

- P**  **PROTECTION**
Avoid activities and movements that increase pain during the first few days after injury.
- E**  **ELEVATION**
Elevate the injured limb higher than the heart as often as possible.
- A**  **AVOID ANTI-INFLAMMATORIES**
Avoid taking anti-inflammatory medications as they reduce tissue healing. Avoid icing.
- C**  **COMPRESSION**
Use elastic bandage or taping to reduce swelling.
- E**  **EDUCATION**
Your body knows best. Avoid unnecessary passive treatments and medical investigations and let nature play its role.
- &**
- L**  **LOAD**
Let pain guide your gradual return to normal activities. Your body will tell you when it's safe to increase load.
- O**  **OPTIMISM**
Condition your brain for optimal recovery by being confident and positive.
- V**  **VASCULARISATION**
Choose pain-free cardiovascular activities to increase blood flow to repairing tissues.
- E**  **EXERCISE**
Restore mobility, strength and proprioception by adopting an active approach to recovery.

E-Learning Course 1.10 PEACE & LOVE

Scientific References

- 2020-Dubois, B. & J.-F. Esculier. Soft-tissue injuries simply need PEACE and LOVE. *British Journal of Sports Medicine* 54 (2): 72-73. 4
- 2019-Duchman, K. R., D. B. Lemmex, S. H. Patel, L. Ledbetter, G. E. Garrigues & J. C. Riboh. The Effect of Non-Steroidal Anti-Inflammatory Drugs on Tendon-to-Bone Healing: A Systematic Review with Subgroup Meta-Analysis. *The Iowa Orthopaedic Journal* 39 (1): 107-119. 5
- 2018-Borgeat, A., C. Ofner, A. Saporito, M. Farshad & J. Aguirre. The effect of nonsteroidal anti-inflammatory drugs on bone healing in humans: A qualitative, systematic review. *Journal of Clinical Anesthesia* 49: 92-100. 6
- 2018-Vuurberg, G., A. Hoorntje, L. M. Wink, B. F. W. van der Doelen, M. P. van den Bekerom, R. Dekker, C. Niek van Dijk, R. Krips, M. C. M. Loogman, M. L. Ridderikhof, F. F. Smithuis, S. A. S. Stufkens, E. A. L. M. Verhagen, R. A. de Bie & G. M. M. J. Kerkhoffs. Diagnosis, treatment and prevention of ankle sprains: update of an evidence-based clinical guideline. *British Journal of Sports Medicine* 52 (15): 956. 7
- 2018-Wheatley, B. M., K. E. Nappo, D. L. Christensen, A. M. Holman, D. I. Brooks & B. K. Potter. Effect of NSAIDs on Bone Healing Rates: A Meta-analysis. *Journal of the American Academy of Orthopaedic Surgeons* 27 (7): e330-e336. 8
- 2018-Zhao-Flemming, H., A. Hand, K. Zhang, R. Polak, A. Northcut, D. Jacob, S. Dissanaike & K. P. Rumbaugh. Effect of non-steroidal anti-inflammatory drugs on post-surgical complications against the backdrop of the opioid crisis. *Burns & Trauma* 6 (25): s41038-018-0128-x. 9
- 2017-Doherty, C., C. Bleakley, E. Delahunt & S. Holden. Treatment and prevention of acute and recurrent ankle sprain: An overview of systematic reviews with meta-analysis. *British Journal of Sports Medicine* 51 (2): 113-125. 10
- 2017-Duchesne E., S. S. Dufresne & N. A. Dumont. Impact of Inflammation and Anti-inflammatory Modalities on Skeletal Muscle Healing: From Fundamental Research to the Clinic. *Physical Therapy* 97 (8): 807-817. 11
- 2017-Morelli, K. M., L. B. Brown & G. L. Warren. Effect of NSAIDs on Recovery From Acute Skeletal Muscle Injury: A Systematic Review and Meta-analysis. *The American Journal of Sports Medicine* 46 (1): 224-233. 12
- 2017-Singh, D. P., Z. Barani Lonbani, M. A. Woodruff, T. J. Parker, R. Steck & J. M. Peake. Effects of topical icing on inflammation, angiogenesis, revascularization, and myofiber regeneration in skeletal muscle following contusion injury. *Frontiers in Physiology* 8: 93. 13
- 2016-Shibaguchi, T., T. Sugiura, T. Fujitsu, T. Nomura, T. Yoshihara, H. Naito, T. Yoshioka, A. Ogura & Y. Ohira. Effects of icing or heat stress on the induction of

