GAME READY®

Cost Analysis of Cryotherapy and Compression Products

Objective

To establish the scientific basis for applying cryotherapy and compression, review a variety of products that address this therapeutic need and analyze their relative health economics.

Summary

Discussion The RICE regimen (rest, ice, compression and elevation) is the commonly accepted best practice for the treatment of musculoskeletal pain, injury or post-operative recovery. The function of cold therapy (the "ice" portion of the equation) is primarily to control swelling and moderate pain and muscle spasms. Traditionally applied static compression – such as an ACE bandage – aids the mitigation of edema formation and removal of swelling achieved through cryotherapy. While the therapeutic value of these two treatments in moderating pain and swelling has long been recognized by front-line practitioners, a substantial amount of literature also exists today to support the use of these therapies for management of these symptoms.

Further, there is growing evidence that active or intermittent forms of pneumatic compression have demonstrated the ability in clinical studies to go beyond moderation of symptoms to stimulate tissue healing, and to help optimize and accelerate the body's natural repair mechanisms. A novel form of pneumatic compression intermittently applied in systematic conjunction with cold therapy is available with a technology called ACCEL™ (Active Compression and Cold Exchange Loop) found in a modality called Game Ready®.

Conclusion Upon review of the available forms of cold and compression modalities, there is a broad spectrum of costs and relative value for those with interest in patients' care. When reviewing healthcare expenses from the time of injury to return to pre-injury activity levels, there appears to be value in higher up-front investments in effective methods of cold and active compression therapies which may result in reduced expenses throughout the patient's overall recovery.

The application of cold therapy applied in systematic conjunction with active pneumatic compression using a technology such as ACCEL may result in less post-operative manipulations and interventions, less physical therapy expenses, improved pain relief, greater likelihood of independence from narcotic use, and a quicker return to work and daily activities.

Introduction

Cryotherapy (the application of cold therapy) and compression in accordance with the RICE regimen (Rest, Ice, Compression, Elevation) is the commonly accepted best practice for the treatment of musculoskeletal pain, injury, or post-operative recovery. In recognition of these benefits, a wide variety of cryotherapy products have been developed, some of which additionally offer static compression. Further, due to growing scientific evidence that intermittent compression has positive, beneficial effects on tissue healing and improved tissue quality following connective tissue injury, another technology has been developed which offers an active pneumatic form of compression.[1, 2, 3]

The breadth of these cryotherapy-based products is as varied as their pricing and value. We will discuss the scientific basis for applying cryotherapy and compression, describe some products that address this therapeutic need, and review the relative health economics.

The Clinical Benefits of Cold and Active Compression Therapy

Soft tissue trauma from injury, overuse, or surgery initiates an inflammatory response that increases the local tissue temperature. Characteristics of inflammation include increased blood flow, edema accumulation, and passage of leukocytes into the tissue spaces. While leukocytes play a central role in removal of infectious agents and tissue debris, they can also be responsible for cellular injury and necrosis.[1]

Research findings have confirmed the benefits of cryotherapy and static compression to control pain, swelling, muscle spasms and edema, but the addition of active (or intermittent) forms of compression enhance lymphatic function, encourage blood flow, and stimulate tissue healing to optimize and accelerate the body's natural repair mechanisms.[1]

The Importance of Cryotherapy

Cold therapy is typically prescribed for two primary reasons:

- To control swelling
- To moderate pain

Cryotherapy has long been recognized as a beneficial posttrauma treatment modality, which provides a short-term analgesic effect, reduces metabolic activity, and decreases cellular oxygen demand. A marked reduction in local metabolic enzymatic activity and a profound local vasoconstriction occur in response to cold application. The analgesic effect of cryotherapy has been attributed to a combination of decreased production of pain mediators and slower propagation of neural pain signals.[1]

Additionally, in vivo research findings suggest that cryotherapy reduces posttrauma endothelial dysfunction (contributing to the impediment of blood flow), which ultimately reduces the intensity of the inflammatory response.[1]

Evidence of the Healing Benefits of Cryotherapy

Several authors have undertaken reviews of published reports of clinical studies in search of evidence-based support for clinical practice, including Bleakley, Hubbard, Block, and more recently, Adie, who studied cryotherapy in Total Knee Arthroplasty, specifically.

