombotic brain infarction, cardiogenic cerebral embolism, and intracerebral hemorrhage, in that order. Elevation tended to start later in subarachnoid hemorrhage after surgical clipping or endovascular coiling for ruptured aneurysm.

As indicated by the above findings, caution should be used for some patients such as those with large-vessel occlusion. However, considering the increased risk of complications associated with lying flat, such as aspiration pneumonia, there is little need to uniformly maintain acute stroke patients in a lying-flat position.

#### Clinical Question 1-2

■ What is the appropriate time after onset to start range of motion training in bed for acute stroke patients (mainly ischemic stroke)?

#### Answer 1-2

■ Starting range of motion training in bed soon after onset appears to result in no significant adverse events. Therefore, starting this training within 24 h of onset can be considered.

#### Commentary

There have been very few studies that have investigated the time for starting ROM training in bed. In a randomized study that investigated training initiation with the Bobath approach in bed within 72 h or 1 week of onset in 85 patients with hemiparetic ischemic stroke, the group that started training earlier showed significantly better neurological outcomes.<sup>13)</sup> In a randomized study that assigned 40 patients with ischemic stroke to start exercise training in bed within 24 or 48 h after onset, the patients that started training earlier had significantly higher scores on the Berg Balance Scale and higher BI after 7 days.<sup>14</sup>)

A questionnaire survey on acute stroke rehabilitation conducted in Japan in 2022 found that in patients with any type of ischemic stroke, in-bed training (maintaining functional position, positioning, and ROM training during bed rest) was started on the day of admission at approximately 60% of the facilities.<sup>12</sup>) By the second day of hospitalization, in-bed training had been started at nearly all facilities. In patients with intracerebral hemorrhage (nonoperative patients), inbed training was started on the day of admission at slightly less than 50% of the facilities and, by the second day of hospitalization, had been implemented at more than 90% of facilities. In patients with subarachnoid hemorrhage (after ruptured aneurysm treatment), the training tended to start later.<sup>12)</sup> These findings indicate that starting in-bed ROM training early after onset does not result in an increase in adverse events and may improve functional outcome, although further evidence is required.

#### Clinical Question 1-3

• What is the appropriate time after onset to start mobilization (training to leave bed) in patients with acute stroke (mainly ischemic stroke)?

#### Answer 1-3

■ At present, it may be appropriate to start mobilization 24–48 h after stroke onset.

• For patients with mild symptoms or those with nonelderly ischemic stroke, if consideration is given to treatment adjustments, such as shortening mobilization time and increasing its frequency, starting mobilization within 24 h of onset can be considered.

#### Commentary

In this section, the initiation of mobilization is defined as the initiation of sitting training (including sitting on the edge of the bed), transfer training, standing training, and gait training. This section mainly discusses the studies of acute ischemic stroke. In the reviews published in 2006, mobilization was defined as all physical activity regardless of posture within 3 days of stroke onset. At that time, the concept of early mobilization had not been established.<sup>15–17)</sup> In the AVERT II study,<sup>18)</sup> which was conducted at two stroke units in Australia and published in 2008, all 71 stroke patients (87% were ischemic stroke) were randomized to standard care plus very early mobilization (within 24 h of onset) or standard care only, and rehabilitation was continued for up to 14 days. There were no significant differences with respect to death within 3 months (primary endpoint; very early mobilization group, 8/38; standard care group, 3/33), adverse events, or worsening of symptoms.<sup>18)</sup>

In the AVERT III study, 2014 patients with acute ischemic stroke or intracerebral hemorrhage (1828 with ischemic stroke) in 56 acute stroke units in five countries were randomized to a very early mobilization group (within 24 h of onset) or to a usual-care group. Mobilization was started within 24 h of onset for 92% of patients in the very early mobilization group and 59% of those in the usual-care group. In the very early mobilization group, the frequency of mRS score of 0–2 after 3 months (primary endpoint) was significantly smaller than those in the usual-care group (46% vs. 50%). Moreover,

the results were similar for patients with ischemic stroke and those with intracerebral hemorrhage. However, there was no significant difference in the frequency of death within 3 months (very early mobilization group, 8%; usual-care group, 7%). There was also no difference in the frequency of non-fatal adverse events (19% and 20%, respectively).<sup>19)</sup> An additional analysis of adverse events within 14 days of onset showed a significantly increased risk of death with very early mobilization in patients with intracerebral hemorrhage and those aged 80 years or older. However, there was no significant intergroup interaction.<sup>20)</sup>

In the Early Sitting in Ischemic Stroke Patients (SEVEL) study<sup>21)</sup> published in 2016, 138 patients with ischemic stroke were randomized to an early sitting group (sitting at the earliest possible time but no later than 1 day after onset) or a progressively sitting group (head elevation of 30 degrees on day 0, followed by 45 degrees on day 1, 60 degrees on day 2, and sitting on day 3). The results showed no significant difference in the frequency of mRS score of 0-2 after 3 months (76.2% vs. 77.3%, P=0.52) and no difference in adverse events between the two groups.<sup>21)</sup> In a study of 340 patients with ischemic stroke who received mobilization as either proprioceptive neuromuscular facilitation or cognitive therapeutic exercise, Morreale et al.<sup>22)</sup> showed that very early mobilization (within 24 h) was associated with better outcomes after 12 months when compared with late initiation of mobilization (after 24 h) for both techniques.

The results from the AVERT III study contradicted the expectation that very early mobilization would result in improved outcomes, prompting widespread debate. For example, it was noted that the initiation of mobilization differed from that in the control group by only 4 h. That is, in many of the clinical studies that examined early mobilization, including the AVERT III study, randomization was used not only for differences in the timing of mobilization initiation, but also for the subsequent continuation of mobility rehabilitation. Therefore, the amount of rehabilitation provided, rather than the timing of mobilization initiation, may have affected the results. The results of an additional analysis examining the effect of timing and dose of mobilization on its efficacy and safety irrespective of the assigned treatment group showed that increased amount of mobilization reduced the likelihood of a good outcome, whereas more frequent mobilization resulted in a positive effect.<sup>23)</sup> It is argued that very early mobilization cannot improve outcomes unless mobilization time is shortened and the frequency of mobilization is increased. In support of this idea, the study by Tong et al.<sup>24</sup>) published in 2019 randomized 300 patients with ischemic stroke into three groups: patients that underwent very early intensive mobilization (mobilization for  $\geq$ 3 h/day within 24 h); patients that underwent early intensive mobilization (mobilization for  $\geq$ 3 h/day within 24–48 h); or patients that underwent early usual mobilization (mobilization for  $\leq$ 1.5 h/day within 24–48 h). They showed that outcomes were the poorest in the group that underwent very early intensive mobilization, whereas outcomes were the best in early intensive mobilization group (proportion of patients with mRS score 0–2 after 3 months: 37.8% vs. 53.5% vs. 45%, respectively).<sup>24)</sup> Therefore, in considering the significance of very early mobilization, it may be necessary to take into account the effects of mobilization time and intervention frequency on outcomes.

