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Content

Past, Present and Future of ASEAN Journal of Rehabilitation Medicine

In 2019, the Journal of Thai Rehabilitation Medicine changed it's name to the ASEAN Journal of Rehabilitation Medicine (ASEAN J Rehabil Med). In line with the change of name, representatives from Malaysia and Indonesia, were invited to join the Editorial Board. The aim and scope of the journal are "to promote improvement of science and education in the field of rehabilitation medicine as well as medical rehabilitation service, system and policy in ASEAN countries." This is of paramount importance as research and publication are key to scientific progress and serve as foundation to creating strong academic culture. The ASEAN J Rehabil Med publishes original articles, short communications, case reports, review articles, and special articles related to rehabilitation medicine including education, services, system, policy, and innovation which would benefit not only rehabilitation professionals but also their patients/consumers especially persons with disability. The journal has no publication charge and the online version is freely accessible through the journal website (https://www.tci-thaijo.org/index.php/aseanjrm/).

The year 2019 was the transition year and there was considerable effort spent on redefining the scope and organization of this new journal. We are proud to announce that in the year 2020, the journal successfully published three issues (total of 20 articles), all in English. Two-third were original articles while the rest was on innovation related to medical rehabilitation. The first issue for year 2021 is published in February, two months ahead of schedule. The range of contributors and types of articles submitted to the journal shows changing landscape, which is a positive indication of growth. Although the main contributors were from Thailand, contributors from other countries like Indonesia, Malaysia and Singapore are slowly trickling in. Whilst majority of the authors were PMR trainees, who need to do research as part of their program requirement, experience rehabilitation physicians and rehabilitation professionals such as physical therapists are beginning to explore the opportunity to publish in this journal. We do hope that there will be more articles from other ASEAN countries and professions to which reflect diversity in geographical distribution of authors.

Our peer-review process is rigorous to uphold the quality and validity of each submitted articles. Each submitted manuscript will be blinded and reviewed by two reviewers, one from our editorial board and the other is an expert from different institutes. Generally, the process of peer-review process is about a month; most of the reviewers were able to complete the reviews on time. Reviewers' comments have been very helpful and made the revised manuscripts better in quality and readability. In the year 2020, out of the 22 reviewers, three were non-Thais (1 Indonesian and 2 Malaysian). We seek to diversify the reviewers in the future. Average duration from submission to acceptance decreased from 4 months in 2019 to 3 months in 2020. Unfortunately, there were few manuscripts rejected in 2020 because they did not fit the scope of the journal and not written in English. To improve clarity, readability and quality of publication, we have revised the journal templates, one for original article and one for case report, and criteria for review for original article and for case report. We hope that authors will follow the new templates and peer-reviewers will use the new criteria for review, and these are expected to shorten the peer-review process and facilitate the revision and the publication processes.

The free online access would promote citation of articles published in the journal. Currently the journal is in Tier 1 of the Thai Citation Index (TCI) and also in the ASEAN citation index (ACI). If rehabilitation physicians and professionals in ASEAN submit their quality research papers to the journal, and these articles can be cited by other journals in international citation index such as Scopus and PubMed. The journal aims to be a regional and international journal in medical rehabilitation in the next 3-5 years. Together we urge the ASEAN rehabilitation community to join us in this valuable journey.

Apichana Kovindha, MD, FRCPhysiatrT
Editor-in-chief

Review Article

Applications of Transcranial Magnetic Stimulation in Post-Stroke Dysphagia

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ABSTRACT

Objectives: To summarize the main findings of using transcranial magnetic stimulation (TMS) and repetitive TMS (rTMS) in physiologic swallowing response and to review the parameters related to rTMS protocols in post-stroke dysphagia (PSD) treatment.
Study design: English-language literatures published from 1st January 1999 to 20th August 2020 were sought using PUBMED, MEDLINE, and Web of Science; and MeSH terms of transcranial magnetic stimulation, swallowing, deglutition, dysphagia, and stroke. Nineteen randomized control trials (RCT), six non-RCT, and one systematic review article were included.
Setting: Rehabilitation centers and university hospitals in Europe or Asia.
Subjects: Normal population and post-stroke dysphagia patients.
Methods: A narrative review of all the relevant papers related to TMS or rTMS was conducted.
Results: TMS is used to investigate swallowing physiology and to treat dysphagia. Several experiments have shown positive outcomes of swallowing functions without any serious complications. Two parameters: frequency and stimulation side, have different effects. Low-frequency stimulation has an inhibitory effect by decreasing the cortical excitability while high-frequency stimulation has the opposite effect by increasing the excitability. Low-frequency stimulation applied over the unaffected hemisphere inhibits interhemispheric interaction. High-frequency stimulation applied over the unaffected or the affected hemisphere might facilitate the recovery. Bilateral hemispheric stimulation by using high-frequency was shown to improve outcomes. To alter the cortical signal in swallowing, rTMS can be applied on both pharyngeal cortical hemisphere and the cerebellum.
Conclusion: rTMS is one intervention which may facilitate neurological recovery after dysphagic stroke. Although there was weak evidence to support dysphagia treatment, the recent studies showed positive effects. rTMS may be beneficial adjunctive therapy in post-stroke dysphagia treatment if a strong evidence protocol is addressed.

Keywords: transcranial magnetic stimulation, deglutition, dysphagia, stroke

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Introduction

Deglutition is an important process of living and it influences quality of life. Dysphagia is a difficulty in swallowing which in turn, results in malnutrition, dehydration, and aspiration pneumonia. Causes of dysphagia can be categorized into neurological, mechanical, infection, iatrogenic, and neuromuscular disorders. Cerebrovascular accident is one of the important causes.[1]

Nowadays, common therapeutic methods for post-stroke dysphagia (PSD) include, oral-lingual-pharyngeal muscles training, compensatory techniques, and dietary modification.[2] Neurofacilitation is an approach of muscle training. Apart from muscle training, repetitive transcranial magnetic stimulation (rTMS) is an important machine which has been used, successfully, to study deglutition physiology and treatment over a long period of time. Some studies believed it may help accelerate brain recovery.[3]

In the past 20 years, there were many research studies regarding rTMS in swallowing. Therefore, the purpose of this narrative review is to summarize the main findings of using transcranial magnetic stimulation (TMS) and rTMS in physiologic swallowing response and to review the parameters related to rTMS protocols in post-stroke dysphagia treatment; with an appropriate protocol, it could be used as an adjunctive treatment in the future.

Methods

Search strategy

PubMed, MEDLINE, and Web of Science were sought to identify the relevant clinical studies published in English from 1st January 1999 to 20th August 2020. The following MeSH terms: transcranial magnetic stimulation, swallowing, deglutition, dysphagia, and stroke, were used in combinations for database searches.

Inclusion criteria

- Clinical trials associated with usage of TMS and rTMS in protocol finding in physiologic swallowing response.
- Clinical trials, meta-analysis, or systematic reviews

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related to the use of rTMS as an intervention in PSD.

- TMS or rTMS as an intervention in human

Exclusion criteria

- The dysphagia caused from other diseases such as Parkinson's disease, cancer, and traumatic brain injury.
- Reviews, case series, case reports, and preliminary studies
- Other non-invasive brain stimulations such as transcranial direct current stimulation or theta burst stimulation, etc.
- The experiments or the results involved other conditions, for example, communication or hemiparesis.

Quality assessment

The author read the articles in full and analyzed the quality markers by using the Joanna Briggs Institute (JBI)[4] for clinical trials and systematic review articles. This is one of the standard tools for critical appraisal in medical research. Nineteen RCT, six non-RCT and one systematic review article were assessed for quality.

Data extraction

This narrative review was conducted in accordance with the Scale for the Assessment of Narrative Review Articles (SANRA).[5] There were no specific protocols for this review. The extracted data included the rationales, the processes of the studies, and the outcomes of the experiments.

Results

Five hundred and fifty-one of the literatures were found in the databases. The duplicated articles (n = 322) were excluded. The reviewer assessed the studies (n = 229) following the inclusion and the exclusion criteria. There were eleven articles related to TMS and rTMS in physiologic swallowing response and fifteen studies in post-stroke dysphagia treatment. The experiments were done in the university hospitals or the rehabilitation centers in Europe or Asia. For physiologic swallowing studies, the subjects were healthy. For stroke studies, patients had a unilateral cerebrovascular disease for the first time.

TMS in physiologic swallowing studies

Muscles and nerves can be activated by electrical stimulation. Following Faraday's law, Polsen in 1982 and Barker in 1985 invented a machine called TMS. TMS produces magnetic field via a coil which changes to an electrical field. The electricity passes through the skull, the cortex, subcortical white matter, and neuron projections. The current produced is sufficient to depolarize neural axons and hence, activation of target muscles at last.[6] (Figure 1)

The very first TMS studies were done in motor limbs. Later on, there were researchers who focused more on swallowing. Ertekin was the first researcher who used TMS and needle electromyography (EMG) in cricopharyngeal muscle of the upper esophageal sphincter and found linkage of the cortical pharyngeal cortex to pharyngeal muscles.[7] Paine found the pharyngeal amplitudes were also larger when the intensity was increased.[8] Hamdy and colleagues suggested that the precentral motor cortex plays a major role of deglutition and the pharyngeal motor control in both hemispheres were asymmetrical, showing one side to be more dominant (dominant pharyngeal hemisphere) than one other (non-dominant pharyngeal hemisphere). Moreover, the dominant pharyngeal hemisphere was independent of handedness.[9,10]

rTMS in physiologic swallowing studies

rTMS uses multiple pulses with equal intensity and a specific frequency applied over the brain cortex. The rTMS can produce cortical excitability and cause a prolonged effect for several minutes.[6] Many studies indicate that rTMS can produce excitability from the motor cortex via cortico-bulbar projections to activate pharyngeal musculatures.[3,11]

rTMS in cortical excitability inhibition studies

Mistry et al. established that using the 1 Hz frequency, at 120% of pharyngeal resting motor threshold (PRMT), 600

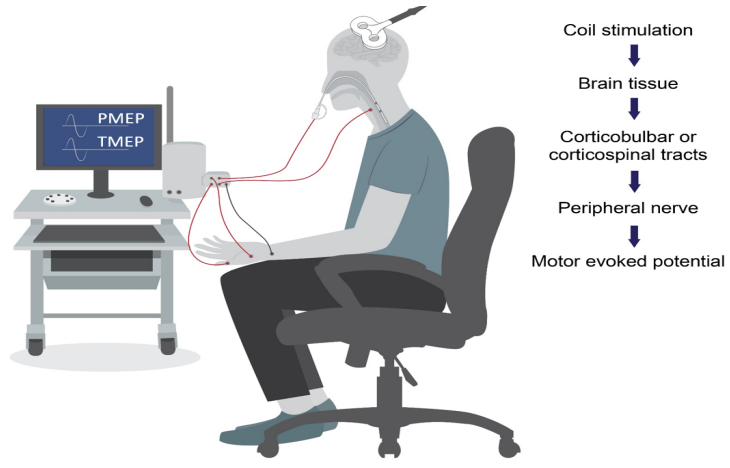

Figure 1. TMS set-up

pulses for 10 minutes over the dominant pharyngeal motor cortex caused a reduced cortical excitability for 45 minutes. The outcomes showed a significant change in pharyngeal motor evoked potential (PMEP) and swallowing behaviors.[12] Verin et al. followed this protocol and found oral transit time (OTT) was delayed and pharyngeal reaction time increased significantly by evaluating from video fluoroscopic swallow study (VFSS).[13] They concluded that the frequency at 1 Hz produced the inhibitory effect. The neurophysiologic effect was called 'virtual lesion' which temporary acted like a true lesion. Furthermore, the virtual lesion occurred only in the dominant pharyngeal hemisphere. If applied this frequency of rTMS over the non-dominant pharyngeal hemisphere, the PMEP and the swallowing behaviors measured from VFSS would not change significantly.[12,13] This finding concurs to what Hamdy et al. found in patients who had brain lesion in the non-dominant swallowing hemisphere but had no dysphagia. It was concluded that oropharyngeal dysphagia might be a result of the damage in the dominant pharyngeal hemisphere only.[1,9]

Additionally, the studies explained more details about the pharynx and the esophagus. In the limbs, they are a predominantly unilateral representation. In contrast to the pharynx and the esophagus, both midline structures are bilateral cortical representation.[9,12] When there is a lesion in one hemisphere, the signal from the contralesional hemisphere inhibits the ipsilesional hemisphere less than what it does in the limbs. This phenomenon implied that transcallosal interactions between the two pharyngeal motor areas were not strongly competitive, and indeed were most likely synergistic.[12]

rTMS in cortical excitability stimulation studies

Gow et al. found that setting frequency at 5 Hz, 80% of PRMT, 100 pulses could increase cortical excitability of pharyngeal motor cortex for the longest duration: 60 minutes, measured by pharyngeal EMG.[11] To use this finding in more clinical setting, Jefferson tried to reverse the virtual lesion in healthy subjects. Several studies had concluded that functional recovery of dysphagia in PSD patients was associated with increased cortical signal only in the unaffected hemisphere.[3,9,14] So, Jefferson applied rTMS over the unaffected hemisphere and found that 250 pulses at 5 Hz frequency were the optimal protocol to reverse the virtual lesion. The effect could last up to two hours.[10] However, in the limbs of stroke patients, more than or equal to 3 Hz of frequency can produce cortical excitability.[6] Therefore, it was also be used by some researchers in swallowing studies.[15,16]

rTMS in cerebellar stimulation studies

Cerebellum is another part which controls the swallowing process. Although the main role is still unclear, it might relate to sequencing, feed-forward control, and internal coordination of oral-lingual and pharyngeal muscles.[1] Impairment in deglutition will occur when stroke lesions are present on this area such as Wallenberg syndrome.[16] One hypothesis indicated that the cerebellum was supplied by vertebrobasilar circulation which was the same branch to the brain stem where the central pattern generator (CPG) was located.[1,16]

Vasant et al. suggested that using 250 pulses at 10 Hz could increase the PMEPs when stimulated over posterior fossa. If the frequency was set to more than 10 Hz, the excitability would not increase anymore due to its ceiling effect.[17] Thereafter, Sasegbon also conducted a study in normal population which was applied to the virtual lesion over the dominant pharyngeal motor cortex. After using 250 pulses at 10 Hz, 90% of thenar resting motor threshold applied over each side of cerebellum (posterior fossa), the cortical inhibition could be reversed when applied over either side compared to sham.[18] A year later, they found that using the same protocols of rTMS applied over both cerebellar hemispheres alternatively could produce the cortical excitability more than only over one side.[19] It could be implied that there were projections from cerebellum passing brain stem to higher brain which control the swallowing processes; neuroplasticity was facilitated by stimulating cerebellar pathways.[18-20]

The advantages of cerebellar stimulation were promoting brain recovery by stimulating at the posterior fossa directly. The anatomical landmark was easy to find and required less intensive training. Serious complications such as seizure also occurred less than stimulating over the cortex.[18]

rTMS in post-stroke dysphagia

rTMS in dysphagia was studied in many experiments. The figure-of-eight coil which released the current focally to the brain was used in all studies. The outer diameter of the coil loop was approximate 70-90 mm. The inclusion and the exclusion criteria were rather similar among of the studies and summarized in the table below.

