

ORIGINAL ARTICLE

Generalizability of Eccentric Exercise for Patients with Subacromial Pain Syndrome to Real-world Clinical Practice: A Propensity Score-based Analysis

Akihisa Watanabe, RPT ^a Qana Ono-Matsukubo, RPT ^a Tomohiko Nishigami, RPT, PhD ^b Toshiki Maitani, RPT ^c Akira Mibu, RPT, MS ^d Takahiko Hirooka, MD ^e Hirohisa Machida, MD, PhD ^a

Objectives: Subacromial pain syndrome is a common problem in primary care. Although several randomized controlled trials have shown that eccentric exercise is effective in patients with subacromial pain syndrome, its generalizability to real-world clinical practice is unknown. This study aimed to investigate, using propensity score analysis, the generalizability of eccentric exercise for patients with subacromial pain syndrome to real-world daily clinical practice. **Methods:** In this study, 78 patients underwent eccentric exercise in addition to traditional exercise, and 77 patients underwent only traditional exercise for 4 weeks. Outcomes measured using a visual analog scale (VAS) and American Shoulder and Elbow Surgeons Society Standardized Shoulder Assessment Form (ASES) scores were assessed at baseline and at 4 weeks. **Results:** In the propensity score-matched analysis, 65 patients in each group were successfully matched (130 of 155 patients, 84% overall). After 4 weeks of exercise, pain intensity was lower in the eccentric exercise group than in the traditional exercise group (VAS -14.5, 95% CI -21.2 to -7.9, $P < 0.001$). No significant difference in the improvement in function was found between the two groups (ASES 4.1, 95% CI -2.0 to 10.2, $P = 0.18$). **Conclusions:** Eccentric and traditional exercise in combination could reduce pain in patients with subacromial pain syndrome to a greater extent than traditional exercise alone. These findings have clinical relevance to primary care practitioners who provide conservative treatment for patients with subacromial pain syndrome.

Key Words: daily clinical practice; eccentric exercise; pain control; propensity score analysis; subacromial pain syndrome

INTRODUCTION

Shoulder pain is a common problem. Studies have suggested that shoulder pain is the third most common musculoskeletal problem in primary care.¹⁻³ Subacromial impingement syndrome (SIS) can be treated in many ways, including exercise therapy, manual therapy, injection, and surgery. Many studies have indicated that eccentric exercise

is effective for SIS,⁴⁻¹⁴ and several randomized controlled trials (RCTs)^{5,8-13} and systematic reviews have supported its effectiveness.^{15,16} However, there are concerns about the generalizability of the results of such studies to real-world clinical practice.

The first concern is the translation from basic research to real-world clinical practice. The effects seen in RCTs do not always manifest in real-world clinical practice. An

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^a Department of Rehabilitation, Machida Orthopedics, Kochi, Japan

^b Department of Physical Therapy, Faculty of Health and Welfare, Prefectural University of Hiroshima, Hiroshima, Japan

^c Department of Rehabilitation, Utsumi Orthopedics Clinic, Kagawa, Japan

^d Department of Physical Therapy, Konan Woman's University, Kobe, Hyogo, Japan

^e Department of Orthopaedic Surgery, Onomichi Municipal Hospital, Hiroshima, Japan

Correspondence: Akihisa Watanabe, RPT, Department of Rehabilitation, Machida Orthopaedics, 1-6-3 Tennou-Minami, Ino-town, Agawa-gun, Kochi 781-2123, Japan, E-mail: ak.watanab@gmail.com

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observational study found that one therapy that was effective in several RCTs was not effective in real-world clinical practice.¹⁷⁾ That study noted that patient access, therapist training and expertise, staffing schedules, non-specific aspects of treatment, and non-treatment-related issues can all affect the outcome.¹⁷⁾

The second concern is the difference in research settings. It is unclear whether eccentric exercise is appropriate for primary care patients because many previous studies were conducted in university hospitals.^{5,7–10,12)} Patients with shoulder problems in primary care may have less severe symptoms than those in university hospitals. The only previous study of primary care patients was a single-subject experimental design, not a comparison with a control group.⁶⁾

The third concern is the difference in patient factors. Previous eccentric exercise studies often included patients with SIS who were awaiting surgery. Therefore, to our knowledge, whether eccentric exercise is effective in patients without SIS has not been investigated.