In a pooled analysis of nine randomized trials provided in the *Cochrane Database of Systematic Reviews* published in 2018,<sup>25)</sup> the odds ratio for death or poor outcome with very early mobilization was 1.08 (95% confidence interval, 0.92–1.26), and no differences were observed in mortality or complications. However, significant improvements in ADLrelated scores and reduction in the length of hospital stay were found. A post hoc network meta-analysis suggested that around 24 h after onset (interquartile range, 22–29 h) is the appropriate timing for mobilization in view of the neurological outcomes and mortality at 3 months after onset.<sup>25)</sup>

Although the 2019 AHA/ASA guidelines recommended early rehabilitation itself (recommendation class I, evidence level A), they indicated that high-dose very early mobilization should not be performed within 24 h of onset [recommendation class III ("harm"), evidence level B-R].<sup>10</sup> Moreover, the systematic review by NICE in the United Kingdom in 2019 reported that although the evidence was difficult to interpret, high-dose mobilization should not be performed very early (within 24 h of onset).<sup>11</sup> However, the review also indicated that in the view of the panel, this should not impede the mobilization of patients with mild strokes.<sup>11</sup>

In 2022, a meta-analysis of six randomized trials of mobilization within 48 h of onset, which included the study of Tong et al.<sup>24)</sup> in 2019, showed fewer favorable outcomes (mRS score of 0–2) at 3 months after onset in patients who received early mobilization (48% vs. 52%, P=0.005). There was no difference in mortality or BI between those with and without early mobilization.<sup>26)</sup> However, perhaps in response to the results of the AVERT III study, a study focusing on mobilization (within 24–48 h of onset rather than very early mobilization (within 24 h) was conducted. The study of 57 patients with ischemic stroke published in 2021 showed better outcomes with mobilization within 24–48 h of onset than within 24 h.<sup>27)</sup> Another study of 120 patients with ischemic stroke published in 2022 showed a higher frequency of mRS score of 0–2 for mobilization within 24–48 h after onset than for mobilization within 72–96 h after onset.<sup>28)</sup> In another study published in 2022, 103 patients with ischemic stroke who had undergone mechanical thrombectomy were randomized to a group that underwent mobilization within 48 h of onset or a group that underwent normal care mobilization. The respective median times to mobilization were 42 h and 101 h. Although there was no difference in neurological outcomes or mortality at 3 months after onset, the frequency of non-fatal complications at 3 months was significantly lower and BI at 3 months was significantly higher with early mobilization.<sup>29)</sup>

A questionnaire survey on acute stroke rehabilitation conducted in Japan in 2022 showed that the greatest number of facilities started mobility training (sitting, transferring, standing, and walking) in branch atheromatous disease, atherothrombotic brain infarction, and cardioembolic stroke on hospitalization day 2, followed in descending order of frequency by hospitalization day 3 and the day of admission.<sup>12)</sup> In patients with lacunar infarctions, the timing of starting mobilization was earlier than in other types, with approximately the same proportion of facilities (slightly more than 40%) starting mobilization day 2.<sup>12)</sup>

As indicated above, if one were to suggest the appropriate timing for mobilization, at present it would likely be considered between 24 and 48 h. Very early mobilization within 24 h of onset may be considered for patients with mild symptoms or those with non-elderly ischemic stroke provided that mobilization time is shortened and its frequency is increased.

#### Clinical Question 1-4

• Are the appropriate times for starting head elevation and mobilization in hemorrhagic strokes such as intracerebral hemorrhage or subarachnoid hemorrhage different from those in ischemic stroke?

#### Answer 1-4

■ In intracerebral hemorrhage, head elevation from immediately after admission to at least 24 h after admission is considered to have no effect on outcome. However, mobilization should be started even more carefully than in ischemic stroke, with mobilization between 24 and 48 h likely to be appropriate.

■ In subarachnoid hemorrhage, after appropriate surgery is performed to prevent re-rupture, a transition from head elevation to a stepwise start of mobilization within several days of onset may be considered.

#### Commentary

In the HeadPoST study described previously, there was no relationship between head elevation and neurological outcome or adverse events in intracerebral hemorrhage.<sup>6)</sup> In a randomized trial published in 2014, 243 patients with intracerebral hemorrhage were randomly assigned to start rehabilitation (not limited to mobilization) within 48 h or 1 week after onset.<sup>30)</sup> The study reported a lower mortality rate and better neurological outcomes at 6 months after onset in the early rehabilitation group than in the late group.<sup>30</sup> In the AVERT III study,<sup>19</sup> which studied very early mobilization (within 24 h of onset), 255 patients (approximately 15% of all patients) were patients with intracerebral hemorrhage. Among these patients, there were significantly fewer good outcomes in the very early mobilization group than in the control group (odds ratio, 0.48; 95% confidence interval, 0.25-0.92).<sup>19)</sup> Furthermore, although the increase of death within 2 weeks of onset was not significant in patients with ischemic stroke, the odds ratio in patients with intracerebral hemorrhage was significantly increased with very early mobilization (odds ratio, 4.17; 95% confidence interval, 1.06–16.43). However, there was no significant intergroup interaction.<sup>20)</sup> A study of mobilization within 24-72 h of onset involving 60 patients with intracerebral hemorrhage, which was published in 2020, reported that there were significant improvements with early mobilization in the motor subscale score of the functional independence measure (FIM) and the functional ambulation category (FAC) by 3 months after onset, along with a reduction in the length of hospital stay. However, mRS score was not evaluated in the study.<sup>31)</sup>

In a questionnaire survey on acute stroke rehabilitation conducted in Japan in 2022,<sup>12)</sup> the greatest number of facilities (approximately 50%) responded that they started head elevation on the day of admission in intracerebral hemorrhage (nonoperative patients). In addition, the greatest number (approximately 40%) indicated that they started mobilization on hospitalization day 2, whereas few facilities (<10%) implemented mobilization starting from the day of admission.<sup>12</sup>)

