Combined Application of Electrically Stimulated Antagonist Muscle Contraction and Volitional Muscle Contraction Prevents Muscle Strength Weakness and Promotes Physical Function Recovery After Total Knee Arthroplasty: A Randomized Controlled Trial

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Summary: Background: Osteoarthritis of the knee (KOA) is the most common cause of disability in both the United States and in Japan. The Hybrid training system (HTS) has been developed as a resistance exercise method combining electrical stimulation with voluntary exercise. The purpose of the present study is to compare the effects of a conventional rehabilitation program with or without HTS on knee muscle strength and physical function after Total knee arthroplasty (TKA).

Methods: We conducted a 12-week randomized controlled trial, using standard rehabilitation (the control group, n = 27) or standard rehabilitation plus HTS (the HTS group, n = 26), in 53 female patients after TKA. The HTS group underwent HTS three times per week for twelve weeks after TKA. Muscle strength, thigh circumference, physical functional testing, QOL and knee pain were assessed before surgery, 6 and 12 weeks after TKA.

Results: There was a significant decrease in quadriceps strength and thigh circumference on the operative side in the control group, but not in the HTS group at 6 weeks. Hamstring strength on the operative side in the HTS group significantly increased and thigh circumference was bigger than in the control group at 12 weeks. Physical function improved at 6 weeks in the HTS group, but not in the control group. Knee pain significantly improved in both groups at 6 weeks.

Conclusions: HTS was effective in preventing quadriceps weakness and in improving physical function and QOL after TKA.

Key words atrophy, osteoarthritis, rehabilitation, resistance exercise, electrically stimulated, antagonist muscle contraction

Osteoarthritis of the knee (KOA) is the most common cause of disability in both the United States and in Japan. KOA is associated with pain, quadriceps weak-
ness, swelling, instability, and a decline in range of motion, physical function, and quality of life (QOL) [1]. End-stage KOA results in severe pain and remarkably limited functional activities. Total knee arthroplasty (TKA) is one of the most successful procedures which can relieve pain and improve physical function in patients with KOA [2]. However, the quadriceps are weakened following TKA and do not recover quickly [3]. Furthermore, functional or physical impairments persist in post TKA patients compared with their age- and gender-matched peers [4]. Postoperative quadriceps strength is important for functional recovery after TKA [5]. Therefore, strategies that specifically target strengthening of knee muscle groups are necessary in order to attenuate this muscle strength weakness and improve post TKA outcomes [3]. Neuromuscular electrical stimulation (NMES) is often used to strengthen quadriceps after TKA [6].

NMES activation is considered nonselective with regard to the type of motor unit and synchrony, and it preferentially activates Type II fibers as compared with voluntary muscle contractions [7]. Therefore NMES produces high force at relatively low intensity. However NMES often causes discomfort [8]. Therefore the effect of NMES may prove to be insufficient because the electrical stimulation intensity is determined by the electrical stimulation endurance level of the user. Though the efficacy of NMES is widely reported, in a recent meta-analysis study, evidence for the use of NMES after TKA to increase quadriceps muscle strength is unclear [6]. Therefore the combined application of electrical stimulation and volitional contractions is said to be more effective than electrical stimulation or volitional contractions alone [9]. A hybrid training system (HTS), that resists the motion of a volitionally contracting agonist muscle with force generated by its electrically stimulated antagonist, was developed as a technique to combine the application of electrical stimulation and volitional contractions [10-12] (Fig. 1). Iwasaki et al. studied the efficacy of HTS compared with conventional weight training with 15 repetition maximum (RM) loads for increasing muscle strength around the knee at both slow and fast joint speeds (at 30 and 180°/sec), and reported that HTS is comparable to weight training with the exception of high-speed contractions (HTS + 25 - 28%, WT + 24 - 33%, at 30 °/sec) [10]. In elderly people, HTS has been shown to produce improvements in muscle strength by about 40% and muscle mass by about 10% which is as good as or better than those achieved with a knee flexion machine at 30% of the maximum voluntary contraction [12]. We hypothesized that HTS would prevent post TKA muscle weakness. We further hypothesized that HTS would improve physical function faster than conventional rehabilitation.