- fibrosis and/or regeneration of injured rat soleus muscle. *The Journal of Physiological Sciences* 66: 345-357. 14
- 2015-Jones, P., S. R. Dalziel, R. Lamdin, J. L. Miles-Chan & C. Frampton. Oral non-steroidal anti-inflammatory drugs versus other oral analgesic agents for acute soft tissue injury. *Cochrane Database of Systematic Reviews* (7): CD007789. 15
- 2015-Yerhot, P., T. Stensrud, B. Wienkers & C. Durall. The Efficacy of Cryotherapy for Improving Functional Outcomes Following Lateral Ankle Sprains. *Annals of Sports Medicine and Research* 2 (2): 1015. 17
- 2013-Tseng, C.-Y., J.-P. Lee, Y.-S. Tsai, S.-D. Lee, C.-L. Kao, T.-C. Liu, C.-H. Lai, M. B. Harris & C.-H. Kuo. Topical Cooling (Icing) Delays Recovery From Eccentric Exercise-Induced Muscle Damage. *Journal of Strength and Conditioning Research* 27 (5): 1354-1361. 18
- 2012-van den Bekerom, M. P. J., P. A.A. Struijs, L. Blankevoort, L. Welling, C. N. van Dijk & G. M. M. J. Kerkhoffs. What Is the Evidence for Rest, Ice, Compression, and Elevation Therapy in the Treatment of Ankle Sprains in Adults?. *Journal of Athletic Training* 47 (4): 435-443. 19
- 2011-Takagi, R., N. Fujita, T. Arakawa, S. Kawada, N. Ishii & A. Miki. Influence of icing on muscle regeneration after crush injury to skeletal muscles in rats. *Journal of Applied Physiology* 110 (2): 382-388. 20
- 2007-Ferry, S. T., L. E. Dahners, H. M. Afshari & P. S. Weinholt. The Effects of Common Anti-Inflammatory Drugs on the Healing Rat Patellar Tendon. *The American Journal of Sports Medicine* 35 (8): 1326-1333. 21
- 2004-Bleakley, C., S. McDonough & D. MacAuley. The Use of Ice in the Treatment of Acute Soft-Tissue Injury: A Systematic Review of Randomized Controlled Trials. *The American Journal of Sports Medicine* 32 (1): 251-261. 22
- 2004-Martuzzi, M. & J. Tickner. The precautionary principle: protecting public health, the environment and the future of our children. World Health Organization. 23
- 1989-Sloan, J. P., R. Hain & R. Pownall. Clinical benefits of early cold therapy in accident and emergency following ankle sprain. *Emergency Medicine Journal* 6: 1-6. 24

[2020-Dubois, B. & J.-F. Esculier. Soft-tissue injuries simply need PEACE and LOVE. *British Journal of Sports Medicine* 54 \(2\): 72-73.](#)

Rehabilitation of soft-tissue injuries can be complex. Over the years, acronyms guiding their management have evolved from ICE to RICE, then on to PRICE and POLICE. Although widely known, these previous acronyms focus on acute management, unfortunately ignoring subacute and chronic stages of tissue healing. Our contemporary acronyms encompass the rehabilitation continuum from immediate care (PEACE) to subsequent management (LOVE). PEACE and LOVE outline the importance of educating patients and addressing psychosocial factors to enhance recovery. While anti-inflammatories show benefits on pain and function, our acronyms flag their potential harmful effects on optimal tissue repair. We suggest that they may not be included in the standard management of soft-tissue injuries.

[2019-Duchman, K. R., D. B. Lemmex, S. H. Patel, L. Ledbetter, G. E. Garrigues & J. C. Riboh. The Effect of Non-Steroidal Anti-Inflammatory Drugs on Tendon-to-Bone Healing: A Systematic Review with Subgroup Meta-Analysis. *The Iowa Orthopaedic Journal* 39 \(1\): 107-119.](#)

Background: There is some concern that non-steroidal anti-inflammatory drugs (NSAIDs) may impair the healing of certain musculoskeletal tissues. However, the effect of NSAIDs on the specialized fibrocartilaginous transition at the tendon-to-bone interface remains largely unknown. Thus, the purpose of the present study is to investigate the effect of NSAIDs on tendon-to-bone healing following acute injury or surgery.

Methods: A systematic review was performed according to the 2009 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The PubMed (MEDLINE), Embase, Cumulative Index to Nursing and Allied Health (CINAHL), and SportDiscus databases were searched from the time of database inception to May 14, 2018 to identify all clinical and basic science studies investigating the effect of NSAIDs on tendon-to-bone healing. Methodological quality was assessed using the Methodological Index for Non-Randomized Studies (MINORS) and SYStematic Review Center for Laboratory animal Research (SYRCLE) risk of bias assessment tools for clinical and basic science studies, respectively. A qualitative synthesis of the literature was performed with a subgroup meta-analysis of homogeneous basic science studies.

Results: A total of 13 studies, including three clinical and 10 basic science studies, were included. The overall methodological quality of the included clinical studies was poor, while assessment of the basic science studies revealed consistent areas at high or unclear risk of bias. Of the included clinical studies, a single study reported a higher rate of rotator cuff repair failure with selective (COX-2) NSAID use compared with non-selective NSAID use, while no clinical failures were noted with NSAID use following distal biceps tendon repair. Basic science studies had heterogeneous outcome reporting. A subgroup analysis of homogeneous animal studies revealed no significant effect of all NSAIDs (Standard Mean Difference [SMD] -1.05, 95% Confidence Interval [CI] -2.39-0.30, $p=0.13$) or non-selective NSAIDs on load to failure (SMD -0.62, 95% CI -1.26-0.02, $p=0.06$).