Table 1. The inclusion and the exclusion criteria to participate the experiments

Inclusion criteria	Exclusion criteria
- Unilateral hemisphere stroke (ischemic stroke mostly) - Varied in time of onset - Age more than 18 years old - Can stay in upright position	- Prior head injury /other neurological disorders/ swallowing problems - Unstable medical conditions such as infection - Severe aphasia or cognitive impairment - Prior administration of tranquilizer - Contraindication for TMS (seizure, implanted pacemaker, medication pump, metal plate in the skull, metal objects in the eye, craniectomy state)

TMS, transcranial magnetic stimulation

Protocols in each experiment were different from each other. However, the influential factors were frequency and stimulation side.[21]

1. The stimulation side and frequency

1.1 Ipsilesional stimulation: When stroke happens, the brain is damaged and loses its neurological control in swallowing. High-frequency stimulation (at least 3 Hz) over this hemisphere can awake the sleep circuits or encourage the coordination of synapses.[15,16] Moreover, the lesional hemisphere might be suppressed from the contralesional side via the transcallosal pathway which was also found in extremity hemiplegia. Enhancing the cortical excitability in ipsilesional side could counteract the suppressive effect.[15] Lee et al. reported that using the 10 Hz frequency of rTMS over the suprahyoid cortical area could significantly improve clinical swallowing assessments.[22]

1.2 Contralesional stimulation can be divided into inhibitory and excitatory effects.

Inhibitory effect: The ipsilesional hemisphere is disrupted from the contralesional hemisphere which is called interhemispheric interaction. Low-frequency rTMS applied over the contralesional side can reduce the inhibition effect.[23,24]

Excitability effect: The recovery from dysphagia stroke involves compensatory changes of the contralesional hemisphere.[9,10] High-frequency stimulation on this side might promote the recovery.[10] Muellbacher et al. supported this hypothesis. They studied acute PSD by using high-frequency rTMS applied over tongue cortical area on the contralesional hemisphere. They found that the cortical excitability increased in bilateral hemispheres which measured by tongue MEP.[14] Moreover, Park et al. suggested to stimulate over the contralesional side; it was easy to find the motor hot spot because in severe cases, the neurons in the lesional hemisphere might remain less than those in the opposite side.[25]

1.3 Bilateral stimulation: The damage on supratentorial areas, when one side is disrupted, the surviving neurons related swallowing functions in the other side will also decrease their activity. Bilateral stimulation might reverse this phenomenon (reverse diaschisis).[26] Following this hypothesis, Park et al. found that the improvements of dysphagia by using high-frequency (10 HZ) of rTMS over bilateral cortical hemispheres were better than those from the unilateral stimulation.[27] The recent study used high-frequency rTMS applied over the lesional hemisphere and used low-frequency on the other side. This protocol could also improve the clinical swallowing assessments but the rationale was unclear.[28]

However, the systematic review in 2017 indicated that the swallowing functions were improved more in contralesional and bilateral hemispheres stimulation. Moreover, both high and low frequency of rTMS could improve the outcomes after treatment.[21]

2. The intensity and the resting motor threshold of the muscles

To calculate the intensity, resting motor threshold (RMT) is needed. RMT is defined as the required minimum stimulation intensity over the motor hot spot to evoke the optimum MEP, 5 out of 10 trials, in the given muscle.[6] There are two groups of muscles which are usually used. The first is hand muscles, abductor pollicis brevis (APB)[25] and first dorsal interossei (FDI)[15,16] muscles, and the second is the pharyngeal muscles.[23,25] The intensity to evoke APB or FDI muscles and achieve at least 50 μV was usually at 30-60% of the maximum stimulating output of the rTMS machine[6] while the intensity to evoke PMEP at least 20 μV is around 70-80%.[12] The intensity to evoke pharyngeal muscles is higher. Therefore, the intensity to activate the cortical excitability after brain damage depends on RMT of which muscle is chosen.

Finding RMT of hand MEP is easier because the cortical area of the upper extremity is large.[25] Some studies chose the intensity following the previous rTMS protocols that were used in unilateral hemiplegia studies.[15,16] Khedr et al. in order to activate more neurons, set high intensity (130%) of FDI RMT because the electricity could spread 2-3 cm over the cortex from the center of coil.[16] However, the safety guideline recommends to use the intensity at < 130% of RMT.[29]

Most problems of PSD are associated with oropharyngeal phase.[1] Most of the experiments used rTMS applied over mylohyoid cortical area because these muscles have the most important role in pharyngeal phase.[22,30] Some

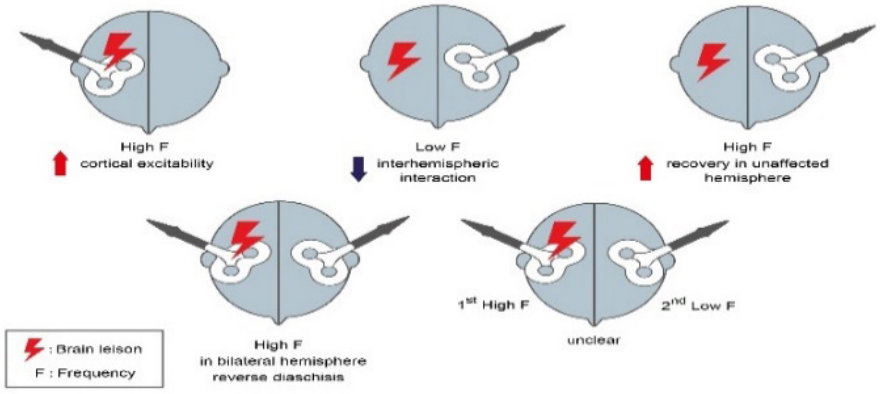

Figure 2. The hypotheses of frequency and stimulation side in rTMS protocols affecting to brain recovery. (F, frequency)

Table 2. Frequencies, intensities, and the cortical motor areas that applied the coil over for rTMS

Frequency and Intensity	Cortical motor area	Position of the coil
- 3 Hz of 120% of FDI RMT over affected side[15] - 3 Hz of 130% of FDI RMT over bilateral hemisphere[16]	Proximal striated muscles of the esophagus[8]	3 cm anteriorly and 6 cm laterally to the vertex[16] In healthy subjects - 3.8±1.4 cm anteriorly and 6.9±1 cm laterally of Rt. side - 3.0±1.7 cm anteriorly and 6.6±0.87 cm laterally of Lt. side[9]
- 3 Hz of 90% of mylohyoid RMT over affected side[30] - 10 Hz of 90% of mylohyoid RMT over bilateral sides[27] - 1 Hz of 100% of mylohyoid RMT over unaffected side[30] - 1 Hz of 90% of mylohyoid RMT over unaffected side[24]	Mylohyoid[24,30]	2-4 cm anteriorly and 4-6 cm laterally from the vertex[24,27,30]
- 5 Hz of 90% of thenar RMT over unaffected side[25]	Pharyngeal muscles[12,25]	Mediolateral and anteroposterior from the vertex 2.5-4 cm from each[12]
- 5 Hz of 90% tongue RMT over affected side[31]	Tongue[31]	0-4 cm anteriorly and 4-6 cm laterally to the vertex[14]
- 10 Hz of 90% thenar RMT[18,19]	Cerebellar hemisphere[18,19]	The central part of coil applied 1 cm below the inion to stimulate the midline, tangentially to the scalp with the handle pointing superiorly[20]

FDI, first dorsal interossei; RMT, resting motor threshold

studies chose tongue muscles because they are mostly involved in oral to initial pharyngeal phase.[14,31] To measure the PMEP directly by transnasal or transoral, pharyngeal intraluminal catheter seemed to be more accurate than surface EMG.[15,16,25] However, some participants felt uncomfortable when the catheter was inserted and wanted to stop the study.[15] Unfortunately, most studies did not describe how the resting motor threshold was determined. This is also important because RMT of any muscle can vary around 20% across studies and across investigators.[8,12] MEP responses also showed a variation according to phase of sleep and intake of ethanol.[8]

3. The duration of effect

Most studies followed up at 3 months and found the effect still lasted.[24,30,32] They hypothesized the long-lasting effect could be from the change of GABAergic circuits in the pharyngeal cortex and enhanced intracortical glutamatergic transmission.[6,25] While some other studies found improved clinical swallowing at 2 weeks,[23,25] 3 weeks,[27] to 4 weeks.[28] However, the systematic review concluded that the results could be maintained over 4 weeks.[21]

4. The outcomes and the adverse effects

Several studies showed positive effects.[21,27,30,32] However, the study of rTMS in chronic PSD did not indicate improvement in swallowing functions (clinical testing, tongue strength, and from VFSS) significantly.[31] Unluer et al. reported that rTMS also improved the quality of life especially in the burden and fear of eating significantly. One hypothesis suggested that diffusing of rTMS signal to prefrontal cortex could affect moods.[24] The small sample size[15,16,21,23,25,31] and the degree of dysphagia (mild to moderate) might impact the exact results in several studies.[22,31] Furthermore, the tools of assessments might have not enough sensitivity to classify the severity of dysphagia clearly.[22,31] Lee et al. reported the clinical rating scale or the Dysphagia Outcome Severity Scale (DOSS). It was used to assess clinical parameters of oral phase more than those of pharyngeal phase whereas the treatment applied over mylohyoid muscles involves more in initial pharyngeal phase.[22] Therefore, the treatments given might not relate well to the parameters assessed.[22] However, rTMS was safe for using in PSD patients due to no serious complications such as seizure. For minor adverse effects, two studies reported dizziness, transient headache,[23,30]and a tingling sensation.[30] Furthermore, pair associated stimulation-combination of rTMS (central stimulation) with neuromuscular or pharyngeal electrical stimulation (peripheral stimulation), might facilitate the speed of neurological recovery.[28,33] More research is still in needed.

Discussion

In the author's aspects, even the protocols were varied and the long-term effects were not clear. However, the results showed the positive effects in both swallowing functions and the swallowing-related quality of life. Using rTMS to promote neuroplasticity in acute and subacute phase combined with traditional therapy might be beneficial. The future study might design a proper methodology including the sample size, outcome assessor blinding, the time of finding RMT, the subtype

Table 3. Recent published studies related to rTMS in post-stroke dysphagia

Study	RCT Participants	Onset	Site of stimulation	Protocol	Duration	Results
Cheng et al, 2017[31]	Double-blinded N = 14	PSD At least 12 months	Affected (active rTMS vs sham)	5 Hz 100 pulses ITI 15 s, 90% RMT of tongue 10 days over 2 weeks	F/U 2,6,12 months	No significant change in VFSS, SAPP and maximum tongue strength
Park et al, 2017[27]	Single- blinded N = 33	Stroke less than 3 months	Bilateral vs affected side vs sham (pre and post treatment)	10 Hz 500 pulses ITI 55 s, 10 min 90% RMT of mylohyoid 10 consecutive days	F/U immedi-ately and 3 weeks	Improved CDS, DOSS, PAS mostly in bilateral stimulation over 3 weeks ($p < 0.05$)
Tarameshlu et al, 2019[32]	Double-blined N = 18	More than 1 month	Unaffected (rTMS + TDT vs TDT vs rTMS)	1 Hz, 1200 pulses + 20% above RMT of mylohyoid 20 min 5 consecutive days	F/U at 5th, 10th, 15th and 18th sessions	MASA: improve all over time ($p < 0.001$) FOIS: improve overall groups ($p < 0.05$), more greater in rTMS+TDT ($p < 0.05$)
Unluer et al, 2019[24]	Single-blinded N = 28	2-6 months	Unaffected (rTMS + TDT vs TDT)	1 Hz, 1200 pulses 90% RMT of mylo-hyoid 20 min, 5 consecutive days	F/U at after, 1 and 3 months	SAFE: improve all at 1,3 months ($p = .000$) PAS: improve over 1 month ($p < 0.05$), no significant in between group
Zhang et al, 2019[28]	Single-blinded N = 64	Less than 2 months	HF at affected LF at unaffected 1. Sham rTMS + NMES, 2. HF of rTMS + NMES 3. LF of rTMS + NMES 4. Bilateral rTMS + NMES	HF: 10Hz, 900 pulses, 110% RMT of mylohyoid ITI 27 s, 15 min LF: 1 Hz 900 pulses, 80% RMT 15 min, 5 days/ week for 2 weeks	F/U at 2 weeks and 1 month	DD score: improve in bilateral rTMS+NMES at 2 weeks ($p = 0.017$) SSA: decrease all groups at 2 weeks, 1 month ($p < 0.05$), bilateral rTMS + NMES greater > HF/LF of rTMS + NMES > NMES

CDS, Clinical Dysphagia Scale; DD, Degree of Dysphagia; DOSS, dysphagia outcome and severity scale; FOIS, Functional Oral Intake Scale; F/U, follow up; HF, high-frequency; ITI, intertrain interval; LF, low-frequency; MASA, the Mann Assessment of Swallowing Ability; NMES, neuromuscular electrical stimulation; PAS, Penetration-aspiration Scale; PSD, post-stroke dysphagia; RCT, randomized controlled trial; RMT, resting motor threshold; rTMS, repetitive transcranial magnetic stimulation; SAFE, the Swallowing Ability and Function Evaluation; SAPP, the Swallowing Activity and Participation Profile; SSA, Swallowing Assess-ment; TDT, Traditional Dysphagia Therapy; VFSS, Videofluoroscopic Swallowing Study

Table 4. Advantages and disadvantages of rTMS

Advantages	Disadvantages
- Safe - Painless - Non-invasive procedure - Well-tolerated procedure - Do not need to be actively engaged during treatment	- High cost - Contraindicated in certain patient groups - Varied treatment protocols - Uncertain outcomes - Uncertain long-term effects

of stroke (the recovery is varied in different locations of the lesion) and the tools of assessments. Moreover, the rTMS studies in PSD tend to be increasing so a meta-analyses and systematic review might be done for certain outcomes in the future.

Conclusion

TMS is one intervention which may facilitate neural re-organization after post-stroke dysphagia. Many studies showed several protocols for treatment. The frequency and the stimulation site seem to be crucial. Although there were weak evidences to support the use in PSD treatment, the recent studies showed positive effects. In designing a study, understanding the swallowing physiology, mechanisms of the swallowing recovery, and the limitation of the previous studies is important. rTMS may be beneficial adjunctive therapy in post-stroke dysphagia treatment if a strong evidence protocol is addressed.

Disclosure

The author has no conflict of interest to declare.

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Original Article

Factors Related to Return to Sport at One Year after Anterior Cruciate Ligament Reconstruction

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ABSTRACT

Objectives: To investigate rates of return to pre-injury sport (RTS) level at around one year after anterior cruciate ligament reconstruction (ACLR) and completing a rehabilitation program for post-ACLR and related factors.
Study design: Retrospective case control study.
Setting: Department Rehabilitation Medicine, Suratthani Hospital.
Subjects: Patients who underwent ACLR and completed the rehabilitation program, had a pre-injury Tegner Activity Scale (TAS) level 5 or higher, had normal Lachman test, and 4 single leg hop tests done.
Methods: Demographic data and results of 4 single leg hop tests were extracted from the recruited patients' medical records. Limb symmetry index (LSI) was calculated from the 4 single leg hop tests. The recruited patients were divided into two groups, the RTS and the non-RTS groups, and data were compared between the two groups.
Results: There were 40 patients in the RTS group and 31 in the non-RTS group. The RTS rates were 56.3% in average, 57.4% for football, 62.5% for running, and 16.7% for basketball. The RTS group had younger age (mean age of 23.5 and 29.0 years, p = 0.01), more athletes (37.5% and 12.9%, p = 0.03), higher percentage of LSI > 90% of all 4 single leg hop tests (77.5% and 29.0%, p = 0.00) than the non-RTS group. Mean duration from operation to the last 4 single leg hop tests was 10.4 months for the RTS group. One reason of being unable to RTS was fear of re-injury (67.7%).
Conclusion: The overall rate of return to pre-injury sport level was 56.3%. Younger age and achieving LSI more than 90% of all 4 single leg hop tests were factors related to RTS at around one year after ACLR and receiving postoperative rehabilitation. Fear of re-injury was a major reason for not returning to pre-injury sports activity.