In his 2004 review Bleakley found 22 publications reporting clinical trials evaluating cold and compression or cold therapy alone. Upon review, he concluded there was, "evidence that ice plus exercise is most effective, after ankle sprain and postsurgery." Few studies assessed the effectiveness of ice on closed soft-tissue injury, and while was no evidence of an optimal protocol for treatment, [2] the author was able to find evidence that "…adequate cooling can reduce pain, spasm, and neural inhibition, thereby allowing for earlier and more aggressive exercises…."

In her 2004 review searching specifically for published evidence of the effect of cryotherapy on return to participation in activities post injury, Hubbard found: "Based on the available evidence, cryotherapy seems to be effective in decreasing pain." She also found "After critically reviewing the literature for the effect of cryotherapy on return-to-participation measures, we conclude that cryotherapy may have a positive effect." [11]

Block performed a review of published studies not unlike that performed by Hubbard and Bleakley and found “Almost without exception, the use of cold compression therapy following either acute musculoskeletal injury or orthopedic surgery results in improved clinical outcomes compared to no treatment.” [3] However, this author grouped the published studies into procedural types and his review of total knee replacement studies found: “Of the seven randomized trials evaluated, five concluded that cold compression therapy was superior to alternative treatment modalities for improving clinical outcomes after knee replacement surgery.” [3]

In a more recent review of randomized studies of cryotherapy in total knee replacement, Adie attempted a meta-analysis that was challenged by the disparity in methodology and outcomes measured across the selected studies. Adie reported in his general discussion: “Our findings are mainly limited by the quality and number of included studies. Trial methods and required data were not always reported, which required calculation or imputation of values.” Yet, in his report of results of subgroup analyses Adie reported: “… When form of intervention/ control was examined, cryotherapy plus compression had additive range of motion benefits to compression alone, which was not apparent in studies comparing cryotherapy alone to neither cold nor compression ($P = .03$).” [1]

There have also been individual published reports that the use of cold as an analgesic results in reduced narcotic intake. In a randomized controlled study of 54 ACL patients, Cohn assessed post-operative pain medication usage and found a statistically significant decrease (53%) in the use of injectable Demerol among patients who were randomized to the cryotherapy arm. Further, he found that while there was no significant difference in the intake of oral Vicodin, the cryotherapy patients converted from injectable to oral 1.2 days sooner [6].

These clinical outcomes represent strong evidence of a positive effect on the time and medication required to the progress in the physical recovery from the trauma of orthopedic injury or surgery when cold is part of the plan of care, permitting an earlier engagement in therapeutic activity/exercise due to reduced pain and swelling.

The Importance of Compression

Static compression is also a commonly recognized means to address musculoskeletal injury. The purpose is to reduce swelling by limiting the pooling of fluid in the injured tissue outside the blood vessels. This pooled fluid interferes with the body’s ability to deliver nutrients to the injury site and limits the mobility that helps the body return to its pre-injury state. External compression helps to restore normal physiologic processes within damaged tissue and it increases the depth of temperature reduction achieved by the application of cold to the body surface.

The Incremental Value of Active Methods of Compression

Although static compression is an effective therapy for edema reduction, intermittent or active compression offers the added benefits of optimizing lymphatic drainage. The utilization of active pneumatic compression has been shown to be effective not just for prevention of edema formation, but for also increasing blood flow, and stimulation of tissue healing. Active pneumatic compression can accelerate recovery especially when the patient is incapable of generating rhythmic muscle contractions. Improved lymphatic function accelerates healing through removal of edema from injured soft tissues.[1]

While cryotherapy modalities available today may help moderate pain and swelling, adding compression may further help control these symptoms. In addition, active pneumatic compression synchronized with circulating cold therapy provides even greater therapeutic – and in turn economic – value than common forms of cold therapy alone by speeding and enhancing the body's natural repair mechanisms.