In the current study, we aimed to investigate the benefits of eccentric exercise in a primary care setting. Can eccentric exercise, which is effective in RCTs in university hospitals, be generalized to patients in real-world primary care? This retrospective observational study used propensity score analysis to examine whether eccentric exercise in clinical practice improved pain and function in patients with and without SIS.

MATERIALS AND METHODS

Study Design

This observational study entailed a retrospective review of medical records in a Japanese primary care outpatient facil-

ity. Therefore, this study presents translational research from an RCT to real-world clinical practice.

Participants

Between January 2013 and March 2016, consecutive patients with subacromial pain syndrome who visited a Japanese primary care outpatient facility were identified. According to recent guidelines, subacromial pain syndrome was defined as “shoulder problems that cause pain, localized around the acromion, often worsening during or subsequent to lifting of the arm”.¹⁸⁾ Bursitis, supraspinatus tendinopathy, partial tear of the rotator cuff, and tendon cuff degeneration are all causes of subacromial pain syndrome, including patients with or without SIS.¹⁸⁾ The eligibility criteria were as follows: (1) diagnosis with subacromial pain syndrome, including SIS, by a shoulder-specialized surgeon; (2) age ≥ 18 years; and (3) had undergone rehabilitation for at least 4 weeks. The exclusion criteria were as follows: (1) the presence of any neurological disease, such as cervical spine disease; (2) the presence of full-thickness rotator cuff tears, calcific tendinitis of the rotator cuff, or biceps tendinitis; (3) scheduled or waiting for surgery; and (4) a history of shoulder surgery. Diagnosis was confirmed by a shoulder-specialized surgeon with more than 30 years of experience who combined various physical examinations including the Neer test, the Hawkins-Kennedy test, the painful arc test, and muscle strength tests.¹⁸⁾ Radiography and magnetic resonance imaging were performed as needed to support patient diagnosis.

Procedures: Overall

All study patients were provided medication, rehabilitation, and information about their shoulder condition (**Table 1**). Non-steroidal anti-inflammatory drugs (loxoprofen) were

Table 1. Treatment undergone by the Ecc(+) group and Ecc(-) group

	Treatment
Common to the Ecc(+) group and Ecc(-) group	Medication Non-steroidal anti-inflammatory drugs, 60–120 mg Information about their shoulder condition Traditional rehabilitation Exercises for the scapula stabilizers Posterior shoulder stretch Manual stretch or mobilizing the glenohumeral capsule Scapulothoracic mobilization Instructions for posture correction Instructions about performing activities of daily living
Ecc(+) group only	Two eccentric exercises Supraspinatus eccentric exercise Infraspinatus eccentric exercise

Ecc(+), eccentric exercises group; Ecc(-), no-eccentric exercises group.

prescribed at 60–120 mg per day (used as needed) for 1 or 2 weeks, according to the patient's pain level, and side effects were monitored.

Patients underwent rehabilitation and were instructed to visit our clinic at least once a week to exercise under the supervision of physical therapists. Patients were routinely advised to continue visiting our clinic for at least 4 weeks because some may elect to stop visiting when their symptoms improve. All exercises were supervised by well-trained physical therapists with experience in treating shoulder disorders.

The exercise equipment was provided in a rehabilitation room in our clinic and consisted of a treatment bed, a chair (42 cm in height), and 1.0- to 3.0-kg wearable wrist weights. Exercise adherence was documented in the medical record by the physical therapists. Patients who performed eccentric exercises in addition to standard exercises were assigned to the Ecc(+) group, and those who performed only standard exercises were assigned to the Ecc(-) group.