Keywords: anterior cruciate ligament reconstruction, rehabilitation, return to sport, single leg hop test

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Introduction

The anterior cruciate ligament (ACL) tears are the most common, complete ligamentous injuries that occur in the knee joint.[1] In the United States, it is thought that over 200,000 ACL injuries occur annually, contributing to in excess of 100,000 ACL reconstruction (ACLR) surgeries.[2] The ACLR is the current standard for those with an ACL tear and considered to be at a high risk of knee instability such as young age, high-level athletes in a contact sport.[3] The primary goals of ACLR are to stabilize the knee to ensure minimized morbidity and allow a safe return to previous level of activity.[4] About 98% of the orthopedic surgeons recommend surgery if patients wish to return to sport (RTS).[5] Unfortunately, ACLR does not guarantee that they are able to achieve RTS.[5] Edwards et al. reported 63% of the patients could return to their pre-injury level of sport at 12 months after surgery.[6] The meta-analysis by Ardern et al. recorded a mean return to pre-injury sports rate of 65%.[7] The narrative review by Doyle recorded average RTS for competitive athletes was slightly lower than recreational athletes (60% vs 64%).[4] Different literatures led to improved understanding of variables influencing patients' ability to achieve RTS such as under 25 years of age, normal body mass index (BMI), professional athletes, short duration of injury, absence of co-commitment injury, grafts type, complete rehabilitation program, less 10% deficit quadriceps and hamstring trength, absence knee pain, more than 90% of limb symmetry index (LSI) and positive psychological factor.[1,4,6-10]

After ACLR, a rehabilitation program is provided to patients so that they could to return to a painless and fully functional daily life.[11] The program consists of neuromuscular control, lower limb muscular strength and sport specific exercise. Before returning to sport, functional tests such as a series of single leg hop tests are recommended for evaluating a lower extremity performance, physical function and readiness to RTS after ACLR.[7,12-14] In patients undergoing rehabilitation following ACLR, the 4 single leg hop tests are reliable measure

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of limb symmetry (intraclass correlation coefficient, ICC = 0.82-0.93)[15] as these tests assess the combinations of muscle strength and power, neuromuscular control, confidence in the repaired knee, and ability to tolerate loads related to sport specific activities.[13] The results of individual tests are frequently reported as LSI.[16] Recent ACLR studies have demonstrated an increased re-injury risk in patients not meeting a minimum 90% LSI on functional and strength tests.[10,17]

At Suratthani Hospital, there are about 80 cases of ACLR per year. All 4 orthopedists have utilized a similar arthroscopic ACLR with hamstring tendon autografts surgical technique consisting of anteromedial portal drilling, tibial screw fixation and femoral endobutton fixation.[18] The reason for hamstring tendon autografts choice was most patients were amateur or low division athlete.[18] Furthermore, the long term study of Webster et al. reported 15 years follow up for comparing patellar tendon and hamstring tendon ACLR. There were no differences in knee laxity and degree of osteoarthritis between both groups that supported this graft choice.[19]

In this present study, we aimed to investigate rates of return to pre-injury sport (RTS) level after ACLR and completing the seven-stage rehabilitation program, and factors related to successful RTS. We hypothesized that 1) age, BMI, meniscus injury, sport activity pre-injury status, duration from injury to ACLR and achievement in the functional tests might be related to RTS, and 2) based on the 4 single leg hop tests, those who could RTS would demonstrate better functional tests than those who failed to RTS.

Methods

Ethical approval was obtained from the Suratthani Hospital Human Research Committee (approval ethical number/RF 33/2563) before starting this retrospective study.

Participants

A total 255 of patients who had undergone an arthroscopic ACLR with hamstring tendon autografts during April 2016 - May 2019 were recruited into this study. Inclusion criteria were age between 15 and 50 years, unilateral ACL injury, and a pre-injury Tegner activity scale[20] (TAS) level 5 or higher. Exclusion criteria were bilateral knee injury, prior knee ligament injury and/or surgery, incomplete rehabilitation program, a history of heart condition and pregnant women. The flow diagram (Figure 1) describes how patients were tracked throughout the study.

Following the operation, 194 patients entered our post-operative rehabilitation program[21] (Appendix) starting in the first post-operative week, and duration of the whole program lasted at least six months after surgery. Before advancing to the next stage, the goals of the present stage were evaluated. However, we had only 71 patients who completed program and met all inclusion criteria. After completing the rehabilitation program, having full knee range of motion (ROM) and having normal knee stability (Lachman test with an end point grade 0 to 1+) evaluated by orthopedists, the patients then performed a series of 4 single leg hop tests which indicated knee joint stability function. According to our protocol, if the patients failed the first-time tests, approximately 8 months after ACLR, they were asked to have the second tests two months later; if they still failed the second-time tests, the third tests were repeated in the next two months. For those who passed the first-time tests, they were asked to repeat the tests at approximate one year after surgery.

According to a previous study by Edwards et al. (2018),[6] a sample size of at least 26 members for each group should be recruited.

Data collection

Medical records of eligible patients were identified and relevant demographic and clinical data were extracted. Demographic data were age, gender, body mass index (BMI); clinical data were meniscus injury, date of injury, date of operation, date of rehabilitation program ended, knee ROM, the Lachman test, the pre-injury and the post-operation sport activity status, results and date of performing the 4 single hop tests after completing the rehabilitation program, and reasons of not RTS.

The 4 single leg hop tests measured 1) single hop distance, 2) crossover hop distance, 3) triple hop distance, and 4) time utilized for a 6-meter hop distance with maximum effort.[14] Base on the tests, a LSI is calculated as a percentage of performance on the operated and the non-operated limb (% = operated limb/non-operated limb × 100). Using the last data achieved approximately one year post- operation, the LSI of each 4 single leg hop tests was calculated.[14] From this study of patients with ACLR, the tests were done between 8 and 14 months after operation.

According to previous study by Edwards et al. (2018)[6] to "pass" the tests in this study, one required to achieve LSI > 90% on the operated limb in all 4 tests, and to "fail" when on one or more of the 4 tests showed LSI < 90%.

Statistical analysis

For statistical analysis, the data were divided into two groups based on patients' report: the "RTS" of those who were able to return to their pre-injury sport levels and the "non-RTS" of those who failed. The levels were classified based on TAS.[20] Using STATA version 12.0 (Stata Corp, College Station, TX), descriptive statistics such as means, standard deviations, proportions, percentage, were calculated for all demographic, physical and functional data of each group. Independent t test was used to assess between-group differences of continuous data, and Fisher exact test for categorical data such as gender, age groups, BMI groups, the pre-injury sport level and the functional tests based on LSI mentioned above. A *p*-value of less than 0.05 was considered statistically significant.

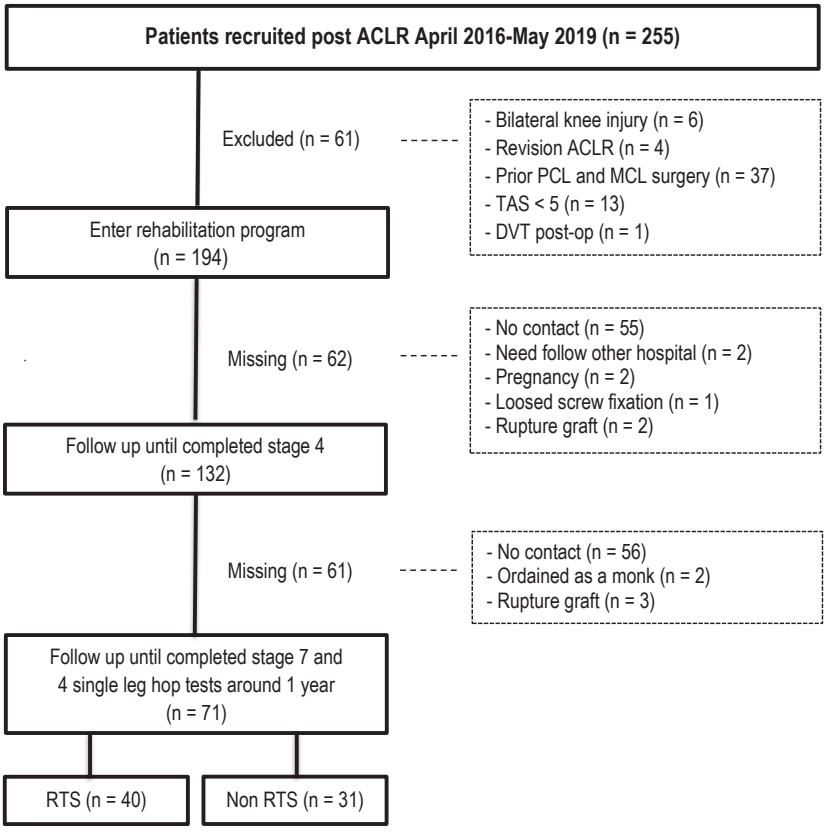

Figure 1. Flow chart diagram for patients recruited post ACLR
ACLR, anterior cruciate ligament reconstruction; PCL, posterior cruciate ligament; MCL, medial collateral ligament; RTS, return to pre-injury sport; DVT, deep vein thrombosis; TAS, Tegner activity scale

Results

A total of 71 patients were included in the study. The rates of return to pre-injury sport level were highest in those below 18 years old (87.5%), followed by those between 26 and 32 years old (62.5%), in those between 18 to 25 years old (50%), and lowest in those over 32 years old (26.7%). The most common sports participants played before their ACL injury were football (76.1%), running (11.3%), and basketball (8.5%); and the rates of RTS were 57.4% for football, 62.5% for running, and 16.7% for basketball. Other sports were volleyball (n = 2) and taekwondo (n = 1), and all could RTS.

Demographic data are shown in Table 1. The RTS group was significantly younger than non-RTS group (mean age of 23.5 and 29.0 years, respectively, p = 0.01). When dividing into four distinct age groups, there was a statistically significant difference between the RTS and the non-RTS groups (p = 0.05). Gender, mean BMI, meniscus injury, and obesity were not different between the two groups. However, the pre-injury sport status was significantly different between the two groups (p = 0.03). Regarding the TAS, the pre-injury level was no difference but the post-injury level was significantly different (p = 0.00), the mean post-operative TAS level was higher in the RTS group than in the non-RTS group. The RTS group had a shorter duration from injury to ACLR but the difference between groups did reach statistical significance (7.0 and 9.9 months, p = 0.24). Mean duration from operation to the last 4 single leg hop tests was similar at 10.4 months for the RTS group and 10.7 months for the non-RTS group (p = 0.61).

There were 31 patients in the RTS group (77.5%) and 9 patients in the non-RTS group (29.0%) who could pass all 4 single leg hop tests with LSI > 90%, and there was statistically significant difference between the two groups (p = 0.00) as showed in Table 2 In addition, the LSI for each 4 single leg hop test and all 4 combined in the RTS group were more than non-RTS group and there were significant differences between the two groups (p = 0.00, 0.05, 0.00, 0.01 and 0.00).

In the non-RTS group, 21 patients (67.7%) reported fear of re-injury or lack of confidence as a primary reason for not returning to pre-injury levels of sports participation, and 10 patients (32.3%) had knee joint symptoms (pain, swelling, and muscle weakness). Muscle weakness was reported by 6 patients (19.4%), knee pain was reported by 3 patients (9.7%) and swelling knee was reported by 1 patient (3.2%). Muscle weakness was the most frequently reported knee joint symptoms.

Discussion

This study investigated the rate of return to pre-injury sport level approximately one year after surgery, 56.3% of

Table 1. Comparison of demographic data between the return to pre-injury sport level (RTS) and the non-RTS groups

Demographic data	RTS (n = 40)	Non-RTS (n = 31)	*p*-value
Age[1] (years)	23.5 (7.4) [16-46]	29.0 (9.6) [17-49]	0.01[a]
Age groups[2] (years)			
< 18	14 (87.5)	2 (12.5)	0.05[b]
18-25	12 (50.0)	12 (50.0)	
26-32	10 (62.5)	6 (37.5)	
> 32	4 (26.7)	11 (73.3)	
Gender[2]			
Male	36 (90.0)	30 (96.8)	0.38[b]
Female	4 (10.0)	1 (3.0)	
BMI[1] (kg/m^2)	23.4 (3.3)	24.8 (4.1)	0.11[a]
BMI groups[2] (kg/m^2)			
< 25	30 (63.8)	17 (36.2)	0.08[b]
> 25	10 (41.7)	14 (58.3)	
Meniscus injury[2]	32 (79.5)	22 (71.0)	0.38[a]
Duration from injury to ACLR[1] (months)	7.0 (6.1) [1-24]	9.9 (13.4) [2-60]	0.24[a]
Duration from ACLR to the 4 single leg hop tests[1] (months)	10.4 (2.1) [8-14]	10.7 (2.3) [8-14]	0.61[a]
TAS[1]			
Pre-injury	7.5 (1.3) [5-9]	7.2 (0.8) [6-9]	0.17[a]
Post operation	7.5 (1.3) [5-9]	5.1 (0.7) [4-7]	0.00[a]
Pre-injury sport status[2]			
Amateur	25 (48.1)	27 (51.9)	0.03[b]
Athlete	15 (79.0)	4 (21.1)	

[1]Mean (SD) [range], [2]number (%)

[a]Independent t test; [b]Fisher exact test

BMI, body mass index; TAS, Tegner activity scale; ACLR, anterior cruciate ligament reconstruction

Table 2. Comparison of means limb symmetry index (LSI) calculated from the 4 single leg hop tests between the return to pre-injury sport level (RTS) and the non-RTS groups

LSI	RTS (n = 40)	Non-RTS (n = 31)	*p*-value
Single hop LSI[1]	95.2 (0.8)	89.6 (1.5)	0.00[a]
Triple hop LSI[1]	95.7 (0.7)	92.6 (1.5)	0.05[a]
Crossover hop LSI[1]	97.0 (0.8)	90.7 (1.6)	0.00[a]
Timed hop LSI[1]	93.8 (1.0)	88.6 (1.8)	0.01[a]
Combined LSI[1]	95.4 (0.7)	90.4 (1.3)	0.00[a]
Pass/Fail[2]	31 (77.5)/9 (22.5)	9 (29)/22 (71.0)	0.00[b]

Pass means achieving LSI > 90% in all 4 tests; Fail means having one or more of the 4 tests with LSI < 90%

[1]Mean (SD), [2]number (%)

[a]Independent t test; [b]Fisher exact test

the patients had returned to their pre-injury level of sport participant, which is in line with the previous research reporting 63% and 65% of patients resumed participation at their pre-injury level of activity by 12 months after surgery.[6,7] Those who participated in running had higher rate of RTS (62.5%) than those who participated in football (57.4%) and basketball (16.7%). One reason of having higher rate of RTS in runners might be due to less injury as running is a non-contact sport. On contrary, basketball had the lowest rate of RTS as basketball is a contact-sport. Similar with Seto et al. reported that athletes who participated in sports involving cutting and twisting motions were less successful in returning to pre-injury activity level after ACLR.[22]

In this study, one factor related to RTS around one-year post ACLR was younger age. Ardern et al. reported that younger age certainly appeared to significantly influence return to pre-injury sport rates, as the RTS rates in their 280 patients divided into four distinct age groups were as follows: 49% in age < 18 years, 57% in age 18-25 years, 44% in age 25-32 years and 33% in age > 32 years; highest in the 18-25 years group and lowest return in the > 32 years group.[23] In our current study, the highest rate (87.5%) was recorded in those < 18 years, while the lowest rate (26.7%) was same in those > 32 years. It has been suggested that people under 18 years of age have a greater opportunity to participate in sports because they are often school athlete and had free

time for recreation activity, whereas those over 32 years of age have more barrier including employment, family commitments and less opportunity to take part in sport.

Ballal et al. displayed that obesity within two years post-operation did not adversely affect functional outcomes as measured by the KOOS and Lysholm scores.[8] However in our study, the percentage of obese patients (BMI > 25 kg/m^2) was less in the RTS group less than non-RTS group (25.00% and 45.16%) and the difference between groups was closely statistically significant (p = 0.08). Hence, we suggest that the obese patients should control their body weight after ACLR and through rehabilitation program as they may fail to RTS.

Another factor concerned was being an athlete. In our study, there was a higher number of athletes in the RTS group than the non-RTS group (37.5% and 12.9%) with statistically significant difference (p = 0.03). Smith et al. displayed the competitive athletes RTS more successfully than recreational athletes.[24] Competitive athletes might be expected to have greater success rates in returning to pre-injury levels of sport than amateur considering that they have a more satisfactory physical status preoperatively, good cooperated with the rehabilitation program, and mental prepare to RTS.

