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Consensus agreement on interpretation of the results of the SINEX study

# Three Months of Physical Therapist-supervised Neuromuscular Shoulder Exercise Program versus Standard Care for Patients with Traumatic Anterior Shoulder Dislocations: An Assessor-blinded Randomized Controlled Trial (The SINEX study)

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## Introduction

This study has a focus on a neuromuscular shoulder exercise programme with the overall goal to improve shoulder-related Quality of Life (QoL), function and pain of patients with traumatic anterior shoulder dislocation (TASD). The hypothesis is that patients with TASD treated with shoulder neuromuscular exercises (intervention, SINEX group) will experience and report larger improvements in shoulder-related QoL, function and pain than those treated with advice in self-managed shoulder exercises (control, Standard Care group). The protocol article is published (Eshoj, Rasmussen, Frich, Hvass, Christensen, Jensen, Sondergaard, et al. 2017), and the statistical analyses plan is available on the web page of Department of Sports Science and Clinical Biomechanics (Eshoj, Rasmussen, Frich, Hvass, Christensen, Jensen, Søndergaard, et al. 2017).

## Aim

The aim of this paper is to document a consensus agreement on the interpretation of the results of the primary outcome, a patient reported outcome (Western Ontario Shoulder Instability Score, WOSI), while all the authors of the primary outcome are still blinded as to the intervention and control group identification, as recommended (Jarvinen et al. 2014). The primary objective in this randomized controlled trial (RCT) was to evaluate the efficacy and safety of a 12-week physiotherapist-supervised neuromuscular shoulder exercise (SINEX) program in comparison with 12-weeks of self-managed shoulder exercise program (standard care) in patients with TASD as measured by the primary outcome being the total score of WOSI.

## Methods

The primary analysis used on the primary outcome, WOSI, is an analysis of covariance (ANCOVA) model based on Intention-To-Treat (ITT). The lost-to-follow-up was 4 patients in total, distributed by 3 patients in group A (0), and 1 patient in group B (1), which, although being a small number in total, may have added bias to the results.
ANCOVA was not invalidated and therefore appropriate to do. Also paired t-test was used with baseline observation carried forward (BOCF). A sensitivity analysis will be carried out with different imputation techniques. Analyses are not adjusted for sex as both groups have an equal distribution for group A (0) (men, 82%) and group B (1) (men, 93%).

## Results

Due to recruitment difficulties and closing of recruitment after 24 months as an a priori decision (Eshoj, Rasmussen, Frich, Hvass, Christensen, Jensen, Sondergaard, et al. 2017) the number of patients did not reach the required sample size.

Group A and B represent: either the SINEX (intervention, active) group or Standard care (control) group with the authors being blinded to identification of the groups.
The results of the primary outcome are:

| | A (0) mean change (SD) | B (1) mean change (SD) | Difference mean change A minus B (mean) (95% CI) | P-value Linear regression model |
|---|---|---|---|---|
| WOSI total | 445.21 (466.14) | 499.04 (337.71) | -53.82 (-271.91; 164.27) | 0.092 |

Group B (1) is improving 53.83 points more compared with group A (0) on WOSI total, however, non-significantly.

## Conclusions

Overall: The linear regression model showed no statistically significant between-group difference in change score in the primary outcome measure WOSI at the primary assessment end point (12 weeks from baseline), nor did the T-test, although close to. However, within-group differences of WOSI Total, for both groups showed improvements to levels above the threshold recognized for minimal clinical important difference (a priori defined to be 250 points) (Eshoj, Rasmussen, Frich, Hvass, Christensen, Jensen, Sondergaard, et al. 2017).
As described above the lost-to-follow-up rate was 4 patients in total, distributed unequally between the groups. Further, compliance of the supervised SINEX sessions is not yet known, but according to non-compliant patients during the 12 weeks of exercise (but completed patient-reported outcomes at 3 mth´s follow-up) at least 5 non-compliant patients were seen, distributed by 4 in group A (0) and 1 in group B (1), which may have added bias to the results. Still the remaining compliance and the amount of home training compliance (from patient dairies) is not yet known.

The main conclusion of this randomized controlled trial involving 2 x 28 patients with TASD, is that the effect of 12 weeks of supervised neuromuscular exercise was similar on shoulder-related QoL, function and pain (as measured by WOSI) when compared with 12 weeks of Standard Care treatment. In terms of short-term shoulder-related QoL, these findings suggest that patients with TASD can be treated with Standard Care since this treatment is less expensive and time-consuming to prescribe. However, the long-term effects are unknown at this point. Both intervention and control were effective in reducing shoulder-related QoL, function and pain (WOSI) to a clinically relevant level. At this point, the effect on secondary outcomes to support this result is also unknown.

**Discussion**

The following topics are suggested as points of discussion.

A intervention group and B control group (B improved mostly, but not significantly more)

Interpretation of the results based upon the ANCOVA analyses, with A as the neuromuscular shoulder exercise programme (SINEX, intervention) and B as those treated with advice only (Standard care, control): showing B (control group) – non-significantly more effective on WOSI than A (Intervention group).