In subarachnoid hemorrhage, early mobilization should be implemented carefully because of the use of emergent surgical treatments in the acute phase, other procedures such as ventricular drainage following emergent treatments, and the risk of cerebral vasospasm. A systematic review published in 2013 investigated mobilization within 4 weeks of the onset in subarachnoid hemorrhage for which surgery was

not indicated or not performed.<sup>32)</sup> However, no randomized trials were included in the review. Based on the results of observational studies, the review indicated only that there was a high risk of rebleeding within 24 h.<sup>32)</sup> In a prospective study published in 2017, 156 patients with subarachnoid hemorrhage were assigned to a group in which conventional treatment was performed or to a group in which a stepwise algorithm for mobilization was initiated on the day that surgery was performed.<sup>33)</sup> Upon comparing the two groups, there was no increase in complications or 90-day mortality with the stepwise algorithm, although neurological outcomes were not examined.<sup>33)</sup> An investigation of 56 patients with subarachnoid hemorrhage,<sup>34)</sup> published in 2019, compared different study phases: phase 0, in which mobilization was not started while drainage was continued; phase I, in which mobilization was started by rehabilitation staff; and phase II, in which mobilization was started by nursing staff. The results showed that all patients in phase II were discharged to their home or a rehabilitation facility.<sup>34)</sup> In another study involving 35 patients with subarachnoid hemorrhage, published in 2021, a multivariate analysis adjusted for severity showed that starting walking training within 2 weeks of onset was significantly associated with good outcomes.<sup>35)</sup> A very recent retrospective, observational study of 68 patients with severe subarachnoid hemorrhage (Hunt and Hess grade 3 or 4) found that patients who underwent a program of aggressive early mobilization that started with head elevation or ROM training (starting from approximately 72 h after admission) had few complications. In this study, however, the evaluation of neurological outcomes was inadequate.<sup>36</sup>)

The abovementioned questionnaire on acute stroke rehabilitation in Japan<sup>12)</sup> showed large differences between facilities with respect to the timing of mobilization in subarachnoid hemorrhage, with no consistent trends evident. However, there was a trend toward delayed head elevation and ROM training in subarachnoid hemorrhage as compared with ischemic stroke and intracerebral hemorrhage.<sup>12)</sup>

As indicated above, the data on the timing of mobilization in subarachnoid hemorrhage are limited to findings from small observational studies, and the methods used to start mobilization and the timing of its initiation differed in the various studies. If the patient has undergone appropriate surgery to prevent re-rupture, starting rehabilitation with head elevation may be considered within several days after onset. However, the evidence for this practice is insufficient.

# Clinical Question 1-5

■ Is the appropriate time to start mobilization (training to

leave bed) different if recanalization therapy, such as intravenous thrombolysis or mechanical thrombectomy, has been performed as an acute therapy?

#### Answer 1-5

■ For patients treated with recanalization therapy, as is the case for patients treated with standard medical therapy, it is appropriate to start mobilization between 24 and 48 h after stroke onset.

#### Commentary

In a 2014 observational study<sup>37)</sup> of 18 patients who underwent intravenous thrombolysis, very early mobilization within 24 h of onset was applied for all patients. The study reported no adverse events that resulted in intracranial hemorrhage or permanent neurological symptoms.<sup>37)</sup> In an observational study that used national administrative claims and discharge abstract data (Diagnosis Procedure Combination database) in Japan, 6153 patients underwent intravenous thrombolysis, of whom 4266 started rehabilitation of any type on the day of admission or the following day. The results of multivariate analysis adjusted for background factors showed an association between starting rehabilitation early and good neurological outcomes.38) Although the AVERT III study included 503 patients who underwent intravenous thrombolysis, there was no significant association between very early mobilization within 24 h of onset and poor outcome or death. There was also no significant intergroup interaction.<sup>19,20</sup> The above findings indicate that for patients treated with intravenous thrombolysis, there is no evidence indicating a need to delay mobilization or to otherwise change its timing from that used for patients treated with conventional medical therapy. It is therefore appropriate to start mobilization for such patients at a time similar to that used in conventional medical therapy.

An observational study of 1126 Chinese patients who underwent mechanical thrombectomy compared patients who underwent mobilization within 1 week with patients receiving normal care.<sup>39)</sup> A multivariate analysis showed no relationship between mobilization within 1 week and mRS scores of 0–2 at 90 days after onset. However, the odds ratio for death in these patients was 0.24 (95% confidence interval, 0.15–0.43) and the length of hospital stay was significantly shortened.<sup>39)</sup> In a randomized trial of 103 patients who underwent mechanical thrombectomy, a comparison of early mobilization within 48 h of onset and conventional therapy showed no differences in neurological outcomes or mortality at 3 months and 1 year after onset.<sup>29)</sup> However, early mobilization led to significant improvements in non-fatal complications and BI. Whether puncture site complications were included in the non-fatal complications is unclear.<sup>29)</sup>

The above findings indicate that in patients with acute ischemic stroke who have undergone acute recanalization therapy, there is no evidence of a need to delay mobilization or otherwise change its timing from that used in conventional medical therapy. It is therefore appropriate to start rehabilitation for such patients at a time similar to that used in conventional medical therapy.

# 2 Acute Complications

# Clinical Question 2-1

• How should rehabilitation training be carried out if hemorrhagic infarction occurs after the onset of ischemic stroke?

#### Answer 2-1

■ If the neurological symptoms do not deteriorate, continuing the training can be considered.

• However, when the training is continued, the patient should be closely monitored by means such as careful blood pressure management, coagulation tests, and imaging tests.

# Commentary

There is no evidence on the question of whether training should be continued if hemorrhagic infarction occurs after the onset of ischemic stroke. Although systemic hemorrhagic complications other than hemorrhagic infarction may also occur after intravenous rt-PA therapy, no studies have addressed whether the training should be discontinued after the occurrence of these complications. The results of a questionnaire survey of 959 primary stroke centers in Japan indicated that at 63% of the facilities, training was continued even if intracranial hemorrhage was observed following intravenous rt-PA therapy as long as the hemorrhage was asymptomatic.<sup>12</sup>

A study of convalescent rehabilitation wards in Japan found that although hemorrhagic infarction occurred in 19% of the patients, training could be continued if the antithrombotic drug in use was not changed and monitoring of blood pressure or monitoring by CT was performed.<sup>40</sup> Numerous reports have indicated that asymptomatic hemorrhagic infarctions do not affect the patient outcome.<sup>41,42</sup> A study involving 1135 patients with ischemic stroke at 60 facilities in Canada<sup>43</sup> showed that asymptomatic hemorrhagic infarctions occurred after intravenous rt-PA therapy in 27% of the patients. The results indicated that although HI-1 hemorrhage on the classification system of the European Cooperative

Acute Stroke Study (ECASS) was not related to outcome, HI-2, PH-1, and PH-2 hemorrhages were significantly associated with the worsening of outcomes.<sup>43)</sup>

No optimal criteria have been established for discontinuing training if a hemorrhagic infarction is observed during the acute phase of ischemic stroke, and the response depends on whether neurological symptoms are present. However, if the hemorrhagic infarction is asymptomatic, continuing training is likely to be more beneficial for the patient.

#### Clinical Question 2-2

• How should rehabilitation training be implemented if delayed cerebral vasospasm occurs after a subarachnoid hemorrhage?