Conclusions: The current literature does not provide sufficient evidence for or against the use of NSAIDs following acute injury or surgical repair of the tendon-bone interface.

[2018-Borgeat, A., C. Ofner, A. Saporito, M. Farshad & J. Aguirre. The effect of nonsteroidal anti-inflammatory drugs on bone healing in humans: A qualitative, systematic review. *Journal of Clinical Anesthesia* 49: 92-100.](#)

Study objective: Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used in postoperative pain management. While an increasing number of in vitro and animal studies point toward an inhibitory effect of NSAIDs on bone healing process, the few existing retro- and prospective clinical studies present conflicting data.

Design: The aim of this qualitative, systematic review was to investigate the impact of perioperative use of NSAIDs in humans on postoperative fracture/spinal fusion healing compared to other used analgesics measured as fracture nonunion with radiological control.

Patients/interventions: We performed a systematic literature search of the last 38years using PubMed Embase and the Cochrane Controlled Trials Register including retro- and prospective clinical, human trials assessing the effect of NSAIDs on postoperative fracture/spinal fusion healing when used for perioperative pain management with a radiological follow up to assess eventual nonunion. Due to different study designs, drugs, dosages/exposition times and different methods to assess fracture nonunion, these studies were not pooled for a meta-analysis. A descriptive summary of all studies, level of evidence, study quality and study bias assessment using different scores were used.

Main results: Three prospective randomized controlled studies and thirteen retrospective cohort human studies were identified for a total of 12'895 patients. The overall study quality was low according to Jadad and Oxford Levels of Evidence scores.

Conclusions: Published results of human trials did not show strong evidence that NSAIDs for pain therapy after fracture osteosynthesis or spinal fusion lead to an increased nonunion rate. Reviewed studies present such conflicting data, that no clinical recommendation can be made regarding the appropriate use of NSAIDs in this context. Considering laboratory data of animal, human tissue research and recommendation of clinical reviews, a short perioperative exposition to NSAIDs is most likely not deleterious. However, randomized, controlled studies are warranted to support or refute this hypothesis.

2018-Vuurberg, G., A. Hoorntje, L. M. Wink, B. F. W. van der Doelen, M. P. van den Bekerom, R. Dekker, C. Niek van Dijk, R. Krips, M. C. M. Loogman, M. L. Ridderikhof, F. F. Smithuis, S. A. S. Stufkens, E. A. L. M. Verhagen, R. A. de Bie & G. M. M. J. Kerkhoffs. Diagnosis, treatment and prevention of ankle sprains: update of an evidence-based clinical guideline. *British Journal of Sports Medicine* 52 (15): 956.

This guideline aimed to advance current understandings regarding the diagnosis, prevention and therapeutic interventions for ankle sprains by updating the existing guideline and incorporate new research. A secondary objective was to provide an update related to the cost-effectiveness of diagnostic procedures, therapeutic interventions and prevention strategies. It was posited that subsequent interaction of clinicians with this guideline could help reduce health impairments and patient burden associated with this prevalent musculoskeletal injury. The previous guideline provided evidence that the severity of ligament damage can be assessed most reliably by delayed physical examination (4-5 days post trauma). After correct diagnosis, it can be stated that even though a short time of immobilisation may be helpful in relieving pain and swelling, the patient with an acute lateral ankle ligament rupture benefits most from use of tape or a brace in combination with an exercise programme.

New in this update: Participation in certain sports is associated with a heightened risk of sustaining a lateral ankle sprain. Care should be taken with non-steroidal anti-inflammatory drugs (NSAIDs) usage after an ankle sprain. They may be used to reduce pain and swelling, but usage is not without complications and NSAIDs may suppress the natural healing process. Concerning treatment, supervised exercise-based programmes preferred over passive modalities as it stimulates the recovery of functional joint stability. Surgery should be reserved for cases that do not respond to thorough and comprehensive exercise-based treatment. For the prevention of recurrent lateral ankle sprains, ankle braces should be considered as an efficacious option.

2018-Wheatley, B. M., K. E. Nappo, D. L. Christensen, A. M. Holman, D. I. Brooks & B. K. Potter. Effect of NSAIDs on Bone Healing Rates: A Meta-analysis. *Journal of the American Academy of Orthopaedic Surgeons* 27 (7): e330-e336.

Introduction: NSAIDs inhibit osteogenesis and may result in delayed union or nonunion. The purpose of this meta-analysis was to determine whether their use leads to delayed union or nonunion.

Methods: We systematically reviewed the literature reporting the effect of NSAIDs on bone healing. We included studies of pediatric and adult patients NSAID exposure and healing bone. The outcomes of interest were delayed union, nonunion, or pseudarthrosis with at least six months of follow-up. A maximum likelihood random-effects model was used to conduct meta-analysis and meta-regression.

Results: NSAID exposure increased delayed union or nonunion (odds ratio [OR], 2.07; confidence interval [CI], 1.19 to 3.61). No effect was noted in pediatrics (OR, 0.58; CI, 0.27 to 1.21) or low dose/short duration of exposure (OR, 1.68; CI, 0.63 to 4.46).