Procedures: Ecc(-) Group

Our comprehensive rehabilitation program applies the results of several recent RCTs of eccentric exercise for SIS.^{8,9} However, subjects in the Ecc(-) group carried out traditional rehabilitation exercises, including strengthening and stretching exercises, which consisted of two exercises for the scapula stabilizers (middle and lower trapezius and serratus anterior) and the posterior shoulder stretch. Each exercise was carried out as three sets of 15 repetitions, and the posterior shoulder stretch was done for 30 s and repeated several times for a minimum of 4 weeks. If needed, therapists manually stretched or mobilized the glenohumeral capsule and helped with scapulothoracic mobilization; therapists also provided instructions for posture correction and instructions about performing activities of daily living as exercise to all patients.^{9,19,20}

Procedures: Ecc(+) Group

In addition to the exercises carried out by the Ecc(-) group, we provided eccentric rotator cuff muscle exercises for some patients. We investigated previous studies in advance of our clinical practice to determine which patients were more likely to respond to eccentric exercise.^{4–16} However, we could not find any patient characteristics for which eccentric exercise was known to be particularly effective. Therefore, a bidirectional decision was made between the therapist and the patient whether to add eccentric exercise to the rehabilitation program. Regarding this decision, a recent

review suggested that “clinicians should consider including an eccentric-exercise component in shoulder rehabilitation programs to help improve shoulder function, decrease pain levels, and reduce requests for surgical intervention”.²¹ This is a clinical methodology in line with the decision-making process on whether to use optional treatment.²²

For those opting to undertake the additional exercises, two eccentric exercises were provided that were fully assisted by the therapist during the concentric contraction phase but not during the eccentric contraction phase: (1) Supraspinatus eccentric exercises⁸ were carried out as follows: (1–1) with the patient in a seated position, a 1.0-kg weight was wrapped around the patient's wrist; (1–2) the patient's arm was passively elevated with the help of the therapist in 90° of abduction and 30° of horizontal adduction with the thumb facing downward; (1–3) the arm was slowly lowered in the scapular plane eccentrically without the help of the therapist; and (1–4) the arm was then passively returned to the elevated position with the help of the therapist. (2) Infraspinatus eccentric exercises⁸ were performed as follows: (2–1) with the patient lying on their side, a weight was wrapped around the patient's wrist; (2–2) the shoulder joint was placed at 0° of adduction and passively maximal external rotated with the help of a therapist; (2–3) the arm was slowly internally rotated eccentrically without assistance; and (2–4) the arm was then passively returned to the maximal external rotation position with the help of the therapist. These two exercises were provided in three sets of 15 repetitions for 1–3 days per week for at least 4 weeks and were carried out only when the patient came to the clinic; exercises were not directly done at home. The weight applied during the eccentric exercises was based on the pain monitoring model.^{23,24} That means that patients were allowed to tolerate some pain while exercising but were not allowed to exceed 5 on a 0–10 pain scale when performing the exercises. If the patient was able to perform an exercise without pain, the exercise load was increased by 1.0 kg.

Data Collection

The primary outcome was pain during an activity (defined as the intensity of pain that is usually perceived in daily activity) in a 0- to 100-mm visual analog scale (VAS) in which 0 indicates no pain and 100 indicates the worst possible pain. The secondary outcome was the American Shoulder and Elbow Surgeons Society Standardized Shoulder Assessment Form (ASES) score, a measurement tool that assesses both pain and function. Additionally, the patient's age, sex, duration of symptoms, affected side, and VAS pain intensity (at

rest and at night) were collected. VAS and ASES scores were collected at baseline and after 4 weeks of exercise treatment. Furthermore, we examined whether patients were diagnosed with SIS and their adherence to the eccentric exercise regimen.

The above variables are used routinely in our daily clinical practice. The patients' characteristics, VAS scores, and ASES scores were collected before the physical therapy sessions by an assistant therapist who was not involved in the treatment of the patients or in this study. All other data were extracted from the medical records.

Statistical Analyses

We used propensity score matching in the main analyses. Propensity score matching is a standard technique to control for confounding factors in nonexperimental studies in medicine because it is difficult to carry out an RCT in real-world clinical practice. The purpose of propensity score matching is to create two similar groups for which the only difference is whether they have been "treated" or not. Therefore, if we observe a significant difference in outcomes between these two groups using propensity score matching, we can confirm that it is the "treatment" that caused the difference.²⁵⁾