#### Answer 2-2

• Some studies have indicated that the frequency of cerebral vasospasm does not increase even if early mobilization is performed after a subarachnoid hemorrhage.

■ In the case of asymptomatic cerebral vasospasm, continued training, including mobilization, can be considered.

# Commentary

Delayed cerebral vasospasm is a reversible stenosis of a major cerebral artery that occurs 4-14 days after a subarachnoid hemorrhage. The Japan Stroke Society Guideline 2021 for the Treatment of Stroke indicates that cisternal or lumbar drainage is recommended or can be considered to prevent delayed cerebral vasospasm. Managing this drainage limits the patient's activity level, which is contrary to early mobilization. The results of a questionnaire survey of 959 primary stroke centers in Japan showed that in-bed training and head elevation tended to start later in patients with subarachnoid hemorrhage than in those with cerebral infarction and intracerebral hemorrhage (nonoperative patients).44) However, no evidence has been presented regarding whether training can prevent cerebral vasospasm or whether continuing training in the presence of cerebral vasospasm improves the patient outcome.

In a study on the early mobilization of step-wise progression (from head elevation to sitting on the edge of the bed and then to walking in the hospital ward within 4 days) after surgery for subarachnoid hemorrhage, early mobilization showed no increase in complications and caused fewer and milder cerebral vasospasms when compared with conventional therapy.<sup>33)</sup> Similarly, a study of 111 patients with subarachnoid hemorrhage in Japan compared an early rehabilitation group with a group placed on a conventional training program.<sup>45)</sup> The conclusion was that attempting mobilization and starting walking training as soon as possible after arterial aneurysm surgery was safe and did not increase the frequency of complications.<sup>45)</sup> Another study in patients with severe subarachnoid hemorrhage (Hunt and Hess grades 3 and 4) reported that fewer cases of cerebral vasospasm were observed in patients with early mobilization compared with those without mobilization (14.71% vs. 41.18%, respectively).<sup>36)</sup>

Two studies used transcranial Doppler ultrasound<sup>46</sup>) and near-infrared spectroscopy<sup>47</sup>) to investigate the effects of head elevation on cerebral blood flow in patients with sub-arachnoid hemorrhage. Both studies concluded that head elevation did not affect cerebral blood flow and that early mobilization could be performed without increasing the frequency of cerebral vasospasm.

As the above findings indicate, there is no consensus regarding the relationship between delayed cerebral vasospasm and the continuation of training, including early mobilization. However, training in the acute phase does not increase the frequency of cerebral vasospasm. Moreover, in cases where the cerebral vasospasm is asymptomatic, training can be continued if the patient is carefully monitored for vital signs and neurological symptoms.

#### Clinical Question 2-3

• How should rehabilitation training be implemented if intracranial hypertension is suspected?

#### Answer 2-3

There have been no studies that have addressed whether training should be discontinued in acute cases of intracerebral hypertension.

■ The intensity of training can be modified by paying attention to changes in blood pressure and neurological symptoms while trying to maintain cerebral perfusion pressure.

#### Commentary

A questionnaire survey of 959 primary stroke centers in Japan indicated that training was continued at 74% of the facilities in patients with asymptomatic obstructive hydrocephalus for which drainage was not performed.<sup>12)</sup> Training was continued at 27% of the facilities in patients with symptomatic obstructive hydrocephalus for which drainage was performed.

In patients who underwent ventricular drainage for subarachnoid hemorrhage, mobilization could be safely implemented by clamping the drain for up to 3 h while monitoring for blood pressure, headache, and neurological symptoms under the guidance of nurses.<sup>34)</sup> The outcomes were better in patients who received mobilization than in those treated with conventional management.

To maintain cerebral perfusion pressure in situations that suggest intracranial hypertension, it seems reasonable to elevate the head position 30 degrees. This position can be expected to avoid excessive flexion and rotation of the neck, which may hinder venous return, and avoid breath-holding to prevent any increase in intrathoracic pressure. However, this suggestion is based on findings in severe head trauma.<sup>48)</sup>

#### Clinical Question 2-4

• How should rehabilitation training be implemented if vital signs such as body temperature, blood pressure, heart rate, and arterial oxygen saturation are abnormal?

#### Answer 2-4

• When abnormal values of vital signs are observed, the required treatment and identification of the cause should take precedence over continued training. However, if the cause is established and the patient's condition is stable, training can be continued while symptoms and vital signs are closely monitored.

■ Because training discontinuation and bed rest can lead to other complications, the training intensity should be appropriate for the patient's condition.

#### Commentary

There have been no detailed reports regarding the safety of ROM training in the supine position, which is not associated with an exercise load. However, it seems that the effects of training on the general condition of the patient are limited. Therefore, it is considered that ROM training can be implemented even if the implementation criteria are not fully satisfied.

The results of a questionnaire survey of 959 primary stroke centers in Japan<sup>12)</sup> indicated that less than 40% of the facilities proceeded with training when the patient had a fever (temperature  $\geq$ 38 °C), hypertension that was difficult to control (systolic blood pressure  $\geq$ 160 mmHg even with medication), or symptomatic orthostatic hypotension. When heart failure symptoms that required oxygen administration or hypoxemia (room air SpO<sub>2</sub>  $\leq$ 90%) were observed, training was delayed or discontinued at approximately 90% of the facilities.<sup>12</sup>)

With regard to fever, urinary tract infection and aspiration pneumonia have been reported as frequent causes.<sup>49)</sup> If fever

occurs suddenly, the cause should be investigated, and its treatment should be given priority.

Under normal conditions, blood vessels have the capacity for autoregulation, and cerebral blood flow is maintained when systolic blood pressure is systemically between 70 and 150 mmHg. However, the capacity for autoregulation breaks down in acute stroke, and cerebral blood flow is dependent on systemic blood pressure. In the acute phase, the possibility that a patient's condition may be associated with stenosis or occlusion of a major cerebral artery or complicated by a coronary artery lesion must be kept in mind, and the patient's neurological symptoms should be carefully monitored.

Orthostatic hypotension is also a frequent problem in acute stroke rehabilitation. Long-term bed rest puts the patient at risk of orthostatic hypotension, and this can be prevented by early mobilization. It is therefore desirable to continue training in the acute phase.

Although there is no consensus regarding heart rate, training is generally discontinued if the patient's heart rate is less than 40 beats/min. Many patients with ischemic stroke also have atrial fibrillation, and many patients with subarachnoid hemorrhage also have increased parasympathetic activity. However, although such patients are susceptible to an abnormal heart rate (mainly tachycardia), training can be continued if the abnormality is not new, did not occur suddenly, and other vital signs are stable.

An abnormal arterial oxygen saturation or rapid respiratory rate in acute stroke can result in a serious emergency. In such cases, training should be discontinued, and treatment and investigation of the cause should be started immediately. Possible causes include airway obstruction, aspiration pneumonia, expectoration difficulty, heart failure, recurrent stroke, and chronic obstructive pulmonary disease. Particular caution is required for pulmonary embolism, which is associated with high mortality.