The last but important factor related to RTS found in this current study was the functional tests i.e., the 4 single leg hop tests. There were 22.5% of our patients who had returned to sports even but failed the functional test, and they were at high risk of graft ruptures. According to Kyritsis, et al. athletes who did not meet the required clearance criteria before returning to sport had a 4-fold greater risk of sustaining an ACL graft rupture compared with those who had met the discharge criteria e.g., single leg hop had LSI > 90%, agility running T test < 11 seconds and quadriceps deficit < 10%.[10]In this current study, younger age was a significant predictor of return to sport, with 65% of patients aged < 25 years having already returned to sports at the time of the clinical evaluation but younger age was a significant risk factor for secondary injuries after ACLR as Paterno et al. reported 29.5% of athletes who under 25 years of age suffered a second ACL injury within 24 months of RTS, with 20.5% sustaining a contralateral injury and 9.0% suffering a graft re-injuring.[25] In a systematic review, Wiggins, et al. identified younger patients (< 25 years) and those who returned to a high level of activity, especially in high-risk sports, to be at an increased risk to the secondary ACL injury rate was 23%.[26] The reasons for the increased risk are likely to be younger patients and returning to high-risk sports that involve cutting, jumping, and pivoting movements.[14] We observed 6 of the patients aged < 25 years and who were back playing sport with failed functional tests, potentially putting them at risk of the secondary ACL injury. Patient education seems very important to younger athletes. Rehabilitation physicians (physiatrists) should closely observe and evaluate them through all seven stages of rehabilitation program, and perform follow-up functional tests closely until they achieve all discharge criteria to reduce the re-injury risk.

When exploring the reason why, the patients in this current study who had passed the functional tests but not return to pre-injury sport level fear of re-injury and lack of confidence were the dominant psychological factors. According to the systematic review by Ardern et al. positive psychological responses including motivation, confidence and low fear were associated with a greater likelihood of returning to the pre-injury level of participation and returning to sport.[27] Rehabilitation physicians should encourage positive psychological responses during post-operative rehabilitation program when setting goal for RTS.

This current study had some limitations as it was a retrospective study. The number of patients recruited into the study was rather small when comparing with the number of cases per year which indicated that many patients were missing from the rehabilitation program. We expected causes that 1) some patients had a problem of travelling long distance to Suratthani Hospital because they lived in other provinces e.g., Chumphon, Ranong and Phuket and Samui Island, 2) after operation 2-3 months, patients returned to work or school they found it was difficult to take day off for coming to hospital, and 3) some patients did exercise by themselves after they sought technique from online media and asked their friends.

In conclusion, after ACLR and completing the seven stages out-patient rehabilitation program at Suratthani Hospital, the overall rate of returning to pre-injury sport level at approximately one year after surgery was 56.3% in patients having pre-injury level 5 or higher of Tegner activity scale. Younger patients and achieving a limb symmetry index more than 90% in all 4 single legged hop tests were good predictive factors of RTS at approximately one year after ACLR and completing post-operative rehabilitation program. Fear of re-injury was a psychological barrier of returning to sport.

Disclosure

No potential conflicts of interest relevant to this article were reported.

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Appendix

Home based post ACLR rehabilitation program[21]

Time frame	Rehabilitation goal	Activities
Stage 1 Week 0-2	ROM: full extension Good quadriceps contraction Weight bearing as tolerated with crutches Except repaired meniscus group non weight bearing first 6 weeks	On knee brace full extension all times Isometric quadriceps exercise Ankle pump SLR (flex, abduct, extend) Stretching hamstring and gastrocnemius muscle Prone hang, pillow under heel Gait training Patellar mobilization
Stage 2 Week 2-4	ROM: 0°-90° Closed chain quadriceps exercise Walk without crutches	Knee brace 0°-90° PROM 0°-90° Heel slide Prone hamstring exercise Wall slide knee flex 45°
Stage 3 Week 4-6	ROM: 0°-120° Increased muscle strength and endurance Enhance proprioception, balance, neuromuscular control	Unlocked knee brace PROM 0°-120 stationary bike Step up 4-step forward and lateral Toe rises Wall slide knee flex 90° Shift weight, standing single leg
Stage 4 Week 6-8	ROM: 0°-140° Normal gait pattern Increased muscle strength and endurance With meniscus repaired titrate weight bearing	Off knee brace PROM 0°-140° Step up 8-step forward and lateral Wall slide knee flex 90° with weight and ball Wall slide single leg 45°-90° Backward walking Leg press exercise (0°-60°)
Stage 5 Week 8-12	Full ROM Enhance propriception, balance, neuromuscular control Good single leg squat test	Treadmill walking (flat only) Forward lunge exercise Wobble board balance two legs Single leg squat
Stage 6 Week 12-18	Full ROM Restore functional capability and confidence Good single leg squat test	Reverse lunge exercise Jogging and light running Knee extension exercise Agility exercise Outdoor bike on flat road
Stage 7 Week 18-24	Maintained muscle strength and endurance neuromuscular control Return to sport	Running, jumping, hoping Agility exercise Sport specific exercise

ROM, range of motion; SLR, straight leg raising; PROM, passive range of motion

Reference: Janewanitsataporn S. The functional tests after ACL reconstruction with and without meniscal repair. J Health Sci Med Res. 2020;2:73-9. (with permission)

Original Article

Immediate Effect of Repetitive Peripheral Magnetic Stimulation in Hemiplegic Patients with Arm Paresis: A Pilot Study

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ABSTRACT

Objectives: To compare the immediate effects of repetitive peripheral magnetic stimulation (rPMS) on upper extremity (UE) function of hemiplegic patients with different severity.
Study design: Experimental pilot study.
Setting: Rehabilitation Center at Ramathibodi Hospital, Mahidol University, Thailand.
Subjects: Thirteen participants (10 males and 3 females) with subacute to chronic UE paresis due to central nervous system lesion.
Methods: Each subject received one session of 12 minutes rPMS equally distributed over six hemiparetic shoulder-arm muscles (supraspinatus, infraspinatus, deltoid, biceps, triceps and pectoralis major). The train of stimulation was delivered to the affected arm with a figure eight coil at approximately 120% intensity of motor threshold at 20 Hz frequency in pulses of 4 seconds on alternating with 4 seconds of rest. Motor functions were assessed with upper extremity Fugl-Meyer motor (UE-FMA) scale, modified Ashworth Scale (MAS), and arm reach test (ART) before and then again 5 minutes after the stimulation. Patients with UE- FMA score of 16 or lower and those with score more than 16 were classified as more-severe and less-severe respectively. Statistical analysis was made comparing the difference between before and after of UE-FMA score, MAS, and ART of each group.
Results: The mean (SD) of UE-FMA score before and after rPMS stimulation were 21.6 (10.5) and 23.3 (8.9), respectively. Wilcoxon matched-pairs test confirmed that the results reached statistical significance (p = 0.018). The median (Q1-Q3) UE-FMA score before and after the stimulation in more-severe paresis group were 12.5 (9.3 to 13.3) and 16.0 (11.8 to 17.3), respectively. Wilcoxon matched-pairs test confirmed significant between group statistical difference (p = 0.027). The median (Q1-Q3) of UE-FMA score of the less-severe group before and after stimulation were 32.0 (24.0 to 35.0) and 32.0 (25.0 to 35.0), respectively. This difference has not reached significant level (p = 0.317). Analysis of the MAS and the ART, however, did not show any significances between groups.
Conclusion: The rPMS over six hemiparetic shoulder-arm muscles could result in immediate improvement of motor function in patients with severe upper extremity paresis, but not spasticity or arm and reach test.

Keywords: magnetic stimulation, hemiparesis, upper extremity

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Introduction

Arm paresis is a common problem, but currently available treatments are not always satisfactory. Impaired upper extremity motor function and spasticity are two of the most common problems due to central nervous system pathologies. These lead to limited activities daily living (ADLs), increased pain symptom and poor quality of life.[1,2] Severe upper extremity paresis is also one factor indicating poor prognosis for motor recovery in stroke patients.[2] Even though there are many therapeutic interventions for rehabilitation of hemiparetic upper extremity, the recovery of upper extremity after severe stroke is in general less than satisfactory. Available supporting evidence for non-pharmacological treatments for this population were not strong.[1,3-5]

Repetitive peripheral magnetic stimulation (rPMS) to extremities is a novel therapy technique and may offer a new hope for better recovery as evidence were shown to improve motor recovery and to reduce spasticity.[3,6-8] Unlike direct electrical stimulation, magnetic pulses from rPMS could induce electrical current flow in deep neuromuscular tissues without stimulating the cutaneous nerve and receptors.[9,10] For this reason, it is possible to induce strong muscular contraction painlessly.[6,10] During alternating cycles of muscle contraction and relaxation numerous proprioceptive sensory receptors such as the muscle spindles, Golgi tendon organs, and other mechanoreceptors in the muscular and connective tissues can be strongly activated.[6,11] In addition to that, rPMS could also directly generate action potentials in the afferent nerve fibers. These two mechanisms combined, could generate a massive flow of afferent to the central nervous system.[6]

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Previous research has shown that rPMS could modulate frontoparietal cortical motor control network activation,[12] in which increased unilateral activation of supplementary motor area (SMA), premotor cortex (PM), and parietal area (PA) during hand movement were observed.

However, existing evidence to support effectiveness of rPMS are still limited. Even though some studies had shown reduction of spasticity and/or improved motor control after rPMS in various groups of patients, the Cochrane review in 2019 demonstrated little evidence for the use of rPMS in stroke rehabilitation, probably due to small number of high quality research with more subjects, inhomogeneity of population, and differences of stimulation parameters among the rPMS studies might be another factor that diluted the positive outcome of treatment such as spasticity reduction or improvement of motor control.[9]

A new and different stimulation protocol may improve the effectiveness of rPMS. Recovery of motor function tends to follow stereotypical stages as described by Brunnstorm and Twitchell that recovery of proximal muscle tends to precede distal control.[13] In addition, flexor and extensor synergies precede movement of synergistic pattern.[13] Despite of these facts, all rPMS studies of hemiplegic patients, which were included in the Cochrane reviews delivered magnetic stimulation only to wrist and/or hand muscles[7,12,14] except for one single case experimental study which explored effects of EMG triggered rPMS to flexors and extensor muscles of the affected forearm and upper arm.[15] For these reasons, these authors postulated that a rPMS protocol which treated all major shoulder and arm muscle groups within one treatment session, might be a more effective way to induce upper extremity motor recovery of stroke patients.

Therefore, the primary objective of this study was to compare the immediate effect of a novel protocol of rPMS in patients with subacute to chronic hemiparesis. The secondary objective was to evaluate correlation between upper extremity Fugl-Meyer motor (UE-FMA) score improvement after rPMS, change of spasticity, and change of arm reach test.

Methods

The study was approved by the Ethics Committee on Human Rights Related to Research Involving Human Subjects, Faculty of Medicine Ramathibodi hospital, Mahidol University (approval number: 2014/324).

Participants

Patients with hemiparesis from various causes at the Department of Rehabilitation Medicine, Ramathibodi Hospital who gave informed consent and met the following inclusion-exclusion criteria.

Inclusion criteria

- Hemiparetic upper extremity of any severity due to a central nervous system lesion for at least 6 weeks prior to the study
- Stabilized neurological conditions for 6 weeks
- Stable medical conditions

Exclusion criteria

- On pacemaker or metal implanted devices around the stimulation area including chest region.
- History of seizure.
- Unstable fractures of the paretic upper extremity.
- Poor communication and co-operation.
- Received chemodenervation, or adjustment of anti-spastic medication dosage within 3 months prior to the stimulation date.
- Limited active shoulder motion due to pain.

The rPMS protocol

The participants were seated in a chair. They were instructed to relax and not try to initiate or imagine any specific movement of the limbs during the stimulation. A motor threshold of each muscle or the lowest magnetic pulse intensity which induced a visible muscle contraction was separately identified for supraspinatus, infraspinatus, deltoid, biceps brachii, triceps brachii and pectoralis major muscles. In order to save time and reduce unnecessary maneuvering of the stimulation coil, and to stimulate wide area of the muscles as possible, a specific stimulation protocol was designed. The stimulating magnetic coil was alternately placed and moved slowly along three paths over the affected arm (Figure 1).

The first sweeping path started from medial to lateral part of pectoralis major, and then continued distally along the biceps muscle group (Figure 1A). The second path ran along the length of supraspinatus muscles above the spine of scapular, from the medial part just lateral to the medial border of scapular toward the acromial process, and then further down along the length of either lateral, anterior, or posterior deltoid muscles until the insertion point of deltoid muscles on the humerus (Figure 1B). The last sweeping path went along infraspinatus muscles, starting from a point just lateral to the medial border of scapula toward the posterior axillary line, and then down along the triceps muscles toward the olecranon (Figure 1C).

Magnetic pulse was generated with a Neuro MS/D model Magnetic Stimulation which were manufactured by Neurosoft, Ivanovo, Russia 2020. A figure eight magnetic coil model FEC-02-100-C with liquid cooling system was used for all stimulations. The stimulation was delivered at 20 Hz frequency with 4 seconds pulse width and 4 second pause in between (Figure 2). Intensity of stimulation was arbitrarily set at 120% intensity of motor threshold level, to prevent loss of muscle contraction in case a slight change of coil orientation or distance from skin surface during stimulation. Since two muscles were stimulated within the same sweep, the motor threshold was determined from the higher value between each pair of muscles within each stimulation group.

The speed of stimulation coil movement was such that each sweep be completed within approximately 6 seconds. Once a sweep was completed, then the coil was placed back

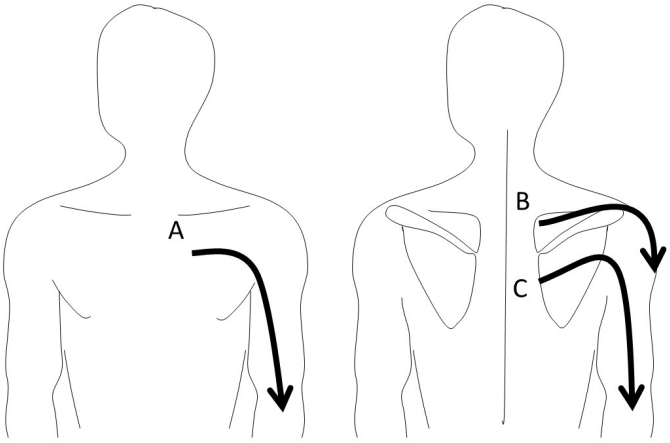

Figure 1. Three rPMS coil sweeping paths: A) pectoralis and biceps brachii, B) supraspinatus and deltoids, C) infraspinatus and triceps brachii

to restart next sweep without a pause. This continued for 4 minutes. Then the intensity was adjusted, and stimulation started again on the muscles of the next stimulation group. Each subject received 2,400 pulses in approximately 12 minutes treatment time (Figure 2).

Assessment tools

To assess the effect of rPMS, each patient underwent two assessments, before and immediately after the stimulation.

Assessment tools consisted of the motor part of upper extremity Fugl-Meyer Assessment (UE-FMA),[16,17] the modified Ashworth Scale (MAS),[18] and the arm reach test (ART). All assessments were done while the patients were in a seated position.

The FMA is a valid and reliable measurement of motor control impairment[16,17] which was designed according to brunnstorm's stage of motor recovery. For the purpose of this study, we only used scores from the UE-FMA, which has a highest possible maximum score of 66. A video recording of each patient during UE-FMA was scored by a blind assessor who was not aware which video was taken before or after therapy. Each of the 33 test items would be scored 0, 1, or 2 in the case that the patient was, completely not able to show the movement, partially do the movement, or show no impairment respectively. The total UE-FMA score was calculated from the sum of all test items.

The MAS is a valid and reliable tool for assessment of spasticity.[18,19] In order to test biceps muscle spasticity, the examiner, passively moves the elbow joint of the patient from fully flexed position to full extension over one second. Next, the elbow is brought from full extension to full flexion at the same speed to test for extensor spasticity. Scores of 0 up to 4 were given according to the well-known MAS scoring criteria.