Conclusion: Analysis of the literature indicates a negative effect of NSAIDs on bone healing. In pediatric patients, NSAIDs did not have a significant effect. The effect may be dose or time dependent because low-dose/short-duration exposure did not affect union rates.

[2018-Zhao-Flemming, H., A. Hand, K. Zhang, R. Polak, A. Northcut, D. Jacob, S. Dissanaiké & K. P. Rumbaugh. Effect of non-steroidal anti-inflammatory drugs on post-surgical complications against the backdrop of the opioid crisis. *Burns & Trauma* 6 \(25\): s41038-018-0128-x.](#)

The USA is currently going through an opioid crisis, associated with tremendous economic and societal impacts. In response to this crisis, healthcare professionals are looking for alternative pain management methods, and non-steroidal anti-inflammatory drugs (NSAIDs) are a sensible choice because of their effectiveness after surgical procedures. However, before surgeons start prescribing NSAIDs in place of opioids, it is crucial to first understand their potential post-surgical complications. The goal of this review is to summarize the data obtained through both animal and human studies, which suggest how a dramatic increase in NSAID use may affect these post-surgical complications. We first provide a short review outlining the mechanisms of action of NSAIDs, followed by a summary of animal studies, which show a trend towards the negative effects of NSAIDs on wound healing and an association between NSAID use and wound infections. Lastly, we present evidence from human studies on the association of NSAIDs with the following complications: anastomotic leaks, necrotizing soft tissue infections, bleeding complications, orthopedic injuries, wound healing, and cancer care. The human studies are much more variable in their conclusions as to whether NSAIDs are beneficial or not, with the only strong evidence showing that NSAIDs inhibit bone healing. This may partially be explained by male and female differences in response to NSAIDs as many animal studies showing the inhibitory effects of NSAIDs were performed on females, while all the human studies were performed with both sexes. We conclude that strong caution should be used in the prescription of NSAIDs, especially in female patients, but larger scale studies are warranted before solid recommendations can be made.

[2017-Doherty, C., C. Bleakley, E. Delahunt & S. Holden. Treatment and prevention of acute and recurrent ankle sprain: An overview of systematic reviews with meta-analysis. *British Journal of Sports Medicine* 51 \(2\): 113-125.](#)

Background: Ankle sprains are highly prevalent with high risk of recurrence. Consequently, there are a significant number of research reports examining strategies for treating and preventing acute and recurrent sprains (otherwise known as chronic ankle instability (CAI)), with a coinciding proliferation of review articles summarising these reports.

Objective: To provide a systematic overview of the systematic reviews evaluating treatment strategies for acute ankle sprain and CAI.

Design: Overview of intervention systematic reviews.

Participants: Individuals with acute ankle sprain/CAI.

Main outcome measurements: The primary outcomes were injury/reinjury incidence and function.

Results: 46 papers were included in this systematic review. The reviews had a mean score of 6.5/11 on the AMSTAR quality assessment tool. There was strong evidence for bracing and moderate evidence for neuromuscular training in preventing recurrence of an ankle sprain. For the combined outcomes of pain, swelling and function after an acute sprain, there was strong evidence for non-steroidal anti-inflammatory drugs and early mobilisation, with moderate evidence supporting exercise and manual therapy techniques. There was conflicting evidence regarding the efficacy of surgery and acupuncture for the treatment of acute ankle sprains. There was insufficient evidence to support the use of ultrasound in the treatment of acute ankle sprains.

Conclusions: For the treatment of acute ankle sprain, there is strong evidence for non-steroidal anti-inflammatory drugs and early mobilisation, with moderate evidence supporting exercise and manual therapy techniques, for pain, swelling and function. Exercise therapy and bracing are supported in the prevention of CAI.

[2017-Duchesne E., S. S. Dufresne & N. A. Dumont. Impact of Inflammation and Anti-inflammatory Modalities on Skeletal Muscle Healing: From Fundamental Research to the Clinic. *Physical Therapy* 97 \(8\): 807-817.](#)

Anti-inflammatory modalities are commonly used for the treatment of various musculoskeletal injuries. Although inflammation was originally believed to interfere with skeletal muscle regeneration, several recent studies have highlighted the beneficial effects of inflammatory cells on muscle healing. This discrepancy is attributable to an evolving understanding of the complex inflammatory process. To better appreciate the paradoxical roles of inflammation, clinicians must have a better comprehension of the fundamental mechanisms regulating the inflammatory response. In this perspective article, cellular, animal, and human studies were analyzed to summarize recent knowledge regarding the impact of inflammation on muscle regeneration in acute or chronic conditions. The effect of anti-inflammatory drugs on the treatment of various muscle injuries was also considered. Overall, this work aims to summarize the current state of the literature on the inflammatory process associated with muscle healing in order to give clinicians the necessary tools to have a more efficient and evidence-based approach to the treatment of muscle injuries and disorders.