There is also the view that training improves respiratory status. In a study from the United Kingdom, training for strengthening respiratory muscles was provided for patients who had suffered a stroke in the previous 2 weeks.<sup>50)</sup> Although the patients that received training showed improved respiratory muscle strength and cough force, no difference was found in the occurrence of aspiration pneumonia within 90 days of onset between the trained group and the controls.<sup>50)</sup>

If an abnormal value is observed for vital signs such as body temperature, blood pressure, heart rate, or arterial oxygen saturation during the acute phase of stroke, investigation of the cause and treatment for the abnormality should take precedence over continued training. Training can be continued if the cause is established and the patient's condition is stable, but constant close attention to changes in symptoms or vital signs is required.

# Clinical Question 2-5

• How should mobilization be implemented if deep venous thrombosis is present?

#### Answer 2-5

• There have been no reports indicating that proceeding with mobilization results in an increase in pulmonary embolism.

■ With appropriate diagnosis and anticoagulant therapy, consideration can be given to proceeding with mobilization.

#### Commentary

Lower extremity paralysis and long-term bed rest increase the risk of DVT in acute stroke.<sup>51)</sup> Furthermore, DVT can cause pulmonary embolism in some patients. The Japan Stroke Society Guideline 2021 for the Treatment of Stroke strongly recommends (recommendation grade A) early mobilization to prevent DVT.

Views are currently divided on whether mobilization should be temporarily discontinued and bed rest maintained in view of the risk of pulmonary embolism or continued unchanged even when DVT occurs. A questionnaire survey conducted in Japan showed that mobilization is temporarily discontinued at 90% of facilities if proximal or unstable DVT (free-floating thrombus) is found.

There is no report of any study that has investigated the effects of discontinuing mobilization on functional outcome after the occurrence of DVT in acute stroke patients. However, a meta-analysis based on 13 randomized, controlled trials in a variety of other disorders found that if anticoagulant therapy was started, the incidence of pulmonary embolism was significantly lower in patients who continued mobilization after DVT onset than those for whom mobilization was temporarily discontinued after the onset.<sup>52)</sup> To date at least, no report has indicated that continuing mobilization after the occurrence of DVT results in a significant increase in pulmonary embolism, and this is true not only for the acute phase of stroke. However, mobilization should be implemented cautiously if anticoagulant therapy has not been started or when coarse or unstable DVT is seen in the proximal lower extremity.

In acute stroke patients, training including early mobilization facilitates DVT prevention. However, it is important to keep in mind that acute stroke patients are at high risk of DVT, and close observation is required for early detection of DVT in such patients.

#### Clinical Question 2-6

• How should rehabilitation training be implemented if convulsions occur?

#### Answer 2-6

• There have been no reports indicating that proceeding with mobilization after the onset of convulsions worsens a patient's functional outcome.

• Proceeding with training and mobilization can be considered if convulsions have already resolved and new neurological symptoms have not persisted.

#### Commentary

A questionnaire survey conducted in Japan found that mobilization was temporarily discontinued at 70% of the facilities if convulsive seizure occurred. However, there have been no reports to date indicating that proceeding with mobilization after the onset of convulsions results in a worsening of the patient's functional outcome. Moreover, there is no evidence that training induces a recurrence of convulsions after the first attack. A recurrence rate of 33% was reported for the 10-year period following symptomatic convulsive seizures that occurred in the acute phase of stroke.<sup>53</sup>

Mobilization can be resumed starting the day after a convulsive seizure if prophylactic administration of an antiepileptic drug has been started and vital signs such as the consciousness level are normal. However, mobilization should be resumed cautiously if consciousness disturbance or Todd's paralysis remains.

# **3 Training Time and Frequency for Acute Stroke Rehabilitation**

# Clinical Question 3-1

• What are the appropriate training time and frequency for acute stroke rehabilitation?

#### Answer 3-1

■ Although the optimal training time is unknown, lengthening the daily rehabilitation training time can be considered.

• Although the optimal training frequency is also unknown, increasing the daily rehabilitation training frequency can be considered.

#### Commentary

The results of a multivariate analysis using a multicenter database of approximately 10,000 patients with ischemic stroke showed that BI improved at discharge when the patients underwent rehabilitation training within 72 h of admission and when the mean training time was 100 min/day or longer.<sup>54)</sup> In a single-center, retrospective study involving 273 patients with intracerebral hemorrhage, improved BI was observed at discharge for patients undertaking training for 150 min/day when compared with patients undertaking 48 min/day.<sup>55)</sup> A questionnaire survey on the status of rehabilitation at primary stroke centers in Japan showed that the greatest number of facilities had an initial training time of 40 min/day, followed by 60–80 min/day, and 20 min/day, in that order.<sup>44)</sup>

A randomized, controlled study<sup>24</sup> compared the following groups with respect to the effects of rehabilitation training on ADL at 3 months after onset: patients that underwent training for less than 1.5 h/day within 24-48 h of onset; patients that underwent training for at least 3 h/day within 24-48 h of onset; and patients that underwent training for at least 3 h/ day within 24 h of onset. Of the three groups, the group with the best result for the proportion of patients with mRS score of 0–2 at 3 months after onset was the group that underwent training for at least 3 h/day within 24-48 h of onset.<sup>24)</sup> A secondary analysis in the AVERT study showed that the daily frequency of training was second only to NIHSS score as an important factor in determining whether patients had good outcome (mRS score of 0–2) at 3 months.<sup>23)</sup> Similarly, a small randomized, controlled trial<sup>27</sup>) (57 patients with ischemic stroke) divided patients into the following nine groups and compared the effects of the different treatments on BI and mRS scores at 1 and 3 months: three groups that underwent training at three different intensities; three groups that underwent training of three different training durations per day; and groups with daily training frequencies of once, two or three times, and at least four times. For all patients, the training started 24-48 h after onset. The results showed that daily training frequency was significantly associated with ADL improvement, with a frequency of two or three times per day the most effective.<sup>27)</sup>

# Clinical Question 3-2

• What is the appropriate intensity for acute rehabilitation training?

#### Answer 3-2

■ Although the optimal training intensity is unknown,

increasing the intensity can be considered.