1) If dropouts/lost-to-follow-ups in A are mainly those improving, results will move towards a smaller effect of SINEX. If dropouts/lost-to-follow-ups in A are mainly those becoming worse, the results will move towards a larger effect of SINEX.

2) SINEX does not improve WOSI more than Control meaning Control is as effective as SINEX. This may be due to the natural course of this musculoskeletal condition, with some patients improving shoulder function just by nature following a primary TASD (Hovelius and Rahme 2016). Also, it may be that advice and self-management only in the control group was just as effective compared with exercises directly targeting shoulder neuromuscular control.

3) The primary outcome, WOSI total, is a patient-reported outcome questionnaire consisting of 4 individual domains (21 items in total). As such, the primary outcome, WOSI Total, is based on an aggregate score and, thus, do not reflect the results of the individual domains.

The WOSI domain 4, targeting shoulder-related "emotions" (3 items), is originally intended to reflect that patients, following shoulder instability treatment (surgical/non-surgical), became less aware/affected by their shoulder symptoms (as a positive change). However, it may be that the patients in the SINEX group (A) become MORE aware of the shoulder due to the intensive physical therapist-supervised SINEX sessions. The WOSI Total score may therefore come out negatively in the SINEX group due to the "negative" outcome of domain 4 (as the positive change). However, at this point, the scores of the individual domains are unknown.

Also, there are no studies to compare WOSI with (as primary outcome) after 3 months of shoulder neuromuscular exercise. Previous RCT studies report mainly on the long-

term effects, such as the number of shoulder re-dislocations, which, in general, do not occur until 2 years after the primary shoulder dislocation for about 50% of the patients (Robinson et al. 2006).

4) SINEX sessions did not have the correct dose or frequency to induce significant differences, or the home exercise compliance in SINEX was not sufficient to show a larger effect than in the control group.

5) Patients doing intensive (and physical therapist-supervised) neuromuscular exercises (as in SINEX intervention group) focus more on their shoulder problems and, therefore, have higher expectations on improvement. This may add to the daily struggle to obtain improvement in shoulder function. On the contrary, advice alone and self-management used for control, and not being directly confronted with problems, may to a higher extent develop a situation of acceptance, releasing new energy and less attention on shoulder function.

6) Lost-to-follow-up is larger in SINEX, and the total compliance in the supervised session and home-training is lower, although at this point unknown. A potentially higher home training compliance rate in control group may be contributing to the better outcome in Control.

7) SINEX is more time-consuming than the control (more visits to the physiotherapist) possibly affecting the motivation for exercising in the SINEX group (lack of compliance).

8) With a sample size of 28 patients per group, SINEX does not have sufficient power to show significant effect of the actual group difference, which was only 54 points in change scores. As described in the protocol (Eshoj, Rasmussen, Frich, Hvass, Christensen, Jensen, Sondergaard, et al. 2017) the study was powered to detect a group difference of min. 250 points in change scores (the minimal clinical relevant difference), with a sample size of min. 36 patients/group. Lack of participants was due to difficulties in patient recruitment and a an a priori final defined endpoint for inclusion.

B intervention group – A control group (B improved mostly, but not significantly more) Interpretation of the results based upon the ANCOVA analyses and with B as the intervention group and A the control group: B – intervention showing non-significantly more effect on WOSI Total than group A – control.

1) If the dropouts in A are mainly those improving, the results will move towards a larger effect of SINEX. If the dropouts in A are mainly those becoming worse, the results will move towards a smaller effect of SINEX.

2) Neuromuscular shoulder exercises (SINEX) reduce QoL, function and pain (measured as WOSI) more than the control due to the positive effect of the supervised guidance and targeted shoulder neuromuscular exercises. This means that improvement of muscle function, balance, and neuromuscular control create improved shoulder function and more resources. However, dose and frequency of the SINEX program may have been sub-optimal.

3) The physical therapist-supervised guidance (SINEX intervention) gives the participants clear feedback on their performance (improvement/worsening) and therefore a feeling of self-management of their shoulder impairments and being in control. This may explain the improvements in QoL, function and pain management (on WOSI Total). However, changes are not significantly larger than in control. Though, for each group the within-group changes are of a clinically relevant size.

4) Placebo effect in SINEX is expected to be larger as the patients have an expectation that they will improve by guided training. The difference in change scores is not large enough to be clinically relevant, but the size of within-group difference is.

5) A potentially higher home training compliance rate (still unknown) in SINEX may be contributing to the better outcome in SINEX compared with control. Distribution of successors and non-successors according to the home training compliance will be studied in the Per-Protocol-analyses.

6) The performed exercises for the control group was not supervised but performed as home exercises. There may be different barriers/facilities for the execution of the home programme in the control group: incorrect interpretation of the instructions, lack of energy, fear avoidance of movement or previous poor training experiences, leading to worse shoulder function in the Control group.

### Perspectives

There was no group difference in the change scores on shoulder-related QoL, function and pain (as measured by WOSI Total). Control and SINEX are equally effective when the effect measure is WOSI. However, both SINEX and control were effective in reducing shoulder-related QoL, function and pain, function from baseline to follow up, corresponding to a clinically relevant level.

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