2017-Morelli, K. M., L. B. Brown & G. L. Warren. [Effect of NSAIDs on Recovery From Acute Skeletal Muscle Injury: A Systematic Review and Meta-analysis. *The American Journal of Sports Medicine* 46 \(1\): 224-233.](#)

Background: There is debate as to whether the use of nonsteroidal anti-inflammatory drugs (NSAIDs) is beneficial after acute skeletal muscle injury. Some studies have suggested that NSAID use may be detrimental to injured muscle.

Purpose: To determine whether NSAID use affects recovery from skeletal muscle injury as assessed by strength loss, soreness, and/or blood creatine kinase level.

Study Design: Systematic review and meta-analysis.

Methods: An extensive systematic review was completed searching 16 databases (eg, PubMed, Cochrane Library, EMBASE). Inclusion criteria were (1) acute injury to skeletal muscle, (2) use of a control condition, (3) certainty of the NSAID dose administered, and (4) use of 1 or more of the 3 desired outcome measures. A total of 5343 study reports were screened, of which 41 studies were deemed suitable for inclusion. The standardized mean difference was used as the effect size (ES) and was calculated such that a positive ES indicated NSAID efficacy. Meta-analyses were run using a random-effects model.

Results: For all studies, time points after injury, and injury markers combined, NSAID use was found to elicit a small to medium, significant decrease in the markers of injury (overall ES = +0.34; P = .0001). Because heterogeneity in study ES was apparent (ie, Q -df = 52.4, P = .000005; I^2 = 57%), subgroup meta-analyses and meta-regressions were run in an attempt to explain the heterogeneity. In human studies, study ESs were higher when lower body muscles were injured (P = .045). In animal studies, study ESs were lower with longer NSAID administration durations (P = .023) and at longer follow-up times after injury (P = .010).

Conclusion: Overall, our analysis supports NSAID use for reducing strength loss, soreness, and blood creatine kinase level after an acute muscle injury, at least for humans and in the short term. Additional research is required to determine why NSAID use appears to be more effective when lower-body muscles in humans are injured. It would also be important to determine why NSAID use appears detrimental at later times after injury in animals but not humans.

[2017-Singh, D. P., Z. Barani Lonbani, M. A. Woodruff, T. J. Parker, R. Steck & J. M. Peake. Effects of topical icing on inflammation, angiogenesis, revascularization, and myofiber regeneration in skeletal muscle following contusion injury. *Frontiers in Physiology* 8: 93.](#)

Contusion injuries in skeletal muscle commonly occur in contact sport and vehicular and industrial workplace accidents. Icing has traditionally been used to treat such injuries under the premise that it alleviates pain, reduces tissue metabolism, and modifies vascular responses to decrease swelling. Previous research has examined the effects of icing on inflammation and microcirculatory dynamics following muscle injury. However, whether icing influences angiogenesis, collateral vessel growth, or myofiber regeneration remains unknown. We compared the effects of icing vs. a sham treatment on the presence of neutrophils and macrophages; expression of CD34, von Willebrands factor (vWF), vascular endothelial growth factor (VEGF), and nestin; vessel volume; capillary density; and myofiber regeneration in skeletal after muscle contusion injury in rats. Muscle tissue was collected 1, 3, 7, and 28 d after injury. Compared with uninjured rats, muscles in rats that sustained the contusion injury exhibited major necrosis, inflammation, and increased expression of CD34, vWF, VEGF, and nestin. Compared with the sham treatment, icing attenuated and/or delayed neutrophil and macrophage infiltration; the expression of vWF, VEGF, and nestin; and the change in vessel volume within muscle in the first 7 d after injury ($P < 0.05$). By contrast, icing did not influence capillary density in muscle 28 d after injury ($P = 0.59$). The percentage of immature myofibers relative to the total number of fibers was greater in the icing group than in the sham group 28 d after injury ($P = 0.026$), but myofiber cross-sectional area did not differ between groups after 7 d ($P = 0.35$) and 28 d ($P = 0.30$). In conclusion, although icing disrupted inflammation and some aspects of angiogenesis/revascularization, these effects did not result in substantial differences in capillary density or muscle growth.

2016-Shibaguchi, T., T. Sugiura, T. Fujitsu, T. Nomura, T. Yoshihara, H. Naito, T. Yoshioka, A. Ogura & Y. Ohira. Effects of icing or heat stress on the induction of fibrosis and/or regeneration of injured rat soleus muscle. *The Journal of Physiological Sciences* 66: 345-357.

The effects of icing or heat stress on the regeneration of injured soleus muscle were investigated in male Wistar rats. Bupivacaine was injected into soleus muscles bilaterally to induce muscle injury. Icing (0 °C, 20 min) was carried out immediately after the injury. Heat stress (42 °C, 30 min) was applied every other day during 2-14 days after the bupivacaine injection. Injury-related increase in collagen deposition was promoted by icing. However, the level of collagen deposition in heat-stressed animals was maintained at control levels throughout the experimental period and was significantly lower than that in icing-treated animals at 15 and 28 days after bupivacaine injection. Furthermore, the recovery of muscle mass, protein content, and muscle fiber size of injured soleus toward control levels was partially facilitated by heat stress. These results suggest that, compared with icing, heat stress may be a beneficial treatment for successful muscle regeneration at least by reducing fibrosis.