First, the differences between the characteristics of patients in the Ecc(+) group and the Ecc(-) group in the unadjusted model were analyzed using Fisher's exact test for categorical data and the non-paired *t*-test for continuous variables. Standardized differences <0.1 were regarded as a balanced distribution of the covariates.²⁶⁾ This retrospective observational study included some confounding biases. To reduce or minimize these confounding effects, propensity score matching (PSM) analyses were performed: propensity scores were calculated for the propensity-score matched model as the main model, and weighting using the inverse probability of treatment (IPTW) was calculated for the submodel. This submodel was used to confirm the robustness of the PSM model and to confirm that the same tendencies were found as in the PSM model. The propensity scores were created using a multivariable logistic regression model that considered variables including baseline data and age, sex, duration of symptoms, affected side, and baseline VAS (at rest, during activity, and at night), ASES scores, and the presence or absence of SIS. All these variables have been postulated to be prognostic factors for shoulder joint disease.²⁷⁻³³⁾

For the PSM model, patients in the Ecc(+) group and the Ecc(-) group were matched 1:1 based on their propensity scores with a caliper of 0.2. For the IPTW model, patients in the Ecc(+) group were weighted using $[1/\text{the propensity$

score], whereas patients in the Ecc(-) group were weighted using $[1/(1-\text{the propensity score})]$. In both models, standardized differences were also calculated to confirm the balance in each group.

We calculated whether the VAS scores during activity (VAS-activity) and ASES scores in the Ecc(+) and Ecc(-) groups improved more than the minimal clinically important difference (MCID) in both the unadjusted and PSM models. The estimated MCID for VAS was 14 mm for conservative treatment of the shoulder,³⁴⁾ and that of ASES was 6.4 points.³⁵⁾ We assessed intra-group comparisons using paired *t*-tests and inter-group comparisons with non-paired *t*-tests.

If the VAS-activity and/or ASES scores improved more than the MCID in the PSM model, we calculated the outcomes in patients with or without SIS. Similarly, we assessed intra-group comparisons using paired *t*-tests and inter-group comparisons with non-paired *t*-tests. A supplementary statistical analysis (a non-paired *t*-test) was performed between the low- and high-frequency eccentric exercise groups to determine if there was a correlation between the frequency of eccentric exercise and the analgesic effect. All statistical analyses were conducted using R (ver. 3.4.1, R Foundation for Statistical Computing, Vienna, Austria), and *P* values <0.05 were considered significant.

Sample Size Calculation

The sample size was calculated according to the estimated MCID for VAS, which was 14 mm.³⁴⁾ We estimated that we needed 52 patients to detect a mean 14-mm difference in VAS between groups, with a standard deviation of 25, a power of 0.80, and an alpha of 0.05. However, the ratio of patients included in the Ecc(+) and Ecc(-) groups was unknown at the study planning stage, and the total number of required patients was impossible to calculate in advance. Consequently, a post-hoc power analysis was performed to determine whether the power was appropriate after taking in patients during the study period and to determine the number of patients in each group in the PSM model.

Ethical Considerations

This study was approved by the institutional ethics committee of Konan Women's University (ID: 24-01). The requirement to obtain written informed consent from patients was waived because of the retrospective nature of this study, and data were analyzed anonymously. The study was conducted in compliance with the Declaration of Helsinki.

Table 2. Patient characteristics before and after propensity score matching analysis

	Unadjusted			PSM		
	Ecc(+) n=77	Ecc(-) n=78	Standardized difference	Ecc(+) n=65	Ecc(-) n=65	Standardized difference
Age, years (SD)	57.8 (17.7)	58.0 (11.8)	0.014	57.3 (17.9)	57.7 (11.3)	0.027
Sex, female (%)	38 (49.4%)	44 (53.8%)	0.142	34 (52.3%)	33 (50.8%)	0.031
Affected side, right (%)	29 (37.7%)	42 (53.8%)	0.329	28 (43.1%)	30 (46.2%)	0.089
Duration, months (SD)	4.3 (5.7)	5.8 (8.2)	0.203	4.6 (6.1)	5.1 (6.6)	0.070
VAS-rest (SD)	29.2 (28.0)	31.0 (23.4)	0.071	29.4 (27.9)	28.6 (21.4)	0.032
VAS-activity (SD)	52.3 (26.8)	59.8 (18.5)	0.325	55.1 (25.4)	57.1 (17.9)	0.090
VAS-night (SD)	37.4 (28.6)	39.9 (25.3)	0.092	36.8 (28.1)	37.1 (24.1)	0.012
ASES (SD)	48.6 (15.2)	46.5 (17.2)	0.127	48.0 (14.6)	47.2 (17.1)	0.050
SIS, n (%)	39 (50.6%)	45 (57.7%)	0.142	33 (50.8%)	34 (52.3)	0.031

Data are presented as the mean (SD) for continuous variables and as a number, (proportion, %) for categorical variables.