The purpose of the present study is to compare the effects of a conventional rehabilitation program with or without HTS on knee muscle strength and physical function.

**METHODS**

**Experimental Approach**

A randomized controlled trial was conducted to assess the effects of HTS on the knee muscle strength and physical function after TKA. Participants were randomly divided into a standard rehabilitation group (control group) or standard rehabilitation plus HTS group (HTS group). Maximal knee muscle strength, thigh circumference, physical function, knee pain, and QOL were measured to assess changes before surgery and 6 and 12 weeks after TKA. The subjects were instructed to accept all medical treatment after TKA during the research period, and to carry on their ordinary daily lives, and daily diet or supplements were not controlled.

**Ethics**

The Ethics Committee of Kurume University ap-
proved the clinical design of this study protocol (Ethi-
cal Review Board approval number: 10136). The sub-
jects were given oral and written explanations of the
study involving the objective of the training method
and its risks, and then read and signed informed con-
sent forms before participation. The study was con-
ducted in adherence to the standards of the Declara-
tion of Helsinki (2008 version) and followed the
European Community’s guidelines for Good Clinical
Practice (111/3976/88 of July 1990) as well as the
Spanish legal framework for clinical research on hu-
mans (Real Decreto 561/1993 on 8 clinical trials).

Setting and Participants

Participants underwent primary unilateral TKA
for knee osteoarthritis by 3 orthopedic specialists at
the Medical Center of Kurume University between
November 2010 and October 2012. All participants
underwent a similar cemented TKA with a medial
parapatellar surgical approach. The participants were
selected according to the criteria shown in table 1.
Computer-generated blocked randomization was used
to ensure balanced assignment of participants to 2
groups with random block sizes of 4. Participants were
randomly divided into a control group or HTS group.

Intervention

All participants received standardized rehabilita-
tion for 40 minutes per day, 5 times (Monday – Fri-
day) per week, at the Rehabilitation Center of Kurume
University by a physical therapist starting 1 day after
TKA. The duration of the rehabilitation program was
12 weeks. The standardized rehabilitation protocol is
shown in Table 2.

HTS Intervention

Participants in the HTS group performed HTS
training 3 times per week. The HTS training was per-
formed in a sitting position without feet touching the
floor, and consisted of alternate flexion and extension
for each knee. The joint range of motion was restricted
to a 90° arc that extended from 10° to 100°. Each ses-
son consisted of 10 sets of 10 reciprocal 3-second
knee flexion and extension contractions. The sets were
separated by a 1-minute rest interval, and one session
exercising both lower extremities required 19 min-
utes. Low impedance gel-coated electrodes (8 cm × 6
cm, Sekisui Plastics Co., Tokyo, Japan) were placed
on the motor points of the bilateral vastus medialis and
lateralis of the anterior thigh, while for the posterior
thigh electrodes were placed on the motor points of
the medial and lateral hamstring. We regulated stimu-
lation intensity so that the exercise intensities were
adjusted to 80% of the maximum tolerable intensity
that would successfully improve muscle strength and
mass without causing pain (8,22). Electrical stimula-
tion parameters were based on a standard Russian
waveform in which a 5,000 Hz carrier frequency was
modulated at 40 Hz (2.4 ms on, 22.6 ms off) to deliver
a rectangular voltage biphasic pulse. The joint motion
sensor (Mutoh Engineering Inc., Tokyo, Japan) trig-
gered stimulation of the antagonist once it sensed the
initiation of an agonist’s volitional contraction.

Outcome Measures

All the evaluations were assessed before TKA and
6 weeks and 12 weeks after TKA.