Lymphatic System Function

Edema is caused by protein leakage as a result of the action of inflammatory mediators. Edema causes tissue congestion that reduces the availability of oxygen, leading to the impairment of the body's natural repair mechanisms and decreasing the availability of energy necessary for proper maintenance of the cells' balanced resting state. Restoration of normal lymphatic flow is essential for the healing process to progress from the acute stage to the repair stage. If lymphatic flow is optimized in injured tissues, normal metabolic processes can be restored sooner.

The accumulation of edema within the interstitial space can also lead to the development of scar tissue, which is less elastic than normal collagenous tissue.[19] The reduction of edema within injured tissues has been shown to improve oxygen delivery.[18] McGeown et al.[15,16] concluded that lymphatic flow was directly proportional to the magnitude of intermittent compression in increasing lymphatic drainage.

Enhanced Blood Flow

Active pneumatic compression has also been shown to enhance the blood flow of the treated area through stimulation of endothelial cell production of nitric oxide. Endothelial cells are responsible for reducing the turbulence of blood flow, allowing blood to be pumped farther. This increased velocity is the probable physiologic mechanism for enhanced nitric oxide production. Nitric oxide production helps to inhibit secondary hypoxic injury and is a neurotransmitter that can influence vascular tone, thereby adding to improved blood flow.

Tissue Healing

Active pneumatic compression appears to provide a therapeutic effect that enhances connective tissue healing. Cyclic application of external pressure results in increased arterial blood flow, decreased venous pressure, and reduced venous stasis. Intermittent compression has been shown to increase the ingrowth of neurovascular tissue within an Achilles tendon rupture in a rat model.[14]

Evidence of the Healing Benefits of Active Compression

In a review of peer-reviewed publications reporting the use of Intermittent Pneumatic Compression (IPC) for soft tissue and/or fracture healing, Khanna noted that "IPC has the potential of enhancing the fracture and soft-tissue healing process with early return to functional activities" [14].

The review, published in the British Medical Bulletin, identified 16 studies (both animal and human) that investigated the use of IPC in [fracture and] soft-tissue healing. The reviewer notes that those studies "…demonstrated that IPC facilitates both fracture and soft-tissue healing with rapid recovery…." The mechanism of action of IPC that enhances the healing process is hypothesized to include:

- improved vascularity (from application of external pressure);
- generation of nitric oxide, a potent inhibitor of smooth muscle cell contractions
- increase in inflammatory mediators

Finally, Khanna notes that "…every fracture or soft-tissue injury is accompanied by direct and indirect implication on the economy of an individual, an establishment and the nation as a whole…." and that rapid recovery could reduce costs to the individual and to the hospital.

In a randomized controlled trial studying fracture management [5], Challis found that when cyclic pneumatic soft-tissue compression was added to the fracture management program, there was an increase in the recovery of muscle strength and joint range of motion.

Stöckle, et al., in a study of 60 patients with foot or ankle trauma, showed the fastest reduction in swelling occurred in those patients treated with IPC that was a true pulsatile pressure [31]. Knobloch et al. and Quillen et al. found similar results in studies of the ankle tendon response to cold and compression (in uninjured volunteers) showing significantly increased tendon oxygenation in contrast to cryotherapy alone [27, 19]. Wilkerson et al. found that subjects attained specified levels of function much earlier than those without compressive treatments (although the sample size was small and statistical significance was not demonstrated) [32]. Sloan et al. found that the addition of mild pressure to cooling significantly reduced swelling on a sustained basis [29].

In summary, these reports represent scientific evidence illustrating that intermittent pneumatic compression has been shown to stimulate tissue healing, increase blood flow and the delivery of oxygen to the injury site, optimize lymphatic drainage, and mimic the body's natural muscle contractions, "pumping" edema out of the injured area to promote the healing process.

Cryotherapy-Based Modalities: An Overview

A bag of ice or a bag of frozen peas is the least expensive and the least effective of any therapies beyond very localized pain control. However, the accepted therapeutic objectives of cryotherapy are pain control AND reduction of edema to enhance pain reduction and facilitate earlier recovery/rehabilitation of the injured limb. Cold packs alone will not be effective at reducing edema. As previously discussed, to reduce edema some degree of compression is required.