PSM, propensity score matching model; VAS, visual analog scale; ASES, American Shoulder and Elbow Surgeons Society Standardized Shoulder Assessment Form; SIS, subacromial impingement syndrome.

RESULTS

During the study period, 221 consecutive patients with subacromial pain syndrome were enrolled; of these, 66 were excluded from the analyses for the following reasons: age <18 years (n=4), neurological disease (n=9), full-thickness rotator cuff tears (n=34), waiting for surgery (n=18), and a history of surgery of the shoulder (n=1). Finally, a total of 155 patients met the inclusion criteria, of which 77 had performed eccentric rotator cuff muscle exercises [Ecc(+) group] and 78 patients had not performed eccentric exercise [Ecc(-) group].

Propensity Score Analysis

Table 2 shows the baseline data of the patients. In the unadjusted model, a difference was found (i.e., a standardized difference >0.1) between the Ecc(+) group and the Ecc(-) group in terms of sex, affected side, duration of symptoms, VAS-activity score, ASES score, and SIS. In the PSM analysis, 65 patients in each group were successfully matched (130 of 155 patients; 84% overall). All the included variables were balanced between the two groups (i.e., all standardized differences <0.1) (**Table 2**). The IPTW analysis showed similar results to the PSM model (**Table 3**). For the PSM model, the post-hoc power analysis yielded a statistical power of 0.93, confirming sufficient power (n=65, delta=14, significance level=0.05).

Table 3. Patient characteristics weighted using inverse probability of treatment analysis

	IPTW		Standardized difference
	Ecc(+) n=155.85	Ecc(-) n=152.95	
Age, years (SD)	57.7 (17.3)	57.4 (11.8)	0.021
Sex, female (%)	81.2 (52.1%)	81.6 (53.4%)	0.025
Affected side, right (%)	71.0 (45.6%)	70.6 (46.2%)	0.012
Duration, months (SD)	4.7 (6.2)	5.0 (7.1)	0.052
VAS-rest (SD)	27.9 (28.0)	28.9 (22.1)	0.041
VAS-activity (SD)	56.9 (26.1)	57.4 (18.1)	0.025
VAS-night (SD)	37.1 (28.2)	37.9 (24.7)	0.030
ASES (SD)	47.4 (14.7)	47.1 (17.0)	0.018
SIS, N (%)	86.9 (55.8%)	84.0 (54.9%)	0.017

Data are presented as the mean (SD) for continuous variables, as a number, (proportion, %) for categorical variables. IPTW, weighting by inverse probability of treatment model.

Table 4. Effect of exercise on VAS-activity with and without propensity score matching

		Baseline	After treatment	Difference before and after (95% CI)	Difference between the two groups (95% CI)
Unadjusted	Ecc(+), n=77	52.3 (26.8)	28.5 (19.8)	-23.8 (-31.3 to -16.3), P<0.001	-14.7 (-21.2 to -8.3)
	Ecc(-), n=78	59.8 (18.5)	43.8 (21.3)	-16.0 (-22.8 to -10.3), P<0.001	P<0.001
PSM	Ecc(+), n=65	55.1 (25.4)	26.7(17.1)	-28.4 (-36.0 to -21.0), P<0.001	-14.5 (-21.2 to -7.9)
	Ecc(-), n=65	57.1 (17.9)	41.2 (20.7)	-15.9 (-22.6 to -9.2), P<0.001	P<0.001

Data represent mean (SD).
CI, confidence interval.

Table 5. Effect of exercise on ASES with and without propensity score matching

		Baseline	After treatment	Difference before and after (95% CI)	Difference between the two groups (95% CI)
Unadjusted	Ecc(+), n=77	48.6 (15.2)	59.0 (18.3)	10.4 (5.1 to 15.8), P<0.001	3.4 (-2.1 to 8.9)
	Ecc(-), n=78	46.5 (17.2)	55.6 (17.8)	9.1 (4.1 to 15.1), P=0.001	P=0.30
PSM	Ecc(+), n=65	48.0 (14.6)	60.4 (17.4)	12.4 (6.9 to 18.0), P<0.001	4.1 (-2.0 to 10.2)
	Ecc(-), n=65	47.2 (17.1)	56.3 (17.6)	9.1 (3.1 to 15.1), P<0.001	P=0.18

Data represent mean (SD).