#### Commentary

A small randomized, controlled study of 57 patients with ischemic stroke compared the efficacy of nine different combinations of rehabilitation training intensity, duration, and frequency, which was started 24-48 h after onset.<sup>27)</sup> The effects of treatment on BI and mRS scores were assessed at 1 and 3 months after onset. Training intensity was significantly associated with ADL improvement, and the training was the most effective when the training proceeded from transfer to sitting, to standing, and then walking.<sup>27)</sup> In a small randomized, controlled study<sup>56)</sup> involving patients with severe stroke (mRS score 4 or 5), a group that underwent repetitive movement training involving standing and sitting (up to 8 to 12 repetitions) for 30 min and ADL training for 15 min was compared with a group that underwent conventional physical therapy for 45 min. No significant differences in BI were observed at weeks 3, 15, 29, or 55 after randomization between the two groups.<sup>56)</sup>

#### Clinical Question 3-3

Does rehabilitation training on non-workdays improve outcomes in stroke patients?

#### Answer 3-3

Training on non-workdays can be used to improve functional outcome.

#### Commentary

A questionnaire survey on the status of rehabilitation at primary stroke centers in Japan showed that training was implemented 7 days a week at 30% of the facilities, 6 days a week at 41%, and 5 days a week at 22%.<sup>44)</sup> A study using a multicenter database of 3072 stroke patients showed a higher proportion of good outcomes (mRS scores of 0–2) at discharge in a group that underwent training 7 days a week as compared with a group that underwent training 5 or 6 days a week.<sup>57)</sup> A single-center analysis of chart data for 661 patients with ischemic stroke found that BI results at discharge were better and DVT during hospitalization was reduced when rehabilitation training was implemented on non-workdays as well as weekdays.<sup>58)</sup>

In a multicenter cohort study of 74,307 stroke patients, a low percentage of the patients who were admitted on a Friday started training within 72 h of admission.<sup>59)</sup> In a study using a multicenter database (2307 stroke patients),<sup>60)</sup> the day of admission was divided into the following five groups, and the groups were compared: admission on a weekday of a week without a holiday; admission on a weekday of a week with a holiday; admission on Friday; admission on Saturday or Sunday; or admission on a holiday. The group admitted on Friday had the lowest proportion of patients whose training was started within 72 h of admission.<sup>60)</sup> Another multicenter, cohort study of 1134 stroke patients<sup>61)</sup> showed that in patients who underwent rehabilitation training on weekdays, a high proportion of weekdays during hospitalization or the first 21-day period (a weekday ratio) was associated with earlier initiation of sitting and standing, and a higher number of days receiving physical therapy. In addition, the weekday ratio was associated with good ADL scores (mRS score 0–1) at discharge.<sup>61)</sup>

# 4 Dysphagia in the Acute Phase

#### Clinical Question 4-1

• What types of personnel should evaluate swallowing function during the acute phase of stroke and at what times?

#### Answer 4-1

• There has been no verification of whether the type of personnel that performs bedside dysphagia screening impacts the effectiveness of screening.

• Dysphagia screening by trained nurses may be effective in preventing aspiration accidents and pneumonia after a stroke and enables screening to be performed earlier than when it is performed by other types of personnel.

■ Dysphagia screening should be performed by a nurse, speech-language-hearing therapist, or physician with knowledge of and training in dysphagia within 24 h of admission, although the evidence for this is inadequate.

# Commentary

Many randomized, controlled studies and studies included in some systematic reviews have focused on the methods used for the initial evaluation of swallowing function. We were unable to identify any studies that verified the relative merits of the types of personnel that should be involved in the initial evaluation of swallowing function, particularly in routine clinical treatment of acute stroke. In much of the literature from other countries, trained nurses performed the initial evaluation of swallowing function according to standardized protocols.<sup>62–68)</sup> In articles from Japan, only a few have discussed the importance of the initial evaluation of swallowing function.<sup>69)</sup> However, no report has mentioned the types of personnel for the evaluation.

A systematic review of swallowing function evaluation

by nurses for acute stroke indicated that management of dysphagia according to formal guidelines may be useful for reducing aspiration accidents, respiratory infections, and mortality.<sup>62)</sup> A premise of many articles is that the combination of detailed examination by a SLHT and VF and VE by physicians is the standard evaluation for swallowing function.<sup>65–67,69–80)</sup> Moreover, many articles mentioned the importance of early comprehensive screening of swallowing function by qualified and trained nurses.<sup>59,67)</sup> The guidelines in the United States recommend that dysphagia screening be performed by SLHTs or other trained healthcare personnel.<sup>81)</sup> Reports from Japan also indicate that dysphagia screening by nurses is useful.<sup>23)</sup> Qualifications for nurses in Japan with regard to swallowing evaluations are the certified nurse in stroke rehabilitation nursing (transition to certified nurse in stroke nursing), the certified nurse in eating and swallowing disorders nursing (transition to certified nurse in dysphagia nursing), and nurse certification by the Japanese Society of Dysphagia Rehabilitation. However, familiarity with these qualifications for nurses is currently inadequate. A practical approach is for ward nurses to perform the initial screening using a general-purpose, standardized evaluation method and for SLHTs and physicians to intervene early for patients suspected of having dysphagia.

Few study reports have mentioned the optimal timing of swallowing evaluations. Studies of swallowing evaluation methods in the acute phase have been varied and have included studies in which the recommended timing of the initial evaluation was immediately after admission, 25, 26, 82, 83) within 24 h,<sup>78,84,85)</sup> 48 h,<sup>67,68,73,86)</sup> 72 h,<sup>23,74,76,79)</sup> 4 days,<sup>87)</sup> or 7 days<sup>64)</sup> after admission. Although it is difficult to establish a uniform time at which the initial screening should be performed, it is important to at least establish a means of initial nutritional provision as early as possible. The United Kingdom's Sentinel Stroke National Audit Programme recommends dysphagia screening within 4 h of admission and evaluation by a dietitian within 72 h of admission.<sup>59,88)</sup> The ASA guidelines recommend dysphagia screening within 24 h of admission and before the first oral food intake.<sup>81,89</sup> The European guidelines recommend screening as early as possible, based on the evidence suggesting that early dysphagia screening reduces mortality in acute stroke patients.<sup>90)</sup> Although the Canadian guidelines do not specify evaluation timing, they recommend performing an evaluation for swallowing function as soon as the patient is alert and ready to attempt oral intake.91)

The results of a nationwide, web-based questionnaire survey of primary stroke centers in Japan showed that the initial swallowing evaluation was performed by a SLHT at 89% of the facilities and by a ward nurse at 59%.<sup>44)</sup> There are presumably few facilities where SLHTs perform swallowing evaluations on non-workdays. Therefore, it can be inferred that there are some facilities where no meal is provided until initial swallowing evaluation by a SLHT or oral food intake is started without any dysphagia screening. Whether facilities in Japan have systematic screening methods, including patient interviews and the timing of the screening, remains unclear.

