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## SHOULD WE UTILIZE ICE FOLLOWING ORTHOBIOLOGIC PROCEDURES?

Morey J. Kolber, PT, PhD<sup>1</sup>, Joseph Purita, MD<sup>2</sup>, William J. Hanney, DPT, PhD<sup>3</sup>, Kristina Martin, DPT<sup>1</sup>

<sup>1</sup>Department of Physical Therapy, Nova Southeastern University, Fort Lauderdale, Florida <sup>2</sup>PUR-FORM, Boca Raton, Florida <sup>3</sup>University of Central Florida, Orlando, Florida

Author for correspondence: Morey J. Kolber: moreykolber@gmail.com

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#### Abstract

Ice applications have been used for centuries to decrease pain and inflammation following orthopedic procedures and musculoskeletal injuries. While there is merit to using ice, more recent advancements in research and recovery have cast doubt on the efficacy of icing. Namely, concerns over suppressing the natural healing process have steered many clinicians away from the routine use of ice. This article presents a balanced perspective on both the merits and limitations of existing research on the use of ice. Recommendations for post-procedural management of patients following orthobiologic procedures and the cellular niche are presented.

Keywords: Cryotherapy, Inflammation, Treatment, Healing, Orthobiologic, Swelling

### SHOULD WE UTILIZE ICE FOLLOWING ORTHOBIOLOGIC PROCEDURES?

Ice applications, also referred to as cryotherapy, have been used for centuries to decrease pain and inflammation following an injury or surgical procedure.<sup>1</sup> The popularity of cryotherapy emerged in 1978 from a textbook entitled the Sportsmedicine *Book* by Dr. Gabe Mirkin,<sup>2</sup> who at the time coined the Rest, Ice, Compression, Elevation (R.I.C.E.) protocol. This protocol was the standard of care following injury and surgery for decades and is still used today. While there is merit to the R.I.C.E. protocol, advancements in research and recovery methods have cast doubt on the once-accepted protocol as a one-size-fits-all response to injury and postsurgical recovery.<sup>3–5</sup> While most would agree that the individual elements of R.I.C.E have merit, more recent commentary and review papers have recommended abandoning post-injury ice applications.

Moreover, the decision to ice has been questioned following orthobiologic procedures. Thus, the scope of this perspective commentary will focus on the decision "to ice or not to ice" following orthobiologic procedures.

A brief, albeit necessary, overview of the relevant literature is presented to provide a foundation for a recommendation in favor of or against ice applications. While local ice applications have been a standard of care in orthopedic practice, the potential for delaying natural post-injury healing processes has been an area of contention.<sup>3,4,6</sup> These concerns, largely unsupported in the outcome-based clinical literature, stem from the potential of ice to cause vasoconstriction of blood vessels,<sup>7</sup> which may limit the ability of healing agents to reach the site of injury.

Opponents of ice applications largely base their position on the aforementioned issue of

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vasoconstriction and previously published animal studies. For example, in one published editorial, the authors state that "even if mostly analgesic, ice could potentially disrupt inflammation, angiogenesis, and revascularization, delay neutrophil and macrophage infiltration as well as increase immature myofibers."<sup>4</sup> While there is merit in the authors' statement, a key point in this statement other than the word "potentially" is the fact that the authors reference a rat study. Most certainly, non-human research should be considered; however, it would be shortsighted to generalize findings from non-human studies to humans. Nevertheless, a brief overview of the research that has cast doubt on the appropriateness of ice applications following injury is presented to understand the decision to ice further or not to ice following orthobiologic procedures.

The opponents of ice routinely reference three key published studies. All three of the studies utilized an experimentally induced injury to rat muscle.5,8,9 In one study, rats with an experimental muscle crush injury were assigned to an ice or no ice group.<sup>5</sup> The study showed that icing immediately after injury suppressed the number of macrophages, insulin-like growth factor (IGF-1) and transforming growth factor (TGF-B1) shortly after the injury. However, after a few days, levels were comparable in both groups. At the 6-12 hour post-injury time points, both groups had characteristic features of necrosis; however, these features were less in the ice group. Muscle cross-sectional area and the size of regenerating muscle cells were larger in the no-ice groups, suggesting that ice may indeed suppress the inflammatory response in the first few days after injury and delay the morphological regeneration of rat muscle. Similar to the aforementioned study, another study on rats following a muscle crush injury showed that rats who received intermittent ice applications every 2 hours after injury for 2 days experienced a suppressed injury response for the first few days compared to rats that did not receive ice.<sup>8</sup> Specifically, changes in macrophages, IGF-1, tumor necrosis factor alpha, and matrix metalloproteinase-9 occurred during the first 3-days; however, differences were no longer present by day seven. Interestingly, the authors reported that icing did not

alter the muscle regeneration process or collagen remodeling. In another study using rats, icing was shown to disrupt inflammation and some aspects of angiogenesis; however, effects did not ultimately result in differences in capillary density or muscle growth when compared to the sham icing group.<sup>9</sup>