Table 6. Changes in VAS-activity and ASES weighted by inverse probability of treatment analysis

		Baseline	After treatment	Difference before and after (95% CI)	Difference between the two groups (95% CI)
VAS-activity	Ecc(+)	56.9 (26.1)	29.2 (19.5)	-27.7 (-31.8 to -23.6), P<0.001	-14.4 (-20.8 to -8.0)
	Ecc(-)	57.4 (18.1)	43.6 (20.5)	-13.8 (-17.1 to -10.5), P<0.001	P<0.001
ASES	Ecc(+)	47.4 (14.7)	57.2 (18.1)	9.8 (7.3 to 12.3), P<0.001	0.2 (-5.6 to 6.0)
	Ecc(-)	47.1 (17.0)	57.0 (17.6)	9.9 (7.1 to 12.6), P<0.001	P=0.95

Data represent mean (SD).

Baseline versus after Treatment

Both VAS-activity and ASES scores had improved after treatment by more than the MCID in the Ecc(+) group and Ecc(-) group for both the unadjusted and PSM models (all P<0.001, **Tables 4, 5**). The IPTW model showed the same tendency as the PSM model (**Table 6**).

Ecc(+) Group versus Ecc(-) Group after Treatment

In both the unadjusted and PSM models, the improvement in the VAS-activity score of the Ecc(+) group over that of the Ecc(-) group was greater than the MCID (unadjusted model, -14.7, 95% confidence interval (CI) [-21.2 to -8.3], P<0.001; PSM model, -14.5, 95% CI [-21.2 to -7.9], P<0.001) (**Table 4**). However, in contrast, no significant differences in the improvements in the ASES scores after treatment were evident between the two groups, and the difference in the improvements was less than the MCID in both models (unadjusted

model, 3.4, 95% CI [-2.1 to 8.9], P=0.30; PSM model, 4.1, 95% CI [-2.0 to 10.2], P=0.18) (**Table 5**).

Patients with SIS versus Patients without SIS

Because the inter-group difference in improvements in ASES scores did not exceed the MCID, we used VAS-activity only to compare patients with and without SIS. The VAS-activity score improved by more than the MCID in all subgroups except for Ecc(-) patients without SIS (**Table 7**). In patients with SIS, the difference in pain improvement between the Ecc(+) group and the Ecc(-) group (-18.0, 95% CI [-27.6 to -9.2], P<0.001) was greater than the MCID. In patients without SIS, a significant difference was found, but the difference was smaller than the MCID (-11.0, 95% CI [-20.8 to -1.2], P=0.02). As part of the post-hoc power analyses of the PSM model, the calculated powers were in the range 0.82–0.96, confirming sufficient power in all subgroup analyses (n=31, 32, 33, 34; delta=14; significance level=0.05).

Table 7. Propensity score matching analysis of VAS-activity changes in SIS(+) and SIS(-) subgroups

	Baseline	After treatment	Difference before and after (95% CI)	Difference between Ecc(+) and Ecc(-) (95% CI)
SIS(+) (n=67)				
Ecc(+), n=33	54.1 (27.9)	20.9 (13.9)	-33.2 (-44.6 to -22.0), P<0.001	-18.0 (-27.6 to -9.2), P<0.001
Ecc(-), n=34	60.9 (18.2)	38.9 (21.9)	-22.0 (-38.9 to -12.1), P<0.001	
SIS(-) (n=63)				
Ecc(+), n=32	56.2 (22.9)	32.6 (18.2)	-24.6 (-33.6 to -12.3), P<0.001	-11.0 (-20.8 to -1.2), P=0.02
Ecc(-), n=31	53.0 (16.8)	43.6 (19.3)	-9.4 (-19.5 to -0.8), P=0.03	

Data represent mean (SD).