[2015-Jones, P., S. R. Dalziel, R. Lamdin, J. L. Miles-Chan & C. Frampton. Oral non-steroidal anti-inflammatory drugs versus other oral analgesic agents for acute soft tissue injury. *Cochrane Database of Systematic Reviews* \(7\): CD007789.](#)

Introduction and aims: Strains, sprains and bruises are common soft tissue injuries, and people with these injuries often require pain relief. This is usually in the form of a tablet taken orally (swallowed). Many different types of oral painkillers are available to treat such injuries, but we do not know whether any of these are any better than any of the others. We sought to identify if there were any differences in people's pain, swelling or function when these injuries were treated with oral non-steroidal anti-inflammatory drugs (NSAIDs) compared with paracetamol, opioids (e.g. codeine), complementary or alternative medicines (CAM), or any combinations of these. We also looked for adverse effects that could occur as a result of using these medicines.

Results of our search and description of studies: We searched different medical databases up to September 2014. We looked for studies that involved people with soft tissue injuries who had been assigned to either an oral NSAID or an alternative oral painkiller. We included 16 studies, with a total of 2144 participants. Seven of these studies included people with ankle sprain only. Two studies included children only. Most of the participants of the other studies were young adults, and there were slightly more males than females. The studies tested three comparisons: NSAIDs versus paracetamol (nine studies); NSAIDs versus opioids (four studies); NSAIDs versus the combination of paracetamol and an opioid (four studies). In many cases, the strength (dose) of one of the drugs being compared was less than recommended. Studies reported outcomes at times varying from one hour after taking medication up to 10 to 14 days.

Quality of the evidence: The evidence available for most outcomes was either low or very low quality. This means that we are unsure of the reliability of these results.

Results: We found no evidence for an important difference between NSAIDs and paracetamol for people with strains, sprains and bruises for pain relief, swelling or return to function at seven days or over. However, there was some evidence that people treated with NSAIDs had slightly more side-effects related to the stomach or intestines.

Although there was some evidence to suggest a greater return to function at seven days and fewer side-effects for people with sprains, strains and bruises using an NSAID compared with an opioid, we cannot say if this would apply to drugs that are currently available. This is

because most of the evidence came from a study that tested an NSAID that is no longer on the market.

We found no evidence for an important difference between NSAIDs and a combination of paracetamol and opioid for people with sprains, strains and bruises regarding pain relief, swelling, return to function at seven days or over, or gut-related side-effects. However, the combination painkiller used in the studies is not now in common use. This means that we cannot be sure that these results would currently apply.

We found no studies comparing NSAIDs and complementary and alternative medicines. Also, no studies looked at the risk of re-injury after treatment.

Conclusions: This review found low or very low-quality but consistent evidence showing no important difference between NSAIDs and paracetamol, opioids or a combination of paracetamol and opioid in pain or swelling after a soft tissue injury. There is low-quality evidence of more gut-related complications with NSAIDs compared with paracetamol. Although there is either low- or very low-quality evidence of better function and fewer adverse events with NSAIDs compared with opioid-containing analgesics, one study dominated this evidence using a now unavailable NSAID and is therefore of uncertain applicability. Further research is required to determine whether there is any difference in return to function or adverse effects between different types of NSAIDs versus paracetamol.

[2015-Yerhot, P., T. Stensrud, B. Wienkers & C. Durall. The Efficacy of Cryotherapy for Improving Functional Outcomes Following Lateral Ankle Sprains. *Annals of Sports Medicine and Research* 2 \(2\): 1015.](#)

Cryotherapy is frequently used to treat acute injuries despite minimal outcomes-based evidence supporting this practice. A thorough review of the literature was conducted to ascertain the efficacy of cryotherapy for improving function after acute lateral ankle sprain (ALAS). Three studies met the inclusion criteria and were selected for review. None of the reviewed studies demonstrated that cryotherapy is more efficacious than control interventions for improving function after ALAS, although their poor methodology, impractical cryotherapy application parameters, and incomplete statistical reporting make it challenging to draw conclusions with any degree of confidence. Despite these methodological shortcomings, the reviewed studies are frequently cited to support the use of cryotherapy as a treatment agent for ALAS. Since the use of cryotherapy is ubiquitous, and a therapeutic “gold standard” against which other interventions are sometimes compared, there is a need to scrutinize its efficacy with high quality outcomes-based research instead of relying on historical convention or anecdotal reports.

2013-Tseng, C.-Y., J.-P. Lee, Y.-S. Tsai, S.-D. Lee, C.-L. Kao, T.-C. Liu, C.-H. Lai, M. B. Harris & C.-H. Kuo. Topical Cooling (Icing) Delays Recovery From Eccentric Exercise-Induced Muscle Damage. *Journal of Strength and Conditioning Research* 27 (5): 1354-1361.