The ART is a novel test invented by Wongphaet P and has been routinely used in the Rehabilitation Clinic at Ramathibodi Hospital as a tool for quick assessment of patient's ability to make upper extremity reaching motion free from primitive synergistic motor patterns. At the beginning of the test, a helper passively places the patient's hand to the patient's own xiphoid process. A vertical support was then applied to the patient's forearm to keep the elbow and hand at the same height as the patient's xiphoid process, but no assistance or resistance were given to the movement in horizontal direction. The patient was then instructed to move his/her hand as far as possible forward without help from the opposite hand. The horizontal distance in millimeters or centimeters from the xiphoid process to the most distal part of the hand was then measured with a plastic measuring tape. All these three assessments were carried out twice by Sukhumvada T without any warm up. Average values were calculated for further analysis. The data was recorded at one decimal place.

Statistical analysis

The statistical analysis was performed using Minitab 19 and IBM SPSS Statistics Version 18. An alpha level of .05 was chosen for all analyses. Because of ordinal scale quality of the outcome parameters, the Wilcoxon matched-pairs test was used for the comparison of the UE-FMA and the MAS scores before versus after stimulation. Spearman's rank correlation coefficient was applied for the analysis of correlation between change of MAS score against change of UE-FMA. Kendall tau-b was applied to calculate correlation between change of ART score against change of UE-FMA.

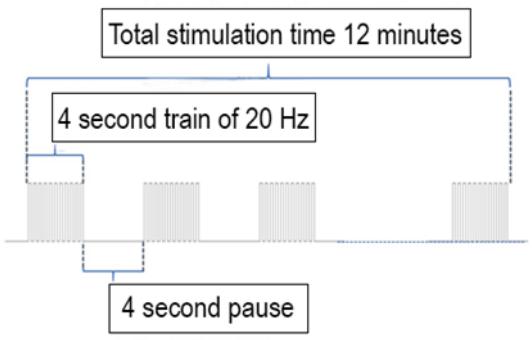

Figure 2. The rPMS stimulation pattern

These correlation coefficients of the whole patient group were calculated without separation between severity groups.

Results

Thirteen patients were included in the study. The clinical and baseline characteristics of the patients were demonstrated in Table 1.

Primary outcomes

The mean (SD) UE-FMA score before and after rPMS stimulation were 21.6 (10.5) and 23.3 (8.9), respectively. Wilcoxon matched-pairs test confirmed that the difference of UE-FMA between before and immediately after treatment reached statistical significance (p = 0.018). An additional subgroup analysis was done in order to see if severity of arm paresis impacted on responsiveness to therapy.

The median (Q1-Q3) UE-FMA score of the more-severe group, before and after the stimulation was 1.5 (9.3 to 13.3) and 16.0 (11.8 to 17.2), respectively. Wilcoxon matched-pairs test confirmed statistical significance at p value =0.027. On the other hand, the median (Q1-Q3) UE-FMA score of the less-severe group before and after stimulation was 32.0 (24.0 to 35.0) and 32.0 (25.0 to 35.0) respectively. This difference has not reached significant level (p = 0.317)

The increased UE-FMA score after stimulation was exclusively from the shoulder and arm motor section. No improvement of wrist, hand, or coordination sub section of FMA was seen in any subject. Individual UE-FMA scores of each subject before and after stimulation are shown in Figure 3.

The median (Q1-Q3) of MAS biceps and triceps muscles change in the more-severe group after stimulation was 0.0 (-0.6 to 0.0) and 0.3 (-0.6 to 1.1) and change of in the less-severe group was 0.0 (-5.0 to 5.0) and 0.0 (0.0 to 0.5). The mean (SD) of ART change of the more-severe and the less-severe groups after stimulation was 0.6 (5.9) cm and -1.1 (5.2) cm respectively. There was no statistically significant difference between all these parameters.

Table 1. Demographic data of all 13 participants

Age[1] (years)	54.23 (14)
Sex[2]	
Male	10 (77)
Female	3 (23)
Pathology	
Stroke	11 (85)
Traumatic brain injury	1 (8)
Progressive multifocal leukoencephalopathy	1 (8)
Seakness	
Right	5 (38)
Left	8 (62)

[1]Mean (SD), [2]number (%)

Secondary outcomes

The number of patients with unchanged, increased or decreased MAS of biceps and triceps muscles are shown in Table 2. Neither treatment nor severity group appeared to correlate with change of MAS. Spearman's correlation coefficient showed no significant correlation between UE-FMA change and MAS change of biceps and triceps muscles with correlation coefficient -0.77 (p = 0.81) and 0.31 (p = 0.30), respectively.

The difference of ART score showed no significant correlation against change of UE-FMA of the whole group at coefficient = 0.07 (p = 0.77). This lack of correlation can be observed from the scatter plot in Figure 4.

Table 2. Numbers of patients with changes in modified Ashworth Scale (MAS) scores of biceps and triceps muscles after stimulation

	MAS change (before-after)		
	Decrease (n)	Same (n)	Increase (n)
Biceps brachii			
Less severe[7]	3	2	2
More severe[6]	0	4	2
Triceps brachii			
Less severe[7]	2	4	1
More severe[6]	3	1	2

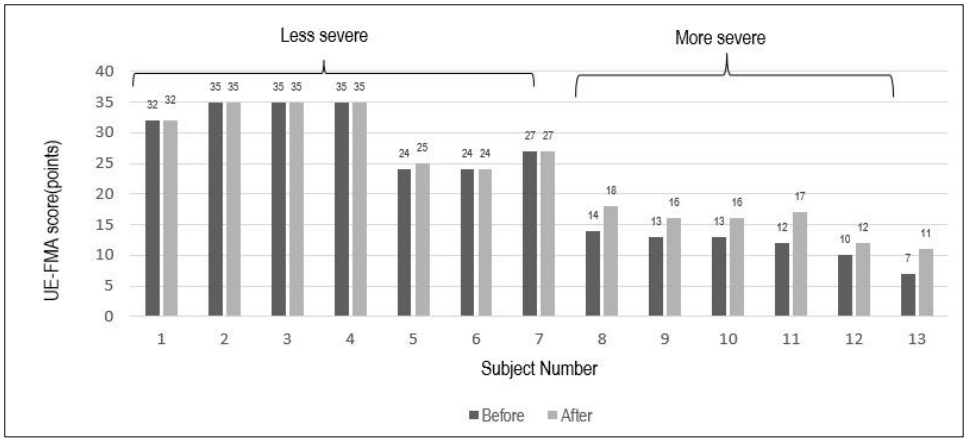

Figure 3. Individual UE-FMA scores of each subject before and after stimulation sorted according to initial FMA scores with the more severely affected cases to the right side.

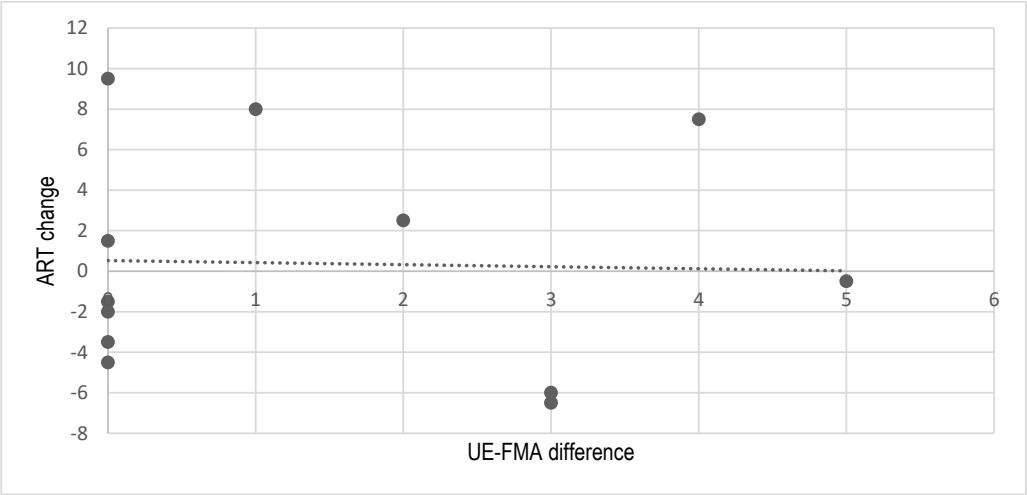

Figure 4. Scatter plot between ART changes versus differences of UE-FMA after stimulation

Discussion

Intensive and variable neural afferent signals, which resulted from this unique protocol of proximal upper extremity rPMS, as described in this research, has a potential to be an effective facilitator of motor recovery. This is the first rPMS study in hemiparetics, which specifically targets proximal upper extremity muscles. The target of rPMS in this study involved not only biceps and triceps muscles like many other previous studies, but also larger numbers of proximal muscles such as pectoralis major, supraspinatus and infraspinatus muscles which were not typical targets of previous studies[7,11,12,14] Movement of magnetic coil during treatment is another important factor because it increased areas of muscle tissues being stimulated. High intensity and variability of afferent input generated through such a stimulation technique is likely much greater than in other studies which stimulated only one or two distal muscle groups without moving the magnetic coil. This could possibly explain the immediate improvement of UE-FMA scores after rPMS in the current study.

Despite the improved UE-FMA score, we have found neither improvement of MAS nor ART. This finding is compatible with a previous study, which showed no change of neurophysiological markers of spasticity such as H-reflex and F-wave and Achilles tendon reflex after rPMS.[8] We speculate that improvement of FMA and spasticity after rPMS may indeed be independent from each other.

Both UE-FMA and ART are measurements of motor impairments. However, these measure different aspects of upper extremity functions. The ART measures only the ability to reach the arm forward away from the chest, which is considered a movement not within the primitive motor synergy pattern. On the other hand, the UE-FMA measures all types of motor patterns. Therefore, the lack of improvement in ART score, despite the improved UE-FMA, suggests that the improvement was likely due to increased ability to move within the primitive motor synergy pattern. Patients gained higher UE-FMA score after rPMS, because they could make bigger and more complete flexor synergy and extensor synergy pattern after rPMS. None of them showed increased selective single joint motor control ability.

So, why did more severely hemiparetic patients respond better to rPMS to proximal muscles than the less severe patients? Motor evoked response to cortical TMS studies has demonstrated that most, if not all of the hemiparetic patients such as the more severe group in this study, sustained a total loss of corticospinal tract on the affected side.[21-24] It is well known that this structure is essential for recovery of meaningful hand functions and perhaps as well as an ability to perform segmented control of a single joint motion.[23,25] All the observed increase of UE-FMA score after rPMS in this study were exclusively from the change of proximal part, (shoulder and arm) motor score. Therefore, the better recovery of UE-FMA scores in the more severe group as found here suggests that the improved function after rPMS may not depend on corticospinal integrity.

In this study we classified patients by their severity according to findings of a study of Woytowicz et al. which identified four distinctive subgroups among 247 subjects with chronic stroke who share a common level of deficit severity and a common residual motor pattern.[20] The FM score range of the groups were: severe (0-15), severe-moderate (6-34), moderate-mild (35-53), and mild (54-66). When such 4-group classification was used, no overlapping of severity group which was assigned by cluster analysis and severity group which was assigned according to UE-FMA score cut points were observed. To avoid confusion with the more commonly used three group classification, in which patients were separated into mild, moderate and severe according to their UE-FMA scores, the patients in this study were divided into two groups based on the pre-stimulation Fugl-Meyer scores. Those with score equal or more than 16, and those with score less than 16 were classified as less-severe and more-severe, respectively[20]

Even without active motor training, sensory stimulation alone can induce long term potentiation (LTP) of the neuron in the central nervous system.[26] Beauliu has proposed that the massive repetitive non-nociceptive proprioceptive afferent from movement related sensors could possibly facilitate greater activation of existing motor related neuronal circuits in recovering stroke patients.[6] We therefore, hypothesized that increased activation of the non-affected hemisphere[26] and/or subcortical motor centers[26-28] are potential contributors to motor recovery of proximal UE motor control in patients with severe UE paresis in this study. This difference of responsiveness to rPMS between the two severity groups, may explain the mixed results of previous rPMS studies in which analysis were not made separately for patients with different severity of arm paresis.[3]

With limited number of subjects, only imprecise estimation of effect can be expected. For example, a false-positive or overestimation of association can be produced.[29] Therefore, firm conclusions cannot be made. To confirm the finding of this small study with no control group, a future prospective randomized controlled trial with adequate number of subjects is needed. Such study should be designed to avoid mixture of different diagnosis and severity of arm paresis among the subjects. A longer treatment and follow up period should also be considered, to study the long-term effects of rPMS in a group of patients with a more homogenous diagnosis e.g., stroke only population.

Conclusion

An immediate effect of rPMS on proximal muscle group could improve motor impairment of hemiparetic patients with more severe upper extremity paresis but not in the less severe group.

Disclosure

The authors declare no conflict of interest with any financial organization regarding the material discussed in the manuscript

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Original Article

A Cross-Sectional Study on Prevalence of Cardiovascular Risk Factors in Persons with Spinal Cord Injury

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ABSTRACT

Objectives: To describe the prevalence of cardiovascular risk factors (dyslipidemia, diabetes, central obesity and smoking) and the current management in persons with spinal cord injury (SCI).
Study design: Cross-sectional study.
Setting: Spinal cord injury rehabilitation clinic of a university hospital.
Subjects: A total of 205 persons with SCI participated in this cross-sectional study between June 2018 and May 2019.
Methods: A self-constructed data collection form was administered via face-to-face interviews. Medical information was extracted from medical records and central obesity was determined by measuring the waist circumference in a supine position, at a point immediately below the lowest rib.
Results: Majority of the participants (91.0%) had at least one cardiovascular risk factor. Dyslipidaemia was the most common cardiovascular risk factor (85.4%), followed by central obesity (59.0%), diabetes (20.5%), and smoking (12.2%). This study revealed that up to 44.0% of the study population did not receive any intervention for dyslipidaemia. Participants who used wheelchairs, motorized or manual, as their main mode of mobility, were three times more likely to have low HDL compared with participants who walked (OR 3.46, 95% CI 1.3-9.4 and OR 3.09, 95% CI 1.4-7.1 respectively).
Conclusion: Cardiovascular risk factors are prevalent among SCI population. Dyslipidaemia was the most common health hazard and approximately one-third of them did not receive any intervention. Users of manual wheelchairs, self-propelled or pushed by others, were three times more likely to have low HDL compared with those who walk.

Keywords: cardiovascular risk factor, spinal cord injury, cross-sectional study, obesity

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Introduction

Due to the advancement of medical care, persons with spinal cord injury (SCI) can experience a longer lifespan but are at a higher risk of contracting cardiovascular-related diseases, which include dyslipidaemia, hypertension, diabetes, smoking and obesity.[1] The leading cause of mortality in persons with chronic SCI is the cardiovascular disease (CVD).[2] Persons with SCI have a higher risk of developing cardiovascular risk factors and the onset is earlier compared with the able-bodied population.[3]

Muscle atrophy and obesity due to paralysis and inactivity in SCI contribute to the development of cardiovascular risk factors.[4] At this point of time, there are no established guidelines available for managing cardiovascular risk factors in individuals with SCI. Muscle atrophy and obesity due to paralysis and inactivity in SCI contributed to the development of cardiovascular risk factors.[4] Studies of the relationship between a lack of physical activity and development of CVD have shown mixed results; the optimal type, intensity and adequate duration of exercises to reduce CVD have yet to be determined.[5] Evidence of an independent risk factor linking to SCI for the development of cardiovascular diseases has been inconsistent. Some studies reported mixed or non-significant associations between SCI characteristics and cardiovascular risk factors.[6,7] Recent studies were done in populations with different dietary and activity norms, which may not be applicable to the local Malaysian population.[1,6,7]

In Malaysia, CVD is the leading cause of death, for both men and women. The local registry of CVD showed that most patients (96.8%) have at least one of the established CV risk factors - hypertension (65%), dyslipidemia (37%) and /or diabetes (46%).[8] Thus, this study aims to investigate and describe the following aspects: the prevalence of cardiovascular risk factors, namely diabetes, smoking, central obesity and dyslipidaemia; the difference in prevalence between various SCI characteristics; as well as current management of dyslipidaemia among persons with SCI. The results of this study could help plan or prioritize future health interventions, and audit the current management to improve the existing practices or develop guidelines if applicable. At this juncture, there are no established guidelines available for managing cardiovascular risk factors in individuals with SCI.