Adherence and Co-interventions

Adherence to exercise was confirmed from the medical records: all patients in the Ecc(+) group performed eccentric exercise for 1–3 days per week for 4 weeks (mean, 8 days; range, 6–10 days). No patient dropped out in this study. Therefore, the patients who underwent eccentric exercise continued until the final evaluation, and no patients were reassigned to the Ecc(-) group midway through the study. Moreover, no patient started eccentric exercise midway through the study. Similarly, all patients in the Ecc(-) group performed traditional exercises for 1–3 days per week for 4 weeks (mean, 8 days; range, 6–12 days). The number of patients using non-steroidal anti-inflammatory drugs was similar in each group [51/65 (78%) and 49/65 (75%) in Ecc(+) and Ecc(-), respectively]. The dosage was common to all patients (60–120 mg per day for 1 week).

Exercise Frequency and Analgesic Effect

In the Ecc(+) group, 36 patients had an exercise frequency of ≤ 8 times and 29 patients had a frequency of ≥ 9 times during 4 weeks. The analgesic effect was not significantly different between these two groups; mean (SD) pain relief was 25.2 (22.2) in the ≤ 8 group versus 32.7 (19.8) in the ≥ 9 group (P=0.16).

DISCUSSION

In this retrospective observational study, pain and function improved more than the MCID regardless of whether eccentric exercises were performed. Furthermore, the Ecc(+) group had an additional benefit for pain improvement compared with the Ecc(-) group. However, no additional benefit of eccentric exercises was found for functional improvement. Therefore, our results showed that eccentric exercises, which are effective in university hospital RCTs, can be useful to patients in primary care clinical practice.

Several previous RCTs have shown that eccentric exercises for patients with SIS had a significant pain improvement effect compared with the control group.^{5,8,12} It is meaningful that eccentric exercises provided the same benefits in daily clinical practice in primary care as they did in RCT studies, indicating that eccentric exercises can be useful in daily clinical practice. Our patients had significantly less pain during activity at baseline than did the patients at university hospitals in the previous studies,^{4,5,8,10,12} which may be explained by the different research settings. However, eccentric exercises had no additional effect on improved function. Several previous studies^{9–11} have shown that eccentric exercises did not provide a superior functional improvement over other treatments, including traditional training,⁹ concentric exercise,¹¹ and scapular-focused treatment.¹⁰ Similar to previous studies in university hospital settings,^{9–11} eccentric exercise, compared to other treatments, may not have a direct effect in further improving function in primary care settings.^{9–11} Regardless of the clinical setting, functional training should still be rigorously executed by patients not adhering to eccentric exercise.

The results of the propensity score analyses showed high generalizability of previous RCT findings to clinical practice in primary care. Validation in the unadjusted model resulted in the smallest variability in the PSM model, leading to a design with the best covariate balance.³⁶ For example, although the pathology of the shoulder and prognosis may differ between patients aged 18 and 70, the age variation was minimized in each group. Furthermore, the results of the IPTW model underlined the robustness of the PSM model. The generalizability of PSM analysis is basically limited to the scope of the PSM model.³⁷ Overall, the number analyzed in the current study was 130 of 155 (84%) in the PSM model, which is one of the strengths of this study because 84% of the participants had common support. Moreover, the study group excluded patients with full-thickness rotator cuff tears

and those on surgical waiting lists, who are often found in primary care. Eccentric exercises may be generalizable to a wide range of patients who undergo primary care, and not limited to those treated in shoulder-specialized medical institutions. To the best of our knowledge, this is the first observational study of eccentric exercise in consecutive primary care patients with shoulder pain.

Even low-frequency eccentric exercises produced sufficient clinical improvement; therefore, the frequency of exercises did not modify the analgesic effect. In our method, it was beneficial that we did not instruct patients to exercise at home. Although no previous studies have directly compared intervention frequency, several studies have shown that exercising twice a week was effective for patients with SIS.^{5,7,8,11} A previous study in patients with Achilles tendinopathy showed no difference in the analgesia effect of patients who performed eccentric exercise 2 days a week and 7 days a week.³⁸ The average of 8 days (range, 6–10 days) in a 4-week course of eccentric exercise, as achieved in the current study, is a clinically feasible frequency. Furthermore, a previous RCT has shown poor adherence to eccentric exercise performed at home, with an adherence rate of approximately 50%⁸); however, in the current study, no patients “dropped out” of eccentric exercise, providing evidence of high clinical feasibility.