It is generally thought that topical cooling can interfere with blood perfusion and may have positive effects on recovery from a traumatic challenge. This study examined the influence of topical cooling on muscle damage markers and hemodynamic changes during recovery from eccentric exercise. Eleven male subjects (age 20.2 ± 0.3 years) performed 6 sets of elbow extension at 85% maximum voluntary load and randomly assigned to topical cooling or sham groups during recovery in a randomized crossover fashion. Cold packs were applied to exercised muscle for 15 minutes at 0, 3, 24, 48, and 72 hours after exercise. The exercise significantly elevated circulating creatine kinase-MB isoform (CK-MB) and myoglobin levels. Unexpectedly, greater elevations in circulating CK-MB and myoglobin above the control level were noted in the cooling trial during 48-72 hours of the post-exercise recovery period. Subjective fatigue feeling was greater at 72 hours after topical cooling compared with controls. Removal of the cold pack also led to a protracted rebound in muscle hemoglobin concentration compared with controls. Measures of interleukin (IL)-8, IL-10, IL-1 β , and muscle strength during recovery were not influenced by cooling. A peak shift in IL-12p70 was noted during recovery with topical cooling. These data suggest that topical cooling, a commonly used clinical intervention, seems to not improve but rather delay recovery from eccentric exercise-induced muscle damage.

2012-van den Bekerom, M. P. J., P. A.A. Struijs, L. Blankevoort, L. Welling, C. N. van Dijk & G. M. M. J. Kerkhoffs. What Is the Evidence for Rest, Ice, Compression, and Elevation Therapy in the Treatment of Ankle Sprains in Adults?. *Journal of Athletic Training* 47 (4): 435-443.

Context: Ankle sprains are common problems in acute medical care. The variation in treatment observed for the acutely injured lateral ankle ligament complex in the first week after the injury suggests a lack of evidence-based management strategies for this problem.

Objective: To analyze the effectiveness of applying rest, ice, compression, and elevation (RICE) therapy begun within 72 hours after trauma for patients in the initial period after ankle sprain.

Study Selection: Eligible studies were published original randomized or quasi-randomized controlled trials concerning at least 1 of the 4 sub-treatments of RICE therapy in the treatment of acute ankle sprains in adults.

Data Sources: MEDLINE, Cochrane Clinical Trial Register, CINAHL, and EMBASE. The lists of references of retrieved publications also were checked manually.

Data Extraction: We extracted relevant data on treatment outcome (pain, swelling, ankle mobility or range of motion, return to sports, return to work, complications, and patient satisfaction) and assessed the quality of included studies. If feasible, the results of comparable studies were pooled using fixed- or random-effects models.

Data Synthesis: After deduction of the overlaps among the different databases, evaluation of the abstracts, and contact with some authors, 24 potentially eligible trials remained. The full texts of these articles were retrieved and thoroughly assessed as described. This resulted in the inclusion of 11 trials involving 868 patients. The main reason for exclusion was that the authors did not describe a well-defined control group without the intervention of interest.

Conclusions: Insufficient evidence is available from randomized controlled trials to determine the relative effectiveness of RICE therapy for acute ankle sprains in adults. Treatment decisions must be made on an individual basis, carefully weighing the relative benefits and risks of each option, and must be based on expert opinions and national guidelines.

[2011-Takagi, R., N. Fujita, T. Arakawa, S. Kawada, N. Ishii & A. Miki. Influence of icing on muscle regeneration after crush injury to skeletal muscles in rats. *Journal of Applied Physiology* 110 \(2\): 382-388.](#)

The influence of icing on muscle regeneration after crush injury was examined in the rat extensor digitorum longus. After the injury, animals were randomly divided into nonicing and icing groups. In the latter, ice packs were applied for 20 min. Due to the icing, degeneration of the necrotic muscle fibers and differentiation of satellite cells at early stages of regeneration were retarded by ~1 day. In the icing group, the ratio of regenerating fibers showing central nucleus at 14 days after the injury was higher, and cross-sectional area of the muscle fibers at 28 days was evidently smaller than in the nonicing group. Besides, the ratio of collagen fibers area at 14 and 28 days after the injury in the icing group was higher than in the nonicing group. These findings suggest that icing applied soon after the injury not only considerably retarded muscle regeneration but also induced impairment of muscle regeneration along with excessive collagen deposition. Macrophages were immunohistochemically demonstrated at the injury site during degeneration and early stages of regeneration. Due to icing, chronological changes in the number of macrophages and immunohistochemical expression of transforming growth factor (TGF)- β 1 and IGF-I were also retarded by 1 to 2 days. Since it has been said that macrophages play important roles not only for degeneration, but also for muscle regeneration, the influence of icing on macrophage activities might be closely related to a delay in muscle regeneration, impairment of muscle regeneration, and redundant collagen synthesis.

2007-Ferry, S. T., L. E. Dahners, H. M. Afshari & P. S. Weinhold. The Effects of Common Anti-Inflammatory Drugs on the Healing Rat Patellar Tendon. *The American Journal of Sports Medicine* 35 (8): 1326-1333.