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Methods

Study design

This cross-sectional study was conducted at the University Malaya Medical Centre (UMMC), which is a tertiary educational research hospital. It is situated in Kuala Lumpur, the capital of Malaysia and provides a comprehensive range of in- and out-patient SCI rehabilitation services.

This study was approved by University Malaya Medical Centre Medical Research Ethics Committee (Approval number: 201826-6010).

Sample size

This study utilizes a universal sampling method by including all the patients who had attended the SCI out-patient rehabilitation clinic throughout the study period (June 2018 and May 2019). A sample size of 216 participants from the expected population size of 500 were required to achieve the 95% confidence level, with a 5% margin of error. A total of 205 persons with SCI participated in this cross-sectional study.

Participants

Inclusion criteria

Individuals with SCI of at least one-year duration, aged more than 18 years old, with traumatic or non-traumatic SCI of all levels, and classified as ASIA Impairment Scale (AIS) A, B, C and D were included in this study.

Exclusion criteria

Individuals with severe traumatic brain injury, metastatic spine disease, and congenital spine disease were excluded in this study.

Data collection

This study used a self-constructed three-part data collection form. The first part contained demographic data (age, gender, race, level of education, and family history of cardiovascular disease). The second part consisted of SCI characteristics (level and severity of injury, aetiology of injury, duration of injury, and main mode of mobility). The third part consisted of comorbidities prior to sustaining SCI, lipid and blood glucose profile parameters, management of dyslipidaemia (if any), smoking history, and measurement of waist circumference. The demographics, SCI characteristics, and morbidity data were collected from the medical records whilst data of family history and mobility were obtained via face-to-face interviews.

Participants were considered to have dyslipidaemia if they had abnormal values of blood lipids within the last one year and/or were taking lipid-lowering drugs. This study used the Malaysian Clinical Practice Guidelines for Dyslipidaemia[8] and Diabetes Mellitus Type 2[9] to determine the cut-off points for diagnosing dyslipidaemia and diabetes. The following lipid levels were used to diagnose dyslipidaemia: total cholesterol > 5.2 mmol/L; high density lipoprotein cholesterol (HDL-C) < 1 mmol/L (males), and < 1.2 (females); triglycerides (TG) > 1.7 mmol/L, and low density lipoprotein cholesterol (LDL-C) > 3.4 mmol/L.[8] Diabetes is diagnosed when venous plasma glucose is more than 7.0 mmol/L (fasting) and > 11.1 mmol/L (random).[9]

The waist circumference, in centimeters (cm), was measured in supine position immediately below the lowest rib[10] after normal expiration. The cut-off point of obesity was taken as ≥ 90 cm in males and ≥ 80 cm in females, according to the WHO guidelines.[11] Lipid profile parameters, glucose level and management records of dyslipidaemia were extracted from the electronic medical records. In the event of no recent blood investigations taken in the last 12 months, the investigator ordered new blood investigations.

Data analysis

Descriptive analyses of categorical variables were expressed in frequencies and percentages. The multiple logistic regression was used to test the relationship between age, level and severity of injury, duration of injury, aetiology of injury, and mode of mobility, with respect to cardiovascular risk factors. Data were analyzed using the SPSS version 24.

Results

A total of 205 persons with SCI participated in this study; the demographic characteristics are presented in Table 1. The mean (SD) age was 51.3 (15.6) years with majority of

Table 1. Participants' demographics and spinal cord injury characteristics

Demographic data	n (%)	Mean (SD)
Age (years)	20-82	51.3 (15.6)
Gender		
Male	147 (71.7)	
Female	58 (28.3)	
Race		
Malay	67 (32.7)	
Chinese	103 (50.2)	
Indian	34 (16.6)	
Others	1 (0.5)	
Education level		
Primary	39 (19.0)	
Secondary	110 (53.7)	
Higher	56 (27.3)	
Family history of cardiovascular disease		
Yes	62 (30.2)	
No	143 (69.8)	
Level and severity of injury		
Complete tetraplegia	19 (9.3)	
Incomplete tetraplegia	43 (21.0)	
Complete paraplegia	56 (27.3)	
Incomplete paraplegia	87 (42.4)	
Aetiology of injury		
Traumatic	127 (62.0)	
Non-traumatic	78 (38.0)	
Duration of injury (range in years)	1-47	11 (10)
Mode of mobility		
Motorized/ pushed by others	37 (18.0)	
Manual wheelchair	99 (48.3)	
Walking	69 (33.7)	

Table 2. Prevalence of cardiovascular risk factors (n = 205)

Risk factor	Yes n (%)	No n (%)
Dyslipidaemia	175 (85.4)	30 (14.6)
High total cholesterol	45 (22.0)	160 (78.0)
High triglyceride	54 (26.3)	151 (73.7)
Low HDL	96 (46.8)	109 (53.2)
High LDL	100 (48.8)	105 (51.2)
Central obesity	121 (59.0)	84 (41.0)
Diabetes	42 (20.5)	163 (79.5)
Smoking	25 (12.2)	180 (87.8)

HDL, high density lipoprotein; LDL, low density lipoprotein

the participants being male (71.7%), and more than half of them received secondary school education (53.7%). Most of the participants (69.8%) had no family history of cardiovascular diseases. Majority of the participants had traumatic SCI (62%) and the most common impairment was incomplete paraplegia (42.4%). The mean (SD) duration post injury was 11 (10) years. The most common mode of mobility was the self-propelled manual wheelchair (48.3%).

Prevalence of cardiovascular risk factors and management of dyslipidaemia are described in Table 2 and Table 3. Majority of the participants (91%) had at least one cardiovascular risk factor; 29% had only one risk factor, 39% had two, 21% had three, and 2% had four cardiovascular risk factors. Overall, the most prevalent cardiovascular risk factor was dyslipidaemia (85.4%). Among those with dyslipidaemia, 48.8% had high LDL, and 46.8% had low HDL. Although dyslipidaemia was common, 44.0% of the study participants did not receive any intervention.

Participants who used motorized wheelchairs or manual wheelchairs pushed by others and self-propelled manual wheelchairs were three times more likely to have low HDL compared with those who walk, with OR 3.46, 95% CI 1.27-9.43, and OR 3.09, 95% CI 1.35-7.08 respectively. There was no difference in the prevalence of diabetes, smoking, waist circumference, high LDL between the participants with paraplegia and tetraplegia, complete and incomplete injury, traumatic and non-traumatic SCI and duration of injury (Table 4 and Table 5).

Table 3. Management of dyslipidaemia in participants (n = 175)

Management	n (%)
Dietician referral	19 (10.8)
Pharmacology	49 (28.0)
Dietician and pharmacology	30 (17.2)
None	77 (44.0)

HDL, high density lipoprotein; LDL, low density lipoprotein

Discussion

This study showed a high prevalence of cardiovascular risk factors among individuals with spinal cord injury; dyslipidaemia (high LDL and low HDL) was the most common risk factor followed by central obesity, diabetes, and smoking. The prevalence found in this study was higher than that of the general population in Malaysia. According to the National Health and Morbidity Survey (NHMS) Malaysia 2015,[12] 63% of the adult population had at least one cardiovascular risk factor. Our finding is consistent with the study by Wahman et al.[1] in which 97% of the study population had at least one risk factor, and 87% had two or more cardiovascular risks. The identified risk factors were dyslipidaemia, hypertension, diabetes, obesity, and smoking.

The current study showed that SCI characteristics such as level of injury, severity of injury, aetiology of injury and

Table 4. Multiple logistic regression tested the relationship between level and severity of injury, duration of injury, aetiology of injury and mode of mobility with dyslipidaemia

	Dyslipidaemia			
	Total cholesterol	Triglyceride	HDL	LDL
Age	0.20 0.97 (0.94-0.99)	0.61 0.99 (0.97-1.01)	0.10 0.98 (0.96-1.00)	0.02 0.97 (0.95-0.99)
Level and severity of injury				
Incomplete para (ref)	0.14	0.13	0.27	0.82
Complete tetra	1.98 (0.36-10.81)	3.02 (0.74-12.25)	1.45 (0.40-5.25)	1.45 (0.40-5.21)
Incomplete tetra	0.32 (0.09-1.06)	1.71 (0.68-4.30)	1.70 (0.74-3.88)	0.82 (0.37-1.81)
Complete para	1.63 (0.63-4.21)	2.82 (1.12-7.09)	2.08 (0.92-4.68)	1.15 (0.53-2.52)
Aetiology of injury			0.61	0.35
Non-traumatic (ref)	0.30	0.75		
Traumatic	1.52 (0.68-3.38)	1.12 (0.53-2.36)	1.18 (0.61-2.30)	1.35 (0.72-2.55)
Duration of injury	0.15	0.06	0.01	0.97
Mode of mobility	0.97 (0.93-1.01)	0.96 (0.92-1.00)	0.95 (0.92-0.99)	1.00 (0.97-1.03)
Walking (ref)	0.23	0.96	*0.01	0.20
Motorized/ pushed by others	0.24 (0.47-1.23)	0.93 (0.30-2.87)	3.46 (1.27-9.43)	0.42 (0.15-1.15)
Manual wheelchair	0.77 (0.30-1.99)	1.08 (0.42-2.80)	3.09 (1.35-7.08)	0.92 (0.43-2.00)

p-value, OR (95% confidence interval)

HDL, high density lipoprotein; LDL, low density lipoprotein; para, paraplegia; tetra, tetraplegia

Table 5. Multiple logistic regression tested the relationship between level and severity of injury, duration of injury, aetiology of injury and mode of mobility with diabetes, smoking and central obesity

	Diabetes	Smoking	Central obesity
Age	0.01	0.17	0.05
	1.04 (1.02-1.07)	0.97 (0.95-1.00)	1.02 (1.00-1.04)
Level and severity of injury	0.10	0.79	0.70
Incomplete para (ref)	0.19 (0.03-1.21)	0.78 (0.71-8.64)	1.26 (0.35-4.52)
Complete tetra	0.39 (0.14-1.07)	1.59 (0.40-6.38)	1.19 (0.52-2.74)
Incomplete tetra	0.43 (0.16-1.19)	1.52 (0.51-4.50)	0.70 (0.31-1.56)
Complete para			
Aetiology of injury			
Non-traumatic (ref)	0.60	0.23	0.02
Traumatic	0.81 (0.38-1.75)	1.97 (0.65-5.91)	0.44 (0.23-0.87)
Duration of injury	0.47	0.17	0.51
Mode of mobility	1.01 (0.97-1.05)	1.03 (0.98-1.07)	1.01 (0.97-1.04)
Walking (ref)	0.34	0.18	0.22
Motorized/ pushed by others	1.56 (0.50-4.89)	0.27 (0.02-2.86)	0.46 (0.17-1.23)
Manual wheelchair	0.68 (0.27-1.68)	1.92 (0.53-6.96)	1.01 (0.45-2.26)

p-value, OR (95% confidence interval)

Para, paraplegia; tetra, tetraplegia

duration post-SCI do not lead to a higher number of cardiovascular risk factors. As such, our findings do not support incorporating SCI status as an independent variable for development of cardiovascular risk factors. Saunders et al.6 and Bauman et al.[13] reported that diabetes, hypertension and dyslipidaemia were associated with injury level and ambulatory status. An evidence report written by Wilt et al.[14] stated that the link between spinal cord injury and the risk of carbohydrate abnormalities was weak, and people with SCI may not be at a greater risk compared with those with able bodies. Hence, the existing guidelines for assessing and managing cardiovascular risk factors in able-bodied individuals should be applicable to persons with SCI as well.

Another important finding of this study is the relationship between mode of mobility and low HDL. This study showed that participants who self-propel their manual wheelchairs have the similar risk of low HDL compared with those who use motorized wheelchairs or manual wheelchairs pushed by others. HDL is known to be an independent risk factor for developing cardiovascular diseases.[15] Manual wheelchair propulsion is often advocated as a form of physical activity to reduce cardiovascular risks, and the finding from this study would have an influence on how clinicians should advise their patients. A compendium examining energy expenditure in wheelchair-related physical activities among wheelchair users showed these comparative figures: propelling a wheelchair on a flat surface at 2 mph or 53.6 m/min has a metabolic equivalent of task (MET) amounting to 3.3 kcal/kgh, while an able-bodied person walking at the same speed has a MET of 2.8 kcal/kgh.[16] However, another study reported that the average speed of wheelchair propulsion among paraplegics was 29.2 m/min, which is considered a slow pace.[17] We did not measure the speed of wheelchair propulsion among manual wheelchair users in this study, but it can be postulated that the speed of propulsion was inadequate to achieve the target heart rate required for reducing cardiovascular risks. Individuals with SCI who normally walk have a higher energy expenditure rate compared with their able-bodied peers; the mean energy expenditure per meter (EE/m) for the SCI participants is 0.33 (± 0.29) calories compared with 0.08 (± 0.02) calories for the able-bodied participants.[18]

This study utilized waist circumference instead of body mass index (BMI) to measure central obesity, which has been associated with an increased risk of cardiovascular diseases.[19] Waist circumference was found to be a better marker for obesity than BMI as the latter can underestimate obesity of a person in the SCI population.[20] This is because individuals with chronic SCI have greater fat mass and less fat-free mass per unit BMI when compared with age-matched able-bodied control subjects.[21,22] Here is another possible reason why BMI tends to underestimate obesity of a person in SCI population: it is difficult to measure a wheelchair-dependent person's height accurately. Ideally, a standing height should be obtained, but this may not be possible for a person with SCI population. Some studies use the subject's recall of height, which is not recommended as it leads to bias and errors.[23] Measuring the length can also be done but it can be quite challenging for persons of the SCI population with limb contractures. The use of waist circumference measurement to estimate central obesity of a person in the SCI population also has its own challenges. There was no standardized method as how to measure the waist circumference of a person in the SCI population. Waist circumference of a person in the SCI population was measured in supine position, but different locations of the body were used in different studies: directly below the lowest rib, narrowest waist, immediately above the iliac crest, and midpoint between the lowest rib and the iliac crest.[7,8,23,24] Measurement taken directly below the lowest rib was the best, due to ease of measuring and it eliminates errors caused by abdominal distension and bowel

impaction, which are common issues of persons with SC.[10] A study by Onat A et al.[19] showed that visceral adipose tissue was found to be higher in people of the SCI population compared with that of the normal able-bodied individuals with the same waist circumference, based on the computed tomography (CT) scan. Thus the cut-off point for waist circumference of persons in the SCI population may not be the same as that of individuals in the non-SCI population.

There are several limitations in our study. First, we did not identify patients who were previously diagnosed with dyslipidaemia, but achieved normal blood lipid levels with non-pharmacological interventions during the recruitment period. Second, there were no standardized methods to measure the waist circumference of a person with SCI or a specific location of the body around which a measurement can be taken. Third, there was no preceding definition of waist circumference for the Asians from the SCI population; as such, prevalence of obesity could be underreported. Finally, we did not take into consideration the level of physical activity, especially time and intensity of using a manual wheelchair of each participant. Thus, it is still possible that different ways of using a manual wheelchair could potentially modify cardiovascular risks in people with SCI.

Our study findings may have some major implications on how we should manage cardiovascular risks in people with SCI. This research does not support the idea of incorporating SCI status as an independent variable for developing cardiovascular risks. Therefore, the existing guidelines for assessing and managing cardiovascular risk factors in able-bodied individuals should be applicable to persons with SCI as well. This study emphasizes that patients with SCI are encouraged to explore opportunities for increasing their physical activities; those who have the potential to walk should be assisted to do some walking, and as the walking ability improves it may eventually become the main mode of mobility. Propelling wheelchair can be physically demanding; hence, there is room for future research to investigate these areas: the intensity and duration of wheelchair propelling, the types of manual wheelchairs, and effects of wheelchair-related activities on cardiovascular disease risks.

In conclusion, this study reveals that cardiovascular risk factors were prevalent among people of the SCI population. Dyslipidaemia was the most common risk factor, but more than one-third of them were not on any intervention. Users of manual wheelchairs, regardless of the operating manners--self-propelled or pushed by others, had low HDL compared with those whose main mode of mobility is walking.