Bilateral maximal volitional isometric knee exten-
sion/flexion strength (KES/KFS) was measured using
the Microfet 2 Load Cell Dynamometer (Hoggan
Health Industries, Draper, Utah, USA). The partici-
pants were seated over the edge of the seat with a pad
placed under the distal femur and the knee flexed to
60°. Participants pushed the attachment of a hand-held
dynamometer which was applied at 4 cm proximal and
anterior/posterior to the lateral malleoli for 3 seconds
at 30 seconds intervals. The scores of three tests were
TABLE 2.
Rehabilitation Exercise Program

Postoperative day 1
- Mobility on the bed and transfer training (bed to/from chair or toilet)
- Quadriceps sets, gluteal sets, hip abduction (supine), foot pumps
- Knee range of motion (ROM): ankle, hip

Postoperative day 2
- Strengthening exercises (eg, ankle pumps, quadriceps sets, gluteal sets, heel slides, straight leg raises, hip abduction), low intensity, 2-3 sets of 10 repetitions for all strengthening exercises
- ROM: active assisted ROM, and terminal knee extension
- Ambulation and standing training with assistive device on level surfaces and functional transfer

Postoperative day 3-14
- Progression of strengthening exercises (eg, ankle pumps, quadriceps sets, gluteal sets, heel slides, straight leg raises, sitting knee extensions, hip abduction) to the patient’s tolerance with progressive resistance exercise, 2-3 sets of 10 repetitions for all strengthening exercises, twice/day
- Progression of ROM with active assisted exercises and manual stretching
- Progression of ambulation distance and stair with the least restrictive device
- Progression of activities-of-daily-living training for discharge to home
- Ice and physiotherapy

From postoperative day 14 to discharge at rehabilitation unit
- Progressive resistance exercise program: hamstring curls, ankle curls, sitting knee extension with weights in addition to contents as before, 2-3 sets of 10 repetitions for all strengthening exercises, twice/day
- ROM exercise with bike (10-15min) in addition to contents as before, seat height and resistance are adjusted with each function
- Knee extension stretch with manual pressure and weights
- Endurance training with gait or bike, progressive duration up to 15 min
- Ambulation training for the purpose of walking without assistive device

TABLE 3.
Subject characteristics by group (mean ± standard deviation)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HTS group (n=26)</th>
<th>Control group (n=27)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>72.8 ± 8.2</td>
<td>74.1 ± 8.6</td>
<td>.22</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>148.8 ± 6.0</td>
<td>148.1 ± 5.6</td>
<td>.66</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>60.2 ± 11.9</td>
<td>59.8 ± 10.9</td>
<td>.87</td>
</tr>
<tr>
<td>Body mass index (kg/m2)</td>
<td>27.0 ± 4.7</td>
<td>27.2 ± 4.6</td>
<td>.84</td>
</tr>
<tr>
<td>Knee extension strength of operative side (N)</td>
<td>151.8 ± 65.5</td>
<td>51.1 ± 59.1</td>
<td>.74</td>
</tr>
<tr>
<td>Knee extension strength of non-operative side (N)</td>
<td>166.9 ± 59.6</td>
<td>1 177.3 ± 66.3</td>
<td>.48</td>
</tr>
<tr>
<td>Knee flexion strength of operative side (N)</td>
<td>72.4 ± 37.7</td>
<td>79.7 ± 40.7</td>
<td>.38</td>
</tr>
<tr>
<td>Knee flexion strength of non-operative side (N)</td>
<td>81.4 ± 34.0</td>
<td>82.1 ± 40.8</td>
<td>.97</td>
</tr>
<tr>
<td>Circumference measurement of operative side (cm)</td>
<td>43.5 ± 5.2</td>
<td>43.7 ± 5.4</td>
<td>.73</td>
</tr>
<tr>
<td>Circumference measurement of non-operative side (cm)</td>
<td>43.7 ± 5.4</td>
<td>43.7 ± 4.7</td>
<td>.66</td>
</tr>
<tr>
<td>10m gait time (s)</td>
<td>13.2 ± 5.5</td>
<td>14.9 ± 5.2</td>
<td>.075</td>
</tr>
<tr>
<td>Timed up &amp; go test (s)</td>
<td>14.5 ± 9.6</td>
<td>14.8 ± 6.1</td>
<td>.62</td>
</tr>
<tr>
<td>Stair climbing test (s)</td>
<td>17.5 ± 5.4</td>
<td>19.2 ± 8.3</td>
<td>.88</td>
</tr>
<tr>
<td>Japan Knee Osteoarthritis Measure total score</td>
<td>77.9 ± 27.3</td>
<td>80.0 ± 19.3</td>
<td>.86</td>
</tr>
<tr>
<td>Visual analog scale score</td>
<td>39.0 ± 29.0</td>
<td>44.4 ± 29.0</td>
<td>.55</td>
</tr>
</tbody>
</table>
The gait was measured to evaluate gait speed. The participants were instructed to walk as fast as possible. The evaluation was performed by two evaluators, and the times provided by the two evaluators were averaged for analysis. The ICC of measurements for 10MW was 0.98 when we measured healthy subjects at our institution.

