de Vries JS, Krips R, et al. Interventions for treating chronic ankle instability. Cochrane Database of Systematic Reviews 2011, Issue 8. Art. No.: CD004124

Design: Meta-analysis of clinical trials

Purpose of study: to compare outcomes of various operative and nonoperative treatments of chronic ankle instability

PICOS:

- Patient population: skeletally mature adults with chronic lateral ankle instability, defined as recurrent sprains or giving way for more than six months
- Interventions and Comparisons:
    - Neuromuscular training programs versus no training
    - Different surgical procedures
        - Anatomical reconstruction of the injured ligaments versus tenodesis using the peroneus brevis tendon
    - Different postoperative rehabilitation programs, comparing early mobilization and range of motion training in a brace versus six weeks of plaster immobilization
- Outcomes: functional outcomes and subjective stability as primary outcomes
    - Secondary outcomes included recurrent injury, use of external support, range of motion, and time of return to work or sports activity
- Study types: both randomized and quasi-randomized studies could be included

Study selection:

- Databases included MEDLINE, EMBASE, and CINAHL through February 2010
- Two authors independently selected articles and graded them for risk of bias using the Cochrane risk of bias system, with emphasis on adequate randomization sequence, allocation concealment, blinding of outcome assessment, completeness of followup, and selective outcome reporting

Results:

- A total of 81 potentially eligible trials were retrieved in the literature search, and 10 studies with a total of 388 patients were used for the analysis of data
    - 3 studies compared neuromuscular training to no training, and 1 study compared two different types of neuromuscular training
    - 4 studies compared different types of surgical intervention
    - 2 studies compared early mobilization and training with plaster immobilization following ankle surgery

        - The early mobilization groups had 2 weeks of immobilization followed by range of motion and use of a prefabricated walking boot which allowed a limited preset range of plantar and dorsiflexion range of motion
- Most of the trials had significant risks of bias; only one study had complete description of the generation of the randomization sequence; none had clear description of allocation concealment, only two studies had adequate blinding
- The authors were able to pool outcome data from three studies comparing neuromuscular training with no training
    - The training groups had significantly higher and better scores than the groups with no training for function at the end of training for both the Ankle Joint Functional Assessment Tool (AJFAT) and for the Foot and Ankle Disability Index (FADI)
    - The one study which compared training with a bi-directional pedal versus training with a standard uni-directional pedal found no differences in outcome
    - None of the studies had followup comparisons past the end of training
- The four studies comparing different surgical interventions found no differences between non-anatomic versus anatomic reconstruction
- The authors were able to pool outcome data from two studies of postoperative rehabilitation comparing early mobilization in a brace versus six weeks of plaster immobilization
    - Fewer patients had an unsatisfactory outcome in the early mobilization group (2 out of 35) than in the plaster immobilization group (7 out of 35)
    - Time to return to work was 2.0 weeks shorter in the early mobilization groups than in the plaster immobilization groups, and return to sports activity was 3.0 weeks shorter in the early mobilization group

Authors' conclusions:

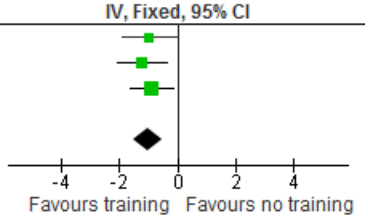
- The review does not provide strong evidence on which to base practice, due to small sizes of study populations, high risk of bias of the studies, and clinical heterogeneity
- Neuromuscular training appears to provide functional benefit in the short term, but it is unclear whether this is clinically relevant and there is no evidence regarding long term outcomes
- There is insufficient evidence to support one surgical intervention over any other, but tenodesis is often impractical due to the insufficient diameter of the peroneus brevis tendons which would be used in the procedures
- After surgical intervention for ankle ligamentous injuries, it is advisable to mobilize the ankle earlier than six weeks using a prefabricated walking boot, since this may shorten time to return to work and may result in fewer unsatisfactory outcomes as rated by patients

Comments:

- The authors are not certain that the differences in outcome for neuromuscular training are clinically relevant even at the end of training, which may be due to uncertainty about what magnitude of effect size constitutes a clinically relevant one
- However, in Analysis 1.1, which displays the outcomes from one study which used the AJFAT with two studies which used the FADI, it might be possible to combine the three studies using a standardized mean difference, even though the AJFAT and FADI use different scales to estimate similar concepts
- If this is done with the data in Analysis 1.1, the forest plot suggests that there is an important functional effect size

	No training			Training				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Clark 2005	13	3	9	16	3	10	25.5%	-0.96 [-1.92, 0.01]
Hale 2007	-0.68	3.91	12	7.3	7.99	13	31.6%	-1.21 [-2.08, -0.35]
McKeon 2008	81.4	18.1	15	93.7	7.4	16	42.9%	-0.88 [-1.62, -0.14]
Total (95% CI)			**36**			**39**	**100.0%**	**-1.00 [-1.49, -0.52]**

Heterogeneity: Chi² = 0.34, df = 2 (P = 0.84); I² = 0%
Test for overall effect: Z = 4.04 (P < 0.0001)



- That is, the three studies have very similar estimates of effect (zero heterogeneity) and the pooled effect size is 1.00 standard deviations in favor of training
- Conventionally, an effect size of 0.80 SD or more is considered to be “large” and an effect size of 0.50 SD or more is considered to be “moderate”
    - The lower end of the 95% confidence interval for neuromuscular training is 0.52, which is at least moderate in size
- The lack of outcome data beyond the training period is an important limitation of the included studies, and the risk of bias could inflate the estimate of the effect of neuromuscular training
    - However, if a “placebo” response to training involves positive patient expectations of benefit arising from their involvement in their own rehabilitation from injury, that contribution to functional improvement could be interpreted as being part of the overall effect of the intervention, and would not necessarily mean that the true benefits were greatly inflated
    - In Analysis 1.1, Clark used 4 weeks of wobble-board training; Hale used 4 weeks of rehabilitation with range of motion, strengthening, and neuromuscular control; McKeon used 4 weeks of progressive balance training with various supervised exercise activities aimed at stabilization of the ankle; the very similar effect sizes indicates that there is no reason to prefer one over any other form of training

Assessment: A methodologically high quality systematic review and meta-analysis of suboptimal clinical trials of treatments of chronic ankle instability, supporting a statement that there is good evidence that 4 weeks of neuromuscular training aimed at improving balance and proprioception

are more effective than no training at producing functional recovery, and there is good evidence that in patients who have undergone surgical repair of the ankle ligaments, early mobilization with a prefabricated walking boot leads to earlier return to work and activity than plaster immobilization for six weeks