Disclosure

The authors declare that there is no conflict of interest.

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Nil

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Original Article

Severity of Erectile Dysfunction in Thai Male Patients with Spinal Cord Injury

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ABSTRACT

Objectives: To examine severity of erectile dysfunction (ED) among Thai male patients with spinal cord injury (SCI) and relevant clinical data.
Study design: A retrospective study.
Setting: Sexual clinic, Sirindhorn National Medical Rehabilitation Institute, Nonthaburi, Thailand.
Subjects: Sixty-two Thai male patients with traumatic SCI.
Methods: The participants' age, duration and level of SCI, relationship status before and after injury, family planning particularly their child wanting, bladder management and catheterization technique, the 5 International Index of Erectile Function (IIEF-5), frequency of sexual intercourse, history of taking oral medications for ED, and ejaculation were retrieved from their medical records.
Results: The mean age was 34 years old and duration of SCI was 50 months. Among all, 60% was complete paraplegia, 16% incomplete tetraplegia,13% complete tetraplegia and 11% incomplete paraplegia; 77% had partners. Regarding bladder management, 11 (36%) used indwelling urinary catheter and had no sexual activity whereas 51 (64%) managed the bladder by themselves and 31 (61%) had regular sexual intercourse. Of those having regular sexual intercourse, 42% used phosphodiesterase type 5 (PDE5) inhibitors. Based on their IIEF-5 scores, 18 patients (35%) with regular sexual intercourse and not taking PDE5 inhibitor, were classified into 5 different severity levels: mild erectile dysfunction (33%), followed by mild to moderate (22%), moderate (22%), severe (17%) and no ED (5%). The prevalence of ED in sexually-active patients was 94% (17 out of 18 patients).
Conclusion: About 35% of Thai SCI men attending a sexual clinic were sexually active without need of PDE5 inhibitor; and among them, one-third had mild erectile dysfunction. All using indwelling urinary catheter had no sexual activity. Preserving their intimate relationship and the use of PDE inhibitors might help impel their sexual activity.

Keywords: spinal cord injuries, erectile dysfunction, prevalence, sex, male

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Introduction

Spinal cord injury (SCI) is a destructive spinal cord that contusion is the most common gross finding.[1] SCI can be categorized into traumatic and non-traumatic according to the causes of injury. Traumatic SCI can be caused by spinal fracture or dislocation from trauma, whereas spinal tumor, vascular ischemia, spinal stenosis, congenital or inflammatory diseases can cause non-traumatic SCI.[2] The incidence of traumatic SCI in Thailand between the years 1989 and 1994 was 23 cases per million per year which were mostly caused by road traffic accidents followed by falls.[3] Between 2008 and 2017, another study found that the average age of Thai patients with SCI was 45.1 years and 67.5% of them were male.[4] The most common site of their injury was cervical spine (54.2%), average length of stay was longest (96.2 days) in cervical complete SCI and mortality rate was 0.4%.[4] Complete injury is the most common type of severity and has the least neurological recovery rate.[3-5] In addition to the ambulation problems following SCI, there are many secondary long-term medical complications such as autonomic dysreflexia, orthostatic hypotension, impaired respiratory function, deep vein thrombosis, bowel and bladder dysfunction, recurrent urinary tract infections, neuropathic arthropathy, osteoporosis, bone fractures, neuropathic pain, spasticity and pressure sores.[6-8] Sepsis from pressure sores was found to be the most common cause of death among SCI patients.[9]

Infertility is also another important problem caused by SCI especially in male patients as inflammation and endocrine changes after injury can affect their spermatogenesis, erectile function and semen ejaculation.[10,11] It was found that only 10% of SCI male patients were able to have children without the help of assisted reproductive technology.[12] The impairment of neurological function can also cause psychogenic and/or reflexogenic erectile function based on level of injury. The reflexogenic erection was usually preserved when the lesion was found above the sacral cord.[13] A previous study

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reported that 82% of SCI patients could achieve some types of erection.[14] However, only 61% of them succeeded in having sexual intercourse, 38% had no sexual activity, and only 11% could ejaculate or reach orgasm.[14] Another previous survey study reported that regaining sexual function was the highest concern for quality of life among both male and female paraplegics, whereas arm recovery function was mostly important for quadriplegics.[15] In Thailand, a study of erectile dysfunction (ED) in SCI patients by Moonla et al. reported that only 28.6% had sufficient erection for sexual intercourse whereas 62.5% of them still had sexual desire.[16] This is in line with Sudsaneha et al. reporting that 84% of Thai chronic SCI men had some degree of ED.[17]

The International Index of Erectile Function (IIEF) is the standard diagnostic tool for ED assessment. The original version provides 15 questions divided into five sexual function domains: erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction.[18] The modified 5-item version of the International Index of Erectile Function (IIEF-5) focuses on erectile function and intercourse satisfaction, especially in men with regular sexual intercourse.[19] In men who reported having had no sexual activity, the score range, 5 to 7, for the severest category of ED will change to 1 to 7. This IIEF-5 has 98% sensitivity and 88% specificity in detecting ED[19] and the Thai version of IIEF-5 (IIEF5-Th) has high validity and reliability for ED analysis in Thai males.[20]

The mission of the sexual clinic at the Sirindhorn National Medical Rehabilitation Institute, Nonthaburi, Thailand is to provide family counseling focusing on sexual behavior and erectile function using multidisciplinary team including rehabilitation physicians (physiatrists), rehabilitation counselors and nurses. The Thai IIEF-5 was used for ED assessment in all male SCI patients at this clinic at their first visit and every follow-up session. However, few studies of this issue in Thailand has been conducted and none of them using the Thai IIEF-5 for ED evaluation.[16,17] Thus, the purposes of this research were to examine severity of erectile dysfunction among Thai male SCI patients in relation to their relevant history and IIEF-5 score.

Methods

This study was approved by the Human Research Ethics Committee, Faculty of Medicine, Ramathibodi Hospital, Mahidol University and the Sirindhorn National Medical Rehabilitation Institute. Informed consent form was waived as this is a retrospective study and the data were retrieved from patients' history files at the clinic.

Participants

Sixty-two male patients, aged over 15 years old, with SCI who came to the sexual clinic at the Sirindhorn National Medical Rehabilitation Institute (SNMRI), Nonthaburi, Thailand, for family counseling between January 2015 and October 2018 were recruited in this study. Almost all of the participants were sent to this clinic by other physicians when they were ready for sexual rehabilitation after their complete general SCI rehabilitation program. Male patients with other medical problems with erectile dysfunction were excluded.

The participants' history in terms of age, onset and level of injury, relationship status, family planning particularly their child wanting, bladder management and catheterization technique, IIEF-5 score, frequency of sexual intercourse, history of oral medications for erectile dysfunction, and ejaculation, meaning patients can ejaculate in orgasmic phase, were retrieved from their first medical files. The patients interested in assisted reproductive technology were recorded as "fertility treatment requirement", while those reporting "in relationship" or "married" were classified as "partner". These demographic and clinical data were considered characteristics of ED patients in this study and the sum IIEF-5 score of each patient was used to classify them into different levels of severity.

Statistical analysis

Statistical analysis was performed using SPSS software version 18.0. The demographic and clinical data were compared among and between groups of severity by using ANOVA, Chi-square test and student's t-test. Statistical significance was defined by $p < 0.05$.

Results

The demographic and clinical data of the overall 62 Thai male SCI patients are displayed in Table 1. The mean patient's age was 34 years old (range 16-57) and duration of injury was 50 months (range 4-187). There were 60% complete paraplegia, 16% incomplete tetraplegia,13% complete tetraplegia and 11% incomplete paraplegia. It was found that 48 out of 62 patients (77%) had partners but only 31 (50%) had regular sexual intercourse.

Table 1. Demographic data of all 62 Thai male SCI patients

Age (years)[1]	34 (9.4)
Onset of SCI (months)[1]	50 (52)
Level of paralysis[2]	
- Complete paraplegia	37 (60)
- Incomplete paraplegia	7 (11)
- Complete tetraplegia	8 (13)
- Incomplete tetraplegia	10 (16)
Relationship status	
- No partner	14 (23)
- Partner	48 (77)
Parenting children	22 (35)
Smoking	20 (32)
Using indwelling urinary catheter	11 (36)
PDE5 inhibitor usage	14 (23)
Regular sexual intercourse	31 (50)
Ejaculation	8 (13)
Fertility treatment requirement	31 (50)

[1]Mean (SD), [2]number (%)

SCI, spinal cord injury; PDE5, phosphodiesterase type 5

The comparison between regular and no sexual intercourse in 51 patients who self-managed bladder is summarized in Table 2. Eleven SCI patients who used indwelling urinary catheter were not included due to no sexual activity from bladder issues. Statistically significant differences between these two groups were found in terms of relationship status ($p < 0.001$) and the use of PDE5 inhibitors ($p = 0.004$) while no statistical differences were found among other characteristics. 97% of patients who had regular sexual intercourse were in relationship, whereas only 50% in patients without sexual intercourse had partner. In addition, 39% had no sexual intercourse, 35% had sexual intercourse without use of PDE5 inhibitor, and 26% took PDE5 inhibitors (see Figure 1).

Table 3 compares the characteristics of IIEF-5 severity groups in 31 SCI patients with regular sexual intercourse. There were no statistically significant differences in terms of age, duration of SCI, level of paralysis, relationship status, parenting children, smoking, PDE5 inhibitor usage, ejaculation and fertility treatment requirement among these 5 groups of patients. The average sexual intercourse per month was lowest (1-2 times per month) in severe group.

Table 2. Characteristics comparison between regular and no sexual intercourse in 51 self-managed bladder patients

	Sexual intercourse		*p*-value
	Regular (n = 31)	No (n = 20)	
Age (years)[1]	34 (7.9)	33 (9.6)	0.719
Duration of SCI (months)[1]	67 (59.2)	39 (43.5)	0.206
Level of paralysis[2]			0.252
- Complete paraplegia	21 (68)	10 (50)	
- Incomplete paraplegia	4 (13)	2 (10)	
- Complete tetraplegia	1 (3)	4 (20)	
- Incomplete tetraplegia	5 (16)	4 (20)	
Relationship status			< 0.001
No Partner	1 (3)	10 (50)	
Partner	30 (97)	10 (50)	
Parenting children	11 (35)	6 (30)	
Smoking	10 (32)	7 (35)	
PDE5 inhibitor usage	13 (42)	1 (5)	
Ejaculation	6 (19)	2 (10)	
Fertility treatment requirement	19 (61)	10 (50)	

[1]Mean (SD), [2]number (%)

SCI, spinal cord injury; PDE5, phosphodiesterase type 5

Table 3. Severity of erectile dysfunction by IIEF-5 in 31 SCI patients with regular sexual intercourse

Severity of ED	Severe (n = 4)	Moderate (n = 7)	Mild to moderate (n = 7)	Mild (n = 9)	No ED (n = 4)	*p*-value
Age (years)[1]	37 (7.4)	36 (9.4)	30 (3.3)	32 (8.1)	37 (11.7)	0.405
Onset of SCI (months)[1]	42 (45.9)	84 (66.9)	53 (58.9)	47 (48.5)	135 (35.8)	0.077
Level of paralysis[2]						0.850
Complete paraplegia	3 (75)	5 (71)	5 (71)	5 (56)	3 (75)	
Incomplete paraplegia	-	1 (14)	1 (14)	2 (22)	-	
Complete tetraplegia	-	-	1 (24)	-	-	
Incomplete tetraplegia	1 (25)	1 (14)	-	2 (22)	1 (25)	
Relationship status[2]						0.471
No partner	-	-	1 (14)	-	-	
Partner	4 (100)	7(100)	6 (86)	9 (100)	4 (100)	
Parenting children[2]	2 (50)	4 (57)	3 (57)	1 (11)	1 (25)	0.343
Smoking[2]	-	2 (29)	5 (71)	2 (22)	1 (25)	0.117
PDE5 inhibitor usage[2]	1 (25)	3 (43)	3 (43)	3 (33)	3 (75)	0.637
Ejaculation[2]	-	2 (29)	-	2 (22)	2 (50)	0.242
Fertility treatment requirement[2]	2 (50)	4 (57)	5 (71)	6 (67)	2 (50)	0.925
Average sexual intercourse per month	1-2	5-6	3-4	5-6	5-6	

[1]Mean (SD), [2]number (%)

IIEF, International Index of Erectile Function; SCI, spinal cord injury; ED, erectile dysfunction; PDE5, phosphodiesterase type 5

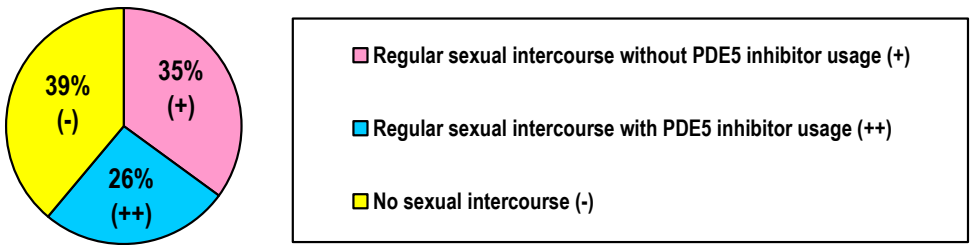

Figure 1. Percentage of regular and no sexual intercourse in 51 patients with self-managed bladder (PDE5, phosphodiesterase type 5) IIEF, International Index of Erectile Function

The characteristics of erectile dysfunction in 18 SCI patients with regular sexual intercourse and no PDE5 inhibitor usage was presented in in Table 4. There were also no statistically significant differences in terms of all clinical data among groups of ED severity.

Based on their IIEF-5 scores, 18 patients with regular sexual intercourse and no PDE5 inhibitor usage were classified into 5 different severity levels. Among these patients, mild erectile dysfunction (33%) was found most, followed by mild to moderate (22%), moderate (22%), severe (17%) and no ED (5%) as shown in Figure 2. The prevalence of erectile dysfunction in this study was 94% (17 out of 18 patients) and 61% of patients (31 out of 51 patients) with self-controlled bladder were sexually-active or having regular sexual intercourse.