For the evaluation of the 10-meter maximal gait time (10MW), 2 meters were added to each end to allow for acceleration before and deceleration after the 10-meter gait. The maximal gait time for the 10-meter gait was measured to evaluate gait speed. The participants were instructed to walk as fast as possible. The evaluation was performed by two evaluators, and the times provided by the two evaluators were averaged for analysis. The ICC of measurements for 10MW was 0.98 when we measured healthy subjects at our institution.

A timed up & go test (TUG) measured the time it took to rise from a standard chair (46 cm seat height), walk a distance of 3 m, walk back to the chair and sit down. The evaluation was performed twice, and the scores of the two times were averaged for analysis. The ICC of measurements for TUG was 0.91 when we measured healthy subjects at our institution.

The maximal time for climbing 18 stairs was measured as a stair climbing test (SCT). The participants were instructed to climb as fast as possible. The ICC of measurements for SCT was 0.99 when we measured healthy subjects at our institution.

The participants answered the Japan Knee Osteoarthritis Measure (JKOM) self-completion questionnaire. JKOM is a self-administered, disease-specific health measure for Japanese patients with KOA [13]. Knee pain during walking on the operated side was evaluated using a visual analog scale (VAS) of 10 cm from no pain to the worst possible pain.

**Data Analysis**

All variables are presented as means and SD. At first we confirmed the normality of the baseline characteristics using Shapiro-Wilk test. According to the results, differences in baseline characteristics between groups were tested by t test or the exact Wilcoxon rank sum test. In order to identify the difference of each evaluation value from preoperative to 6 weeks after TKA or 12 weeks after TKA in each group, we used the exact Wilcoxon signed rank test. For each of the comparisons between groups at 6 weeks after TKA or 12 weeks after TKA, we used the random intercept model. We analyzed whether the intervention effect was different by interaction (group×workload) terms. If p for the interaction term was smaller than 0.25, we judged that there was a different intervention effect between groups and conducted comparisons between groups at 6 weeks after TKA and 12 weeks after TKA. All the statistical analyses were performed using SAS Version 9.3 statistical software (SAS Institute Inc., Cary, NC, USA) and p values ≤0.05 were considered to be statistically significant.

**RESULTS**

A summary of the characteristics and preoperative measures of each group is presented in Table 3. Twenty-six patients in the HTS group and 20 of 27 patients in the control group finished all the evaluations at 12 weeks after TKA (Fig. 2).

In the control group, the KFS on the operated side significantly decreased from preoperation at 6 weeks after TKA. But there were no significant changes in the KES on the operated side in the HTS group. In both groups, the KES on the non-operated side significantly increased from preoperation to 12 weeks after TKA. In the HTS group, the KFS on the operated side significantly increased from preoperation to 12 weeks after TKA and the changes were significantly higher than for the control group. In the HTS group, the KFS on the non-operated side had significantly increased from preoperation at 6 and 12 weeks after TKA. But there were no significant changes in the KFS of the non-operated side in the control group (Fig. 3).

In the control group, the CIR of the operated side significantly decreased from preoperation to 6 and 12 weeks after TKA. But there were no significant changes in the CIR of the operated side in the HTS group. In the control group, the CIR of the non-operated side significantly decreased from pre-operation to 6 and 12 weeks after TKA. But there were no significant changes in the CIR of the non-operated side in the HTS group (Fig. 4).