With regard to evaluations using VF or VF, although their timing has varied widely depending on the study, they have often been performed during the subacute phase. There have been few reports indicating that these evaluations are performed in the acute phase. However, it has been reported that performing VE within several days of onset is useful.<sup>76,92</sup>

In summary, bedside dysphagia screening should be performed within 24 h of admission if possible. The screening should be performed by a nurse with knowledge of and training in swallowing evaluation or by a SLHT or physician. If the findings suggest the possibility of dysphagia, a detailed examination by a SLHT or VF/VE by a specialist physician is recommended. In the future, observational and interventional studies are needed to investigate the optimal timing of dysphagia screening, the types of personnel to perform it, and the methods to use.

#### Clinical Question 4-2

■ What methods should be used to evaluate swallowing function in acute stroke?

#### Answer 4-2

• As with VF and VE, bedside dysphagia screening has been shown by several systematic reviews to be useful in preventing aspiration and pneumonia.

■ Widely used methods of bedside dysphagia screening are the Toronto Bedside Swallowing Test (TOR-BSST), which uses water, and the Gugging Swallowing Screen (GUSS), which uses a viscous substance in addition to water. However, the question of which method is the best has not been adequately verified.

• As methods of dysphagia screening, at the very least, a common procedure and assessment method, which have been shown to be effective in previous reports, should be used uniformly within each facility.

#### Commentary

In many studies, detailed examination by a physician or

SLHT and VF/VE have been regarded as the gold standard for swallowing evaluation.<sup>65–67,69–80)</sup> However, performing these examinations soon after admission is not possible for all patients, and bedside dysphagia screening is therefore recommended. An abundance of multicenter studies and meta-analyses have investigated the usefulness of bedside screening for dysphagia.<sup>62,65,66,70–72,74,75,86,88,93–100</sup>) The results of other studies in Japan have also indicated the usefulness of bedside screening for dysphagia, although they were single-center studies.63,69,78-80,101-103) Manv studies have found that dysphagia screening after admission is useful for predicting the medium-term and long-term risks of pneumonia and death, and that it may reduce the risk for them.<sup>62,64,66,70,71,74,83,85,88,94,99,104)</sup> However, almost no studies have compared the usefulness of some methods of dysphagia screening.

The simplest and most widely used method of dysphagia screening is one that evaluates swallowing function based on changes in respiratory status and whether aspiration is observed after drinking water. A typical method involving drinking water is the Toronto Bedside Swallowing Test (TOR-BSST), which has received strong endorsements in systematic reviews.<sup>65,71,97–100</sup> The method is an evaluation that incorporates assessments of voice quality and tongue movement before and after water is swallowed (5 mL  $\times$  ten times, total of 50 mL). The Gugging Swallowing Screen (GUSS), which is a method that uses a viscous substance as well as water, has been shown to be useful for swallowing evaluation in several studies and systematic revie ws.<sup>64,70,71,99,100,104-107)</sup> In GUSS, the patient is instructed to swallow a half-teaspoon of a semisolid substance five times after swallowing saliva, followed by drinking 3, 5, 10, and 20 mL of water, and then swallowing a small piece of bread five times, in that order. Subsequently, the patient is observed for coughing and changes in voice quality. Based on the results of the evaluation, the types of meals to serve the patient can be selected.<sup>105)</sup> Although they are similar to some extent, evaluations such as the following have also been described as useful: Barnes-Jewish Hospital Dysphagia Screen,<sup>106)</sup> Modified Mann Assessment of Swallowing Ability, 108) Emergency Physician Swallowing Screen,<sup>109)</sup> Oral Pharyngeal Clinical Swallowing Examination,<sup>110)</sup> and Bedside Aspiration Test.<sup>111)</sup>

In the literature from Japan, specialized methods, such as the 2-min spontaneous swallowing test,<sup>63)</sup> tongue pressure assessment,<sup>101)</sup> and use of an ultrasound device,<sup>77)</sup> have been reported to be useful. Other general-purpose methods include the repetitive saliva swallowing test (RSST),<sup>79,80,112)</sup> water drinking test,<sup>78–80,102,103)</sup> and food test.<sup>77,102)</sup>

Although there have been almost no reports of swallowing evaluation by VF in the acute phase, bedside VE can be performed in the acute phase and has been reported to be useful within several days of stroke onset.<sup>73,76,79,92,113</sup> A questionnaire survey conducted in Japan found that 50% of primary stroke centers performed both VF and VE, whereas 24% performed VF alone, and 17% performed VE alone.<sup>44</sup>

In summary, uniform procedures and assessment methods should be used for bedside dysphagia screening within each facility. Evaluation methods should combine some procedures such as evaluation of consciousness level, oral cavity examination, swallowing saliva, drinking water, and swallowing foods of varying viscosity, based on methods that have been shown to be effective in previous studies. It is useful to create an ideal model for an evaluation procedure and assessment method and to validate their effectiveness. However, because circumstances vary considerably depending on the facility, establishing a single evaluation procedure and assessment method may be difficult.

#### Clinical Question 4-3

• What type of initial swallowing training is effective in acute stroke and when should it be started?

#### Answer 4-3

• Several reports have indicated that exercise therapy, transcranial magnetic stimulation, transcranial direct current stimulation, transcutaneous electrical stimulation, and pharyngeal electric stimulation all prevent pneumonia and improve swallowing function.

• Starting swallowing training within 2 weeks of onset may be best for improving dysphagia. Although starting training earlier may be effective, there is still insufficient evidence for establishing a specific starting time, type, or frequency of training.

• Indirect training that includes oral care should be started as early as possible in acute stroke. Training using methods such as exercise therapy and stimulation therapy should probably be started early.

#### Commentary

Several meta-analyses have shown that swallowing training after a stroke is effective in reducing the risk of pneumonia and improving swallowing function.<sup>114–119</sup> However, few studies have investigated the timing at which swallowing training should be started. Nerve stimulation therapy, transcranial magnetic stimulation, transcranial direct current stimulation (tDCS), and transcutaneous pha-

ryngeal electrical stimulation are all effective for improving swallowing function. Moreover, a systematic review showed that starting swallowing training in the acute phase (within 2 weeks of onset) may be effective.<sup>117)</sup> A meta-analysis of two randomized, controlled studies showed that tDCS was effective in restoring swallowing function.<sup>118)</sup> In addition, a meta-analysis of three studies in which mirror-image training was performed in the acute phase found this method to be effective for dysphagia.<sup>119)</sup> However, a Cochrane Review regarding acupuncture therapy for acute stroke showed that there was insufficient evidence of its efficacy for swallowing function.<sup>120)</sup> Some randomized studies of swallowing training in acute stroke found tDCS to be effective.<sup>121,122)</sup> Another, however, found that the use of tDCS for 5 days after admission provided no added benefit over conventional therapy.<sup>123)</sup> A report from Japan indicated that swallowing training including tongue movement training was effective in acute stroke.<sup>124)</sup>

There have been very few reports of the appropriate intensity and frequency of swallowing training. A retrospective cohort study in Japan found that when swallowing training that had been performed only on weekdays was instead performed every day including non-workdays, the time until the patient was capable of oral food intake was shortened.<sup>125)</sup> A recent systematic review of a broad range of studies covering the period from the acute phase to the chronic phase drew no conclusions, given that varied evaluation criteria were used.<sup>95)</sup>

The results of a questionnaire survey of primary stroke centers in Japan showed that SLHTs were involved in swallowing training at 95% of the facilities and ward nurses at 35% of facilities.<sup>44</sup> Although the types of training were unclear, it is surmised that the swallowing training performed by ward nurses was mainly oral stimulation therapy and exercise therapy.