Based on these findings, we provide the following clinical recommendations for eccentric exercise in primary care. Patients should exercise in three sets of 15 repetitions for at least 8 days in 4 weeks. Under these conditions, clinically relevant analgesia can be expected in patients with subacromial pain syndrome. Some previous studies provided interventions for 8 or 12 weeks.^{4,5,8,9,11,13} Although a short duration of 4 weeks is not sufficient for a complete improvement, we believe that it is possible to motivate patients by explaining that pain can be expected to decrease meaningfully in 4 weeks.

In this study, the analgesic effect of eccentric exercise was found in both patients with and without SIS. However, patients with SIS experienced a greater analgesic effect than those without SIS. This result is important because it may reveal the analgesic mechanism of eccentric exercises. Several analgesic mechanisms of eccentric exercise for patients with SIS have been elucidated.³⁹ Histological changes in the rotator cuff in patients with SIS have been found to be similar to those in patients with Achilles and patellar tendinopathies.^{4,19} Eccentric exercises may be associated with increased fibroblast activity, accelerated collagen formation, and increased levels of type I collagen.^{39,40} These mechanisms can explain the improvement in patients with SIS. However, it is unclear

whether tendinous tissue without SIS has the same pathology as SIS or Achilles and patellar tendinopathies. Consequently, the mechanisms described above cannot necessarily be applied to patients without SIS. Recently, 5-week upper trapezius eccentric exercises were shown to reduce central sensitization in patients with neck/shoulder pain,⁴¹ which was presumed to be the result of activation of the descending analgesic system by exercise-induced hypoalgesia.^{41–43} This mechanism may partly explain why pain improved in our patients without SIS. In summary, eccentric exercise may have resulted in increased tendon strength resulting from increased levels of type I collagen and in reduced central sensitization caused by exercise-induced hypoalgesia.

This study has some limitations. First, propensity score analyses cannot control for unmeasured confounders. In particular, measurements of central sensitization variables, such as conditioned pain modulation,⁴¹ will provide better models and more insights into the analgesic mechanisms of eccentric exercise. Furthermore, data on patient expectations for pain relief based on the explanation by the therapists, motivation for recovery, and therapist training and expertise were not collected and might have affected the prognosis. To help mitigate these unmeasured variables, in this study we did not positively state to patients that “eccentric exercise can be expected to provide analgesia”. Consequently, we believe that it was unlikely that patient expectation would lead to analgesia. Habitual physical activity as a predictive parameter may be associated with either a response or non-response to exercise. Although we did not measure habitual physical activity, an individual’s activity capacity was considered by the physical therapists to provide individually tailored and progressed exercise, which presumably helped to mitigate this issue. The therapists in this study were all well-trained physical therapists with experience in treating shoulder disorders, so the difference in co-intervention is probably insignificant. Although there are some unmeasured confounders, as described above, the important thing is that the best propensity score model has the best covariate balance.⁴⁴ Field research advances by making adjustments using the covariates available in the current data, rather than looking for a complete set of covariates. It will be important to further identify feasibly adjustable covariates. Therefore, our analysis results are important as pioneering data in making future research findings, including the central sensitization variables, more robust. Second, we did not collect data regarding the range of motion or muscle strength. The baseline shoulder range of motion and muscle strength may have influenced the choice of treatment program. Further research

is needed to take these factors into account. Third, data on only the short-term effects of the 4-week intervention were collected. However, the pain relief within 4 weeks was clinically relevant in subsequent treatment schedules, because conservative management for 3–6 months is the first-line treatment of patients with SIS, and if this fails, surgery is considered.⁴⁵⁾ Future research on the long-term follow-up effects would be highly relevant.

In conclusion, patients who performed eccentric rotator cuff exercises experienced higher analgesic effects than patients who did not perform eccentric exercises. However, no difference in functional improvement between the two groups was found. Eccentric exercises can be useful for patients in primary care clinical practice. Our findings have clinical relevance for practitioners who provide conservative treatment to patients with subacromial pain syndrome in primary care.

CONFLICTS OF INTEREST

No potential conflicts of interest relevant to this article exist.

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