In the HTS group, the 10MW significantly decreased from preoperation at 6 weeks and 12 weeks after TKA. In the control group, the 10MW significantly decreased from preoperation at 12 weeks after TKA. The 10MW in the HTS group was significantly lower than for the control group at 12 weeks after TKA. In the HTS group, the TUG was significantly decreased from preoperation at 6 weeks after TKA. In the control group, the 10MW significantly decreased from preoperation levels at 12 weeks after TKA. In the HTS group, the SCT significantly de-
Fig. 3. Changes in knee extension/flexion strength.
Changes in knee extension strength in the operative side (A), knee flexion strength in the operative side (B), knee extension strength in the non-operative side (C), and knee flexion strength in the non-operative side (D). Values are means ± SD. * Significant differences from preoperative value, \( p < 0.05 \); ** \( p < 0.01 \). † Significant differences from preoperative value, \( p < 0.05 \); †† \( p < 0.01 \). HTS: hybrid training. Pre; pre-operation. 6wk; 6 weeks after total knee arthroplasty. 12wk; 12 weeks after total knee arthroplasty.
Increased from preoperation at 12 weeks after TKA. The SCT in the HTS group was significantly lower than the control group at 6 weeks after TKA (Fig. 5).

In the HTS group, the JKOM questionnaire results significantly improved from preoperation at 6 weeks and 12 weeks after TKA. In the control group, the JKOM significantly improved from preoperation at 12 weeks after TKA. In the HTS group, the VAS significantly improved from preoperation at 6 weeks and 12 weeks after TKA. In the control group, the VAS significantly improved from preoperation at 6 weeks and 12 weeks after TKA (Fig. 6).

**DISCUSSION**

Although the standard rehabilitation without HTS could not prevent quadriceps weakness, the standard rehabilitation with HTS was able to prevent early quadriceps weakness. Furthermore, the standard rehabilitation with HTS was able to improve physical function.

**Fig. 4.** Changes in thigh circumference.
Changes in thigh circumference in the operative side (A), in thigh circumference in the non-operative side (B). Values are means ± SD. *Significant differences from preoperative value, p < 0.05; ** p < 0.01. HTS; hybrid training. Pre; pre-operation. 6wk; 6 weeks after total knee arthroplasty. 12wk; 12 weeks after total knee arthroplasty.

**Fig. 5.** Changes in physical function.
Changes in 10m walking test (A), timed up & go test (B), stair climbing test (C). Values are means ± SD. *Significant differences from preoperative value, p < 0.05; ** p < 0.01. † Significant differences from preoperative value, p < 0.05; †† p < 0.01. HTS; hybrid training. Pre; pre-operation. 6wk; 6 weeks after total knee arthroplasty. 12wk; 12 weeks after total knee arthroplasty.
function and QOL faster than standard rehabilitation alone. These results indicate that HTS could be effective for rehabilitation after TKA.

There is commonly a general strength deficit of 20% or more after TKA [14]. Quadriceps weakness is a particular problem because quadriceps strength is associated with daily physical function [5,15]. It has been suggested that quadriceps weakness may be caused by a combination of muscle atrophy and neuromuscular activation deficits [16]. It has been reported that there was quadriceps atrophy of 5% to 10% in the first month after TKA as opposed to preoperative values. In this study, quadriceps strength in the control group declined about 28%. Moreover, CIR on the operative side decreased by 3.6% in the control group. This decrease in area seems to indicate a decline in muscle volume by 7% when we assumed the femoral region to be a circle. Thus, muscle weakness after TKA in the control group seemed to occur in the same way as previously reported though the standard rehabilitation was conducted from day 1 after TKA. However, in the HTS group, no muscle weakness was observed. Physical function after TKA normally remains worse than the age-matched healthy population although functional outcome improves after TKA [14, 17]. Finch E et al. suggested that the need for more careful follow up and intensive rehabilitation programs in the first months after TKA and reported that large physical function deficits were present 2 months after TKA [17]. In this study, physical function in the control group hadn’t significantly improved 6 weeks after TKA, but had significantly improved 12 weeks after TKA except for stair climbing. On the other hand, in the HTS group, muscle weakness didn’t occur and physical function had significantly improved 6 weeks after TKA. As the result, QOL seemed to be improved from 6 weeks after TKA. HTS is effective for prevention of muscle atrophy after TKA and improvement in physical function from an early stage.