Discussion

This retrospective study was aimed to identify severity of ED in Thai male SCI patients with regular sexual activity and analyze their relevant clinical data and IIEF-5 score. According to the results, mild ED was found most in overall patients, followed by mild to moderate, moderate, severe and no ED. The findings indicated that mild ED was common among Thai male SCI patients who had active sexual activity. It was also found that those having regular sexual intercourse had partner and tended to use PDE inhibitor more than those with no sexual activity. In addition, in terms of level of paralysis, no statistical difference was found between regular and no sexual activity patients. In contrast to our findings, Akman et al. reported that 87.3% of SCI patients had moderate to severe ED with the mean IIEF-5 score of 5.3 (SD 4.1). This may suggest that when patients who did not have sexual activity (38%) were included, the results might not reflect accurate erectile function scores.[21]

Regarding the prevalence of ED in this study (94%, as shown in Table 5), the prevalence of ED was slightly increased when compared with previous 2 studies in Thailand.[16,17] The explanation for this might be that Erection Hardness Score (EHS) could only be used to assess erectile hardness for penetration, not the completion of intercourse.[22] Consequently, the entire erectile function could not be evaluated. The result reported by the latest study in 2015 using the 6-item erectile function (EF) domain of the IIEF-15 was also slightly different.[17] IIEF-EF was used for assessing ED in

Table 4. Characteristics of erectile dysfunction in 18 SCI patients with regular sexual intercourse and no PDE5 inhibitor usage

Severity of ED	Severe (n = 3)	Moderate (n = 4)	Mild to moderate (n = 4)	Mild (n = 6)	No ED (n = 11)	*p*-value
Age (years)[1]	35 (6.8)	38 (12.7	30 (4.4)	33 (7.8)	26	0.622
Duration of SCI (months)	19 (14.6)	75 (70.3)	24 (16.4)	45 (57.7)	187	0.080
Level of paralysis[2]						0.327
Complete paraplegia	2 (67)	4 (100)	2 (50)	2 (33)	-	
Incomplete paraplegia	-	-	1 (25)	2 (33)	-	
Complete tetraplegia	-	-	1 (25)	-	-	
Incomplete tetraplegia	1 (33)	-	-	2 (33)	1 (100)	
Relationship status						0.447
No partner	-	-	1 (25)	-	-	
Partner	3 (100)	4 (100)	3 (75)	6 (100)	1 (100)	
Parenting children	1 (33)	3 (75)	1 (25)	1 (17)	-	0.343
Smoking	-	2 (50)	3 (75)	-	1 (100)	0.129
Ejaculation	-	-	-	2 (33)	1 (100)	0.078
Fertility treatment requirement	1 (33)	2 (50)	3 (75)	5 (83)	1 (100)	0.497
Average sexual intercourse per month	1-2	5-6	1-2	3-4	5-6	

[1]Mean (SD), [2]number (%)

SCI, spinal cord injury; ED, erectile dysfunction

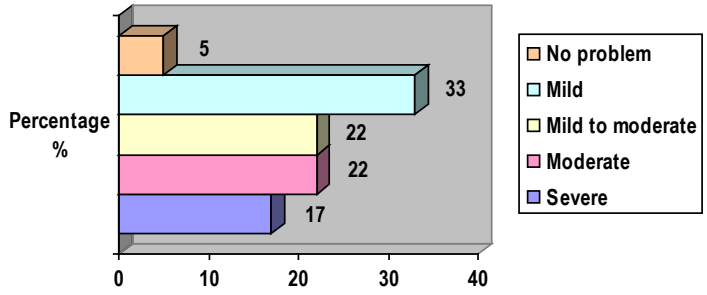

Figure 2. Severity groups found in 18 SCI patients with regular sexual intercourse and no PDE5 inhibitor usage, based on their IIEF-5 scores
IIEF-5, International Index of Erectile Function-5

Table 5. Comparison with other studies in Thailand

Author	Year	N of sexually-active patients	Tool	ED prevalence
Moonla et al.[16]	2010	15	Erection Hardness Score	71.4%
Sudsaneha et al.[17]	2015	25	IIEF-EF*	84%
This study	2020	18	IIEF-5	94%

ED, erectile dysfunction; IIEF-EF, International Index of Erectile Function – Erectile Function

the past 4 weeks and some questions on erection during caressing, foreplay and masturbation were added.[23] Thus, the score from patients who did not attempt sexual intercourse in 4-week period might lower than others.

As mild severity was mostly common (29%) in this study, followed by mild to moderate (22%), moderate (22%), severe (17%) and no ED (5%). These findings slightly differ from Sudsaneha et al.[17] reporting that mild to moderate was found most (32%), followed by severe (28%) and no ED (16%). The differences might be caused by the different tools used for evaluation. The average sexual intercourse in this study which was only 1-2 times per month in the severe group also suggests that an ED-evaluation tool for SCI patients should be designed to assess patients for longer than 4 weeks.

It was also found that patients who received oral drug as erectile dysfunction treatment had more sexual activity (42% in patients with regular sexual intercourse and 75% in patients with no ED). This is similar to the results of a randomized trial conducted by Giuliano et al. who found that sildenafil could improve sexual function in 80% of SCI patients while placebo could improve it in only 10% of the patients.[24] This finding is also in line with Soler et al. who reported that no ED was found in 85% of chronic SCI patients who received oral PDE5 inhibitors or intracavernosal injections of prostaglandin.[25] Moreover, the quality of life improvement after an erectile problem treatment was also denoted.[26]

The findings of this research suggest that sexual education is essential for all SCI patients and their partners as preserved sexual function can maintain their intimacy and relationship. Results from a study in Turkey indicated that only 8.5% of SCI patients were informed about sexuality and fertility after their trauma, and most of them preferred to be trained at the end of their rehabilitation program (74.5%) and by physicians (78.7%).[21] Similarly, a study in Thailand[16] found that only 26.8% of SCI patients reporting having sex education and 80% of them did self-learning from handbooks. Moreover, oral PDE5 inhibitors should be considered in erectile dysfunction patients with close monitoring of some side effects.

Some limitations of this study should be considered. First, as the subjects of this study was only patients in a rehabilitation institute, and the sample size was small, the results may not be generalizable to the larger population especially those in the other regions of Thailand who were unable to approach the rehabilitation program. Second, the influence of other factors such as alcohol use, depression or relationship problems were not being examined in this study. They may affect ED in some ways. Therefore, further research with a larger sample size should include SCI patients from other regions of Thailand, include some other medical issues and relevant factors, and focus more on the outcomes after sexual counseling or medical administration.

In summary, it was found in this study that mild erectile dysfunction was found most in Thai male SCI patients with regular sexual activity and no drug treatment for ED. Moreover, preserving their intimate relationship and the use of PDE5 inhibitors might help impel their sexual activity.

Disclosure

The researchers have no conflict of interest to declare.

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Use of Robotic Gait Training in Hyperglycaemia-Induced Central Pontine Myelinolysis: A Case Report

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ABSTRACT

Objectives: To describe a rarely-seen cause of central pontine myelinolysis (CPM), and the benefits of application of robot-assisted gait retraining (RAGT) in a model of impairment-directed rehabilitation in the management of gait ataxia.
Study design: Case report.
Setting: Inpatient rehabilitation unit of tertiary hospital, Singapore.
Subjects: A 69-year-old male who presented with giddiness, cognitive impairment, and gait ataxia.
Methods: The patient underwent magnetic resonance imaging of the brain which revealed pontine hyper-intensity suggestive of CPM. His diagnostic work-up revealed significant hyperglycaemia.
Results: He underwent treatment for his metabolic derangements and was referred for rehabilitation. We added robot-assisted gait training in the treatment of his ataxia. He was able to ambulate independently subsequently and was discharged uneventfully.
Conclusion: CPM is an uncommon but disabling condition typically seen in rapid correction of hyponatraemia. In our patient this was caused by hyperglycaemia, which likely drives the same osmotic derangements that leads to the dramatic impairments that characterise this condition. Rehabilitation of hyperglycaemia-induced CPM has yet to be described but the condition is becoming more frequently recognised in clinical practice. In addition, given the benefits of RAGT in gait ataxia, there is great potential in the role that RAGT can play in the exploration of best practices beyond CPM in a model of impairment-directed therapy in future.

Keywords: myelinolysis, central pontine, robotics, gait disorders, rehabilitation

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Introduction

Central pontine myelinolysis (CPM) is an uncommon but potentially-fatal presentation of the osmotic demyelination syndrome characterised by oedema and apoptosis of pontine oligodendrocytes resulting from sudden osmolar shifts, such as from rapid correction of hyponatraemia though other associations include renal failure and alcoholism.[1,2] Clinical manifestations, severity, and outcomes are heterogeneous.[1] Hyperglycaemia-induced CPM has only been reported four times prior, and with gait disturbance as a feature.[2-5] We highlight the rare manifestation of hyperglycaemia-induced CPM, and explore the possible role that robot-assisted gait training (RAGT) can play as part of patient-centred and impairment-directed rehabilitation in CPM patients.

Case history

We present a case of a 69-year old Chinese male taxicab driver who was pre-morbidly well, community-ambulant, and lived alone, with a past medical history of hypertension, hyperlipidaemia, diabetes, and transient ischemic attack (TIA). He presented with a progressive one-month history of non-specific leg weakness of gradual onset, which resulted in him becoming homebound and needing to furniture-cruise. Worsening giddiness and swaying while walking led to his attendance at our emergency department. Prior to admission, he had stopped taking his oral diabetic medications for two months as he had run out of supply. Physical examination revealed mild right-sided hemiparesis and gait ataxia. He was forgetful but had normal affect, scoring nine out of ten on the Abbreviated Mental Test. Cranial nerve and sensory examinations were normal.

An urgent magnetic resonance imaging (MRI) scan of the brain on admission was performed for suspected stroke. No infarcts were observed, but new isolated T2-weighted signal hyper-intensity was observed in the central pons (Figure 1) suggestive of CPM. The imaging changes had not been observed a year before when he was diagnosed with TIA. His blood tests including serum sodium were unremarkable except for a serum glucose of 436 mg/dL (24.2 mmol/L) and HbA1c of 138 mmol/mol (14.8%). He was neither dehydrated nor hyponatraemic, and not in in diabetic ketoacidosis. A diagnosis of CPM was made on the basis of his clinical history, lack of physical findings to support alternative differential diagnoses, as well as the severity of his biochemi-

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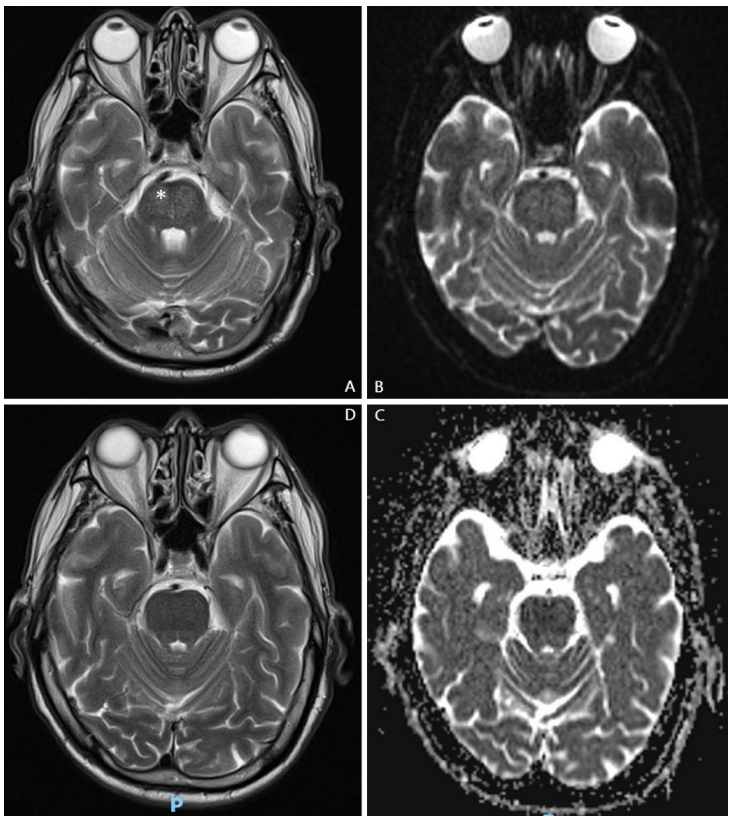

Figure 1. MRI scans of the patient's brain showing (A) T2-weighted signal hyper-intensity in the central pons suggestive of CPM; (B) similar increased signal shown in diffusion-weighted imaging (DWI); (C) signal iso-intensity on apparent diffusion coefficient (ADC) mapping which ruled out an infarct; (D) comparison with the patient's previous MRI findings a year before, showing normal T2-weighted signal, when he presented for a separate neurological complaint (TIA); * represents the lesion of interest.

cal and radiological findings.

He received insulin and was referred for rehabilitation after two days, with transfer to our unit on the fourth day of admission. With correction of his hyperglycaemia, both his weakness and memory had recovered (28/28 on the Mini-Mental State Examination (Chinese)), but despite two days of therapy in the general ward, his standing balance remained poor with retropulsion. He needed assistance to ambulate and perform lower body activities. Quality-of-life (QoL) assessment via the EQ-5D-5L instrument revealed problems in the mobility, self-care, and usual activities domains (health state 23311). He self-scored 50 on the visual analogue scale (EQ VAS).

He underwent conventional physiotherapy and occupational therapy for gait and cognitive training. Conventional gait training in our unit includes both static and dynamic stepping exercises as well as balance perturbation tasks, with promotion to functional walking for performing activities of daily living or going to the inpatient gym. Cognitive training is titrated towards the patients' specific deficits - in his case this memory training through simulation of home tasks.

To address his main impairment of gait ataxia we prescribed overground RAGT with the Andago® V2.0 (Hocoma AG, Switzerland) on the basis of facilitating massed practice. We referred him to ophthalmology for diabetic eye screening and treatment of cataracts. We incidentally diagnosed osteoporosis on bone mineral densitometry and counselled him for anti-resorptive treatment.

He remained clinically-stable and participated well in therapy. After a week in our unit which incorporated seven daily 30-minute sessions of RAGT (Figure 2), he made significant gains in both his gait speed and stability, and subsequently mobilised independently. His functional ambulation category had improved from 1 on admission, to 2 on transfer to rehabilitation, to 5 at the end of his RAGT training. EQ VAS remained at 50 but his health state had improved to 11111. He was discharged home to independent living with outpatient follow-up. At the time of discharge his other mobility indicators were: 315 m on the six-minute walk test (level of assistance 7, no assistive devices, increased from 240 m when measured earlier during his stay in our unit), 10 seconds to complete the Timed Up and Go test, and a score of 53/56 on the Berg Balance Scale (nearly-full functional balance). These had not been charted on admission as they were not routine measurements in our unit for a non-stroke patient.

Discussion

The clinical trajectory of hyperglycaemia-induced CPM varies, from inpatient recovery to intensive care admission, though symptom resolution typically occurs over one to eight weeks.[2,3] The intensity and method of management in such patients also remains heterogeneous, ranging from impairment-directed rehabilitative therapy to purely supportive manage-

Figure 2. Our patient using the robotic gait trainer on the day of his discharge.

ment followed by referral to nursing facility.[3] In our patient his gait improved over the course of a week which was thankfully considered short and he was able to go home.

Just as in treatment of hyponatraemia where there is a need to avoid rapid overcorrection of the patient's serum sodium, we found it important to be wary of large corrections in his diabetic control. Although fluctuations occurred these were generally acceptable and his clinical condition did not deteriorate.

Multi-disciplinary management of CPM is crucial especially in patients with more severe features, to facilitate impairment-directed interventions such as tone management, wheelchair customisation, and communication aids.[6] Our patient's main issues were gait ataxia and memory dysfunction.

His rapid cognitive recovery after reversal of hyperglycaemia suggests delirium rather than a true neurocognitive manifestation of CPM. Management of gait ataxia traditionally comprises balance training, developing postural control, specific gait training, and the use of compensatory orthotics and aids, though treadmill training has not previously shown significant benefits.[7] Using RAGT in the management of gait ataxia in CPM is novel – as an adjunct to conventional physiotherapy in stroke there is moderate evidence that it increases the chance of independent walking (number needed to treat = 7).[8] RAGT also improves gait and endurance in other cardiopulmonary and musculoskeletal conditions. Although there are no precedents in CPM, we applied this understanding in our approach to his gait disturbance.[9] The Andago® is described as a patient-guided suspension system under new classifications of lower limb rehabilitation robotics - these confer mobility to harnessed patients who can then safely practice free-range walking and make errors in a falls-safe environment.[10] The robot leverages on the concepts of intrinsic learning and massed practice to facilitate and accelerate the process of gait retraining in all different phases of gait – when tethered to the robot patients are able to increase the number of steps taken during a therapy session and recognise their own gait abnormalities. The addition of a safety harness helps to prevent falls and promotes confidence, and the mobility of the device allows patients to explore the environment, allowing "real walking", which can motivate participation.[11] Finally, the device also features partial weight supports which allow patients with truncal and lower limb weakness to use it for gait practice. In our patient this translated into a 32% increase in walking speed and also improved balance to the level of unsupervised community mobility.

In CPM there often is a need to evaluate dysphagia and speech but he demonstrated sufficient function in this area and hence we focused more on the gait ataxia.[6] Finally, screening for mood and QoL is essential due to the various activity and participation barriers that can arise – these were addressed through improvement of his walking function and although his gait speed was still considered slow (0.53 m/s), he had regained confidence in his own mobility by discharge.

CPM is increasingly becoming recognised in patients at earlier, less-lethal stages and consequently more of such patients may require rehabilitation services.[1] In addition, given the benefits of RAGT in a model of impairment-directed rehabilitation, there is great potential in its application to a wide variety of other neurological conditions beyond CPM with manifestations of gait ataxia. While we continue to develop best practices in this field, it may prove worthwhile to explore the burgeoning role that robotic therapies could yet play.

Disclosures

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