Many interventional studies to examine the efficacy of swallowing training have investigated such training in the strict sense of the term, as in the case of exercise therapy, stimulation therapy (e.g., magnetic and electrical stimulation), and acupuncture therapy.<sup>114–119</sup> However, approaches such as oral care, oropharyngeal cooling stimulation, tongue movement training, and breathing exercises can be started early after stroke onset even when the patient's general condition is unstable, and are likely to be effective not only in improving swallowing function, but also in improving appetite, preventing pneumonia, and treating disuse atrophy of the swallowing muscles.<sup>124,126</sup> Although these approaches can also be considered swallowing training in the broad

sense, they may appear infrequently in the literature because it is difficult to evaluate their efficacy in randomized, controlled studies and interventional studies. The significance of such swallowing training in its broad sense needs to be investigated in the future.

In summary, indirect training including oral care should be started as early as possible in acute stroke. However, the significance of applying exercise therapy and stimulation therapy more aggressively and starting such training earlier still needs to be clarified. Further work is also required to determine the desirable intensities of these procedures.

# **5** Acute Rehabilitation during Pandemics of Novel and Re-emerging Infections, Particularly Coronavirus Disease 2019 (COVID-19) *Clinical Question 5-1*

■ How should the amount of acute stroke rehabilitation to be provided during pandemics of novel and re-emerging

infections, particularly COVID-19, be determined?

#### Answer 5-1

• The same amount of acute stroke rehabilitation as provided under normal circumstances should be provided during pandemics of novel and re-emerging infections.

#### Commentary

Many reports have indicated that acute stroke rehabilitation was delayed or reduced in volume during the COVID-19 pandemic because resources such as hospital beds and healthcare personnel were temporarily allocated to handling infected individuals or those suspected of being infected.<sup>127–133</sup> In a survey of primary stroke centers in Japan, 61% of the facilities responded that their acute stroke rehabilitation program was affected by the COVID-19 pandemic.<sup>44</sup> The reasons for the reduction in the amount of rehabilitation provided included delays in starting rehabilitation while waiting for patients' negative COVID-test results, infections or suspected infections of therapists and patients, cluster outbreaks, unit closures, and the increased time and work required for infection control.<sup>44</sup>

For similar reasons, acute stroke rehabilitation could be delayed or reduced in volume during pandemics of other novel or re-emerging infections. Multidisciplinary rehabilitation starting early after the onset of stroke is known to improve outcomes. Consequently, even in circumstances where a pandemic may delay rehabilitation or reduce the amount provided, acute stroke rehabilitation should be provided in amounts comparable to those provided under normal circumstances, with priority given to infection control. Some reports have indicated that rehabilitation programs that patients could implement themselves and the use of remote rehabilitation were introduced or considered as part of efforts to address reduced levels of acute stroke rehabilitation.<sup>129–137</sup> Given that the healthcare systems of Japan and other countries differ, this issue should be investigated according to the circumstances of the individual facility and the patients.

#### Clinical Question 5-2

• How should a system to provide acute stroke rehabilitation be established during pandemics of novel and re-emerging infections, particularly COVID-19?

#### Answer 5-2

■ Based on information provided by bodies such as national and local public institutions and relevant organizations and academic societies, the infection control procedures and medical procedures related to acute stroke rehabilitation that are to be implemented during pandemics of novel and reemerging infections should be formulated depending on the circumstances of the community and individual facilities.

■ Infection control procedures and medical procedures related to acute stroke rehabilitation should be formulated in advance depending on the circumstances of the community and individual facilities, with the consideration that pandemics of novel and re-emerging infections may occur in the future.

#### Commentary

During the COVID-19 pandemic, manuals for the pandemic that emphasized infection prevention among healthcare personnel were prepared in Japan and in other countries. This was because ensuring that healthcare personnel were safe from infection helped to protect stroke patients from a collapse of the healthcare system resulting from work restrictions and curtailment of hospital functions caused by infections.<sup>138,139)</sup> In Japan, the Japan Stroke Society published the Protected Code Stroke (JSS-PCS) algorithm,<sup>140)</sup> which was the society's version of the Protected Code Stroke (PCS) algorithm published by a Canadian research team.<sup>139</sup> In addition, the Japanese Association of Rehabilitation Medicine published infection control guidelines.<sup>141)</sup> Formulating infection control procedures and medical procedures for acute stroke rehabilitation based on this information can lead to the creation of a system for providing continuous and effective rehabilitation during the pandemic.

During the COVID-19 pandemic, acute stroke therapy

and rehabilitation were affected, with many reports indicating that infection control and medical procedures were changed.<sup>127,128,131-134,142</sup>) The changes included the introduction of triage systems such as pre-admission PCR tests, the use of personal protective equipment, isolation of infected patients and those suspected of being infected from other patients, and re-allocation of healthcare resources because of the increase in healthcare demand resulting from the spread of infection.<sup>127,128,131-134,142)</sup> In a survey of primary stroke centers in Japan, 61% of the facilities responded that acute stroke rehabilitation at their facility was affected by the CO-VID-19 pandemic, and the effects that impaired the systems for providing rehabilitation included manpower reductions caused by the infection of therapists and close contact of therapists with infected individuals, exclusive assignments of therapists, and restrictions on the use of rehabilitation training rooms.<sup>44)</sup> Such changes in healthcare systems strain healthcare resources and may affect the outcomes of stroke patients.<sup>127,129,133,142)</sup> It has been reported that the effects on outcomes can be minimized by optimizing healthcare resources for stroke patients.<sup>143)</sup>

Healthcare resources may be similarly strained during pandemics of other novel or re-emerging infections because of changes in healthcare systems brought on by the spread of infection; these changes may affect the outcomes of stroke patients. Infection control procedures and medical procedures related to acute stroke rehabilitation should be formulated based on the situations that occur when healthcare systems are limited by a pandemic. The procedures should be designed around the circumstances of the community and individual facilities and should be based on information provided by bodies such as national and local public institutions, relevant organizations, and academic societies. Importantly, it should be kept in mind that pandemics occur suddenly. Therefore, the abovementioned infection control procedures and medical procedures related to acute stroke rehabilitation should be formulated in advance.

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# **CONFLICTS OF INTEREST**

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