While the aforementioned studies do support a short-term suppression of healing responses to muscle injury in rats, their ultimate effect on recovery is uncertain with regard to muscle regeneration in humans. Furthermore, the suppression of healing responses in muscle may not translate to other tissues (e.g., ligament, tendon, cartilage etc.). Of particular interest, and unrelated to the scope of the article, is a body of evidence suggesting that post-exercise ice applications may result in systemic reductions in IGF and protein synthesis following exercise in healthy athletes.<sup>10,11</sup> This body of evidence provides meaningful guidance for recovery methods following exercise; however, the results cannot be generalized to post-injury or post-procedural scenarios.

Unfortunately, at the time of this commentary, there is no convincing evidence that icing alone following an injury or an orthopedic procedure may impede healing in human subjects. However, the absence of evidence does not imply evidence of absence, and clinicians should make decisions based on multiple factors, including the generalizability of studies (e.g., non-human versus human), patients' pain levels, and recovery of function. Thus, a brief overview of the potentially positive outcomes of ice application is warranted.

Evidence of the benefits of cryotherapy after injury has supported a pain-relieving analgesic effect via reduced nerve conduction velocity, with additional benefits that include the potential to reduce swelling, reduced delayed onset muscle soreness from exercise, and enhanced return to sport.<sup>1,12–17</sup> From a surgical perspective, there seems to be evidence in support of post-operative icing following anterior cruciate ligament reconstruction (ACL) surgery. In one study following ACL surgery, patients were randomized into a compression group with ice and ice packs alone. The compression with the ice group significantly reduced pain and joint effusion compared to the ice-only group.<sup>18</sup> These results offer

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a favorable perspective for post-procedural icing and compression. Further evidence from a systematic review indicated that patients receiving ice following an ACL reconstruction surgery had significantly reduced pain compared to patients without ice.<sup>19</sup> A key point here is the word "pain," which would generally not be evaluated in rat studies.

In another study on patients following acute ankle sprains, local ice applications were compared to neurocryostimulation (ice vapor spraying with carbon dioxide) in patients receiving physiotherapy. Results indicated that both groups improved in all outcome measures (edema, range of motion, function, pain) at all follow-up time points, suggesting a favorable cooling and temperature reduction effect, which supports icing.<sup>20</sup> Furthermore, a review on the efficacy of ice following soft tissue injuries and surgeries indicated that ice is effective for pain reduction.<sup>21</sup> However, it is not more effective than compression or physical rehabilitation interventions.

The efficacy of an updated R.I.C.E model referred to as P.O.L.I.C.E, (protection, optimal loading, ice, compression, and elevation) was evaluated in patients following ankle sprain injuries with favorable outcomes when compared to protection, rest, ice, compression, and elevation, suggesting that the addition of optimal loading is a critical consideration following injury.22 Adding optimal loading following injuries and orthopedic surgeries, including orthobiologic procedures, is necessary to a patient's care and should not be overlooked. Optimal loading of tissue, referred to as mechanotransduction, produces cellular and molecular effects synergistic to orthobiologic procedures.<sup>23-28</sup> Specifically, evidence has shown benefits of collagen synthesis, increased IGF-1 and mechano-growth factor, increased interleukin-10, and decreased markers of cartilage degradation from exercises and activities that load the soft tissue and joints.<sup>23–28</sup> Delays in loading may lead to delays in activating mechanotransduction. The caveat here is that optimal loading depends on a patient's pain levels, and one might argue that withholding ice may suppress physical activity. Most certainly, evidence of whether or not to ice following orthobiologic procedures would best be evaluated with patient-based data. Unfortunately, this evidence is unavailable at the time of this perspective writing, and decision making must utilize available evidence from non-orthobiologic studies. Considerations should be made within the context of generalizability of the available evidence and the clinician's goal of maximizing both post-procedural physical function and the cellular and molecular benefits.

In summary, a body of evidence suggests that ice applications suppress the normal muscle injury response in rats; however, the generalizability of these findings to humans is not clear. What is clear is the efficacy of ice for reducing post-procedural pain and swelling. Thus, withholding ice applications for patients in the acute stage of recovery may increase pain levels and potentially suppress physical activity. It is important to promote an environment that encourages early physical activity (protected loading) and the resumption of activities of daily living. Early physical activity improves a patient's ability to function and enhances the synergistic benefit of increasing the cellular and molecular benefits of orthobiologic procedures. Delays in resumption of physical activity (loading) may reduce the desirable cellular and molecular benefits of an orthobiologic intervention. Thus, intermittent 15-minute ice pack applications or cold water immersion for the first few days is recommended<sup>13</sup> to reduce pain and swelling and facilitate protected loading. Lastly, it seems local ice applications following exercise and beyond the acute inflammatory phase is not warranted.

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