Background: Tendon injuries that occur at the osteotendinous junction are commonly seen in clinical practice and range from acute strain to rupture. Nonsteroidal anti-inflammatory drugs are often prescribed in the treatment of these conditions, but the effect that these agents may have on the healing response at the bone-tendon junction is unclear.

Hypothesis: In response to an acute injury at the osteotendinous junction, the healing patellar tendon will have inferior biomechanical properties with administration of anti-inflammatory drugs as compared with acetaminophen and control.

Study Design: Controlled laboratory study.

Methods: A total of 215 Sprague-Dawley rats underwent transection of the patellar tendon at the inferior pole of the patella, which was subsequently stabilized with a cerclage suture. The animals were then randomized into 7 groups and administered 1 of the following analgesics for 14 days: ibuprofen, acetaminophen, naproxen, piroxicam, celecoxib, valdecoxib, or control. At 14 days, all animals were sacrificed, and the extensor mechanism was isolated and loaded to failure. Biochemical analysis of the repair site tissue was performed. Animal activity throughout the study was monitored using a photoelectric sensor system.

Results: The control group demonstrated greater maximum load compared with the celecoxib, valdecoxib, and piroxicam groups ($P < .05$). The acetaminophen and ibuprofen groups were also significantly stronger than the celecoxib group ($P < .05$) but not statistically different than the control group. A total of 23 specimens had failure of the cerclage suture with the following distribution: control (0/23), ibuprofen (0/23), acetaminophen (0/24), naproxen (3/24), piroxicam (4/24), celecoxib (6/22), and valdecoxib (10/24). The difference in distribution of the failures was significant ($P < .001$).

Conclusions: Anti-inflammatory drugs, with the exception of ibuprofen, had a detrimental effect on healing strength at the bone-tendon junction as demonstrated by decreased failure loads and increased failures of the cerclage suture. Acetaminophen had no effect on healing strength. The biomechanical properties paralleled closely with the total collagen content at the injury site, suggesting that these agents may alter healing strength by decreasing collagen content.

Clinical Relevance: Selective and nonselective cyclooxygenase (COX) inhibitors should be used judiciously in the acute period after injury or surgical repair at the bone-tendon junction.

[2004-Bleakley, C., S. McDonough & D. MacAuley. The Use of Ice in the Treatment of Acute Soft-Tissue Injury: A Systematic Review of Randomized Controlled Trials. *The American Journal of Sports Medicine* 32 \(1\): 251-261.](#)

Background: There are wide variations in the clinical use of cryotherapy, and guidelines continue to be made on an empirical basis.

Study Design: Systematic review assessing the evidence base for cryotherapy in the treatment of acute soft-tissue injuries.

Methods: A computerized literature search, citation tracking, and hand searching were carried out up to April 2002. Eligible studies were randomized-controlled trials describing human subjects recovering from acute soft-tissue injuries and employing a cryotherapy treatment in isolation or in combination with other therapies. Two reviewers independently assessed the validity of included trials using the Physiotherapy Evidence Database (PEDro) scale.

Results: Twenty-two trials met the inclusion criteria. There was a mean PEDro score of 3.4 out of 10. There was marginal evidence that ice plus exercise is most effective, after ankle sprain and postsurgery. There was little evidence to suggest that the addition of ice to compression had any significant effect, but this was restricted to treatment of hospital inpatients. Few studies assessed the effectiveness of ice on closed soft-tissue injury, and there was no evidence of an optimal mode or duration of treatment.

Conclusion: Many more high-quality trials are needed to provide evidence-based guidelines in the treatment of acute soft-tissue injuries.

[2004-Martuzzi, M. & J. Tickner. *The precautionary principle: protecting public health, the environment and the future of our children*. World Health Organization.](#)

The purpose of this publication is to provide the background rationale and support for WHO's working paper Dealing with uncertainty - how can the precautionary principle help protect the future of our children?, prepared for the Fourth Ministerial Conference on Environment and Health held in Budapest, Hungary, in June 2004. The debate around the precautionary principle has provided many insights into how to improve public health decision-making under conditions of uncertainty. This publication should further support approaches to attaining the concurrent goals of

1. protecting adults, children and future generations and the ecosystems on which we depend and
2. enhancing economic development, sustainability and innovation in science, research and policy.

1989-Sloan, J. P., R. Hain & R. Pownall. Clinical benefits of early cold therapy in accident and emergency following ankle sprain. *Emergency Medicine Journal* 6: 1-6.

One hundred and forty-three patients presenting with ankle sprains within 24 h of injury were entered into a double blind study. Treatment consisted of a standardized regime of high dose non-steroidal anti-inflammatory medication and an elastic support for all patients, who were then randomly allocated to two groups. One group received immediate cold therapy, the other received simulated therapy. Assessments made at 7 days showed a trend in favour of the group receiving cold therapy, although this did not reach significance. It is concluded that cold therapy together with compression may have a beneficial effect but that a single application in the accident and emergency department is not justified when a background therapy of non-steroidal anti-inflammatory medication is given.