Because there is muscle weakness after TKA despite the fact that a large amount of rehabilitation is conventionally provided postoperatively, a more aggressive and long-term postoperative rehabilitation approach is necessary [14]. In our study, there was quadriceps weakness 6 weeks after TKA in the control group though a relatively aggressive and intense rehabilitation of five days per week was provided from day 1 after surgery. It took 12 weeks after TKA for quadriceps strength to recover to preoperative levels, and physical function and QOL to improve. These results indicate that standard rehabilitation is not able to prevent quadriceps weakness after TKA, and, as a result the recovery of physical function or QOL was delayed. To prevent this early muscle weakness, Meier et al. suggested that an emphasis on muscle weakness countermeasure like NMES was needed in addition to standard rehabilitation [14]. Stevens JE et al. showed the possibility that NMES, which was performed on patients for 6 weeks 2 or 3 times per week starting from 3 to 4 weeks after TKA, improved muscle strength and activation quickly [18]. Earlier intervention using NMES starting from an early postoperative period was also effective [19,20]. Stevens JE et al. reported that NMES, performed for 6 weeks every day twice a day starting 2 days after TKA, resulted in a greater improvement of quadriceps and hamstring strength, physical function such as walking and stair climbing at not only 3.5 weeks but also 52 weeks after
TKA than standard rehabilitation alone [20]. Additionally, Mintken et al. showed in a case report that early NMES, performed for 6 weeks twice a day for the first 3 weeks and once daily for 3 additional weeks starting 2 days after TKA, could increase quadriceps strength from 3 weeks after TKA [19]. However, they could not prevent hamstring weakness because electrodes were placed on quadriceps only. On the other hand, HTS can train both quadriceps and hamstring at the same time [10,12]. Indeed, HTS increased hamstring strength from preoperative values in this study. Of course, conventional NMES can train both quadriceps and hamstring at the same time if electrodes are put on both muscles. However it might cause intense discomfort for the patients since a large amount of electrical current would be applied to the body at one time. On the other hand, electrical stimulation of quadriceps and hamstring which is alternate and intermittent during HTS is easy on the body. Also, a higher intensity NMES is more effective [21]. However a high intensity NMES causes discomfort [8]. It is necessary for us to use effective NMES without discomfort for adherence and safety of patients. Unlike general NMES, HTS uses submaximal stimulation intensity. HTS seems to be an NMES technique that patients in the early postoperative period can easily perform at a relatively low intensity when it is difficult to exercise at a medium-high intensity. Moreover, HTS is effective when used only two or three times a week unlike common NMES which needs to be performed every day. This might contribute to a reduction of not only the time spent with the patients but also health care utilization and costs. Furthermore, HTS has several other potential advantages. There is a significant amount of evidence that an optimal exercise program should involve reciprocal limb movements [22]. HTS can train both legs during the same exercise reciprocally (in fact, muscle strength of both quadriceps and hamstring of the non-operative sides increased). Most patients with KOA have bilateral KOA. Knee muscle strength is important to physical function for patients with KOA [15], and the muscle strength improvement of the non-operative side might contribute to improvement in postoperative physical function. Another potential advantage of HTS is that it includes volitional contractions as well as electrically stimulated contractions. Electrically stimulated contractions and volitional contractions constitute different modes of muscle activation and induce different acute physiological effects on the neuromuscular system [9]. An additional potential advantage is that HTS involves both eccentric and concentric muscle contractions. Gür et al. showed that combined eccentric and concentric exercise affected functional capacity, especially stair climbing in patients with KOA [23].

CONCLUSIONS

In conclusion, this study found that HTS, which resists the motion of a volitionally contracting agonist muscle with force generated by its electrically stimulated antagonist, was able to prevent quadriceps weakness and improve physical function and QOL after TKA. HTS is a useful exercise method for rehabilitation following TKA.

DECLARATIONS

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AUTHORS’ CONTRIBUTIONS: Conceived and designed the experiments: H. Matsuse. Performed the experiments: H. Matsuse, Y. Takano, T, Nago. Performed the management of experiments: H. Matsuse. Performed the experiments: H. Matsuse. Contributed reagents/materials/analysis tools: N. Shiba. Wrote the paper: H. Matsuse.

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