To address these needs, industry has developed cryotherapy devices, including DuraKold®, a "high tech" variation of an ice pack with some amount of static compression as well as devices that use ice water in a pad affixed to the injured limb with an elastic compressive wrap (e.g., Cryo/Cuff®). There are also devices that use cold water continuously circulating through pads affixed with elastic wraps (e.g., Polar Care®). The cost of these three devices ranges from ~$65.00 to ~$250 to as the technology and function increase. They all offer cold and static compression with varying degrees of patient control.

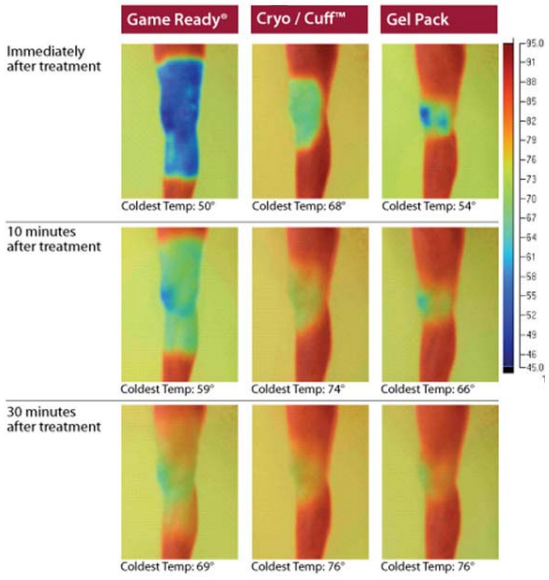
One system, Game Ready®, utilizes a novel technology called ACCEL™ which provides the added benefit of active pneumatic compression in conjunction with rapidly circulating cold water to delivery cryotherapy. The active compression and circulating cold therapy in ACCEL is applied through wraps ergonomically designed to surround each limb of the body. The system offers temperature and compression levels that are fully adjustable. The compression is intermittent and can be set from no compression at all to gradually increasing from a baseline of 5mmHg to 15mmHg, or to 15mmHg up to as much as 75mmHg.

Key features of ACCEL Technology found in the Game Ready modality include:

- Active pneumatic compression that mimics natural muscle contractions, helping the body pump edema away while stimulating blood flow and oxygen delivery to injured limb(s);
- Rapidly circulating ice water through large surface-area wraps, efficiently removing heat and cooling the tissue to reduce edema, muscle spasms, and pain;
- Faster, deeper, longer-lasting intramuscular cooling that slows cellular metabolism, helping the body to minimize secondary tissue damage;
- Air pressure that conforms wrap to the body for better surface contact for improved cooling efficiency and greater comfort for the patient, leading to improved patient compliance.

Exhibit A
Infrared Thermal Images of Cryotherapy Products Applied to the Knee

- Active pneumatic compression and simultaneous cold therapy facilitates faster, longer cooling
- Circumferential therapy covers more surface area and reach key pain points for ACL repair or total knee replacement patients such as the upper shin and back of the knee respectively



Side view shown. First skin temperature measurement immediately after completing 30 minutes of treatment, and subsequent images at ten and thirty minutes post-treatment. All devices applied per manufacturer's instructions and all measurements taken from uniform distance. All devices applied on different days allowing full recovery for "test joint."

The cost for 2 weeks of use for this product retails at $70/day or $980 for a 2-week rental. But the therapeutic value and the cost justification are not determined by the face value of the product alone. The true therapeutic value and, therefore, the true health economics rest in the short and long term therapeutic outcomes of its use.

Clinical Studies

Clinical Study 1: Post-Operative Manipulations and Additional Physical Therapy

In a 2007 random clinical trial (RCT, Level of Evidence 1) was conducted at the Orthopedic Hospital of Indianapolis with 71 total knee arthroplasty (TKA) patients. There were 34 patients in the Test Group (Game Ready) and 37 patients in the Control Group (DuraKold).

The DuraKold patients had 8 post-operative interventions (6 manipulations) that required hospitalization and general anesthesia at a conservative estimated cost of approximately $3,000 and 1 DynaSplint ($500) and 1 scar excision ($500). Each of these would also result in extended PT of 6-12 visits (@$200 each). Thus, 21.6% of the patients in this group were exposed to additional costs of, on average $5,975 independent of the loss in “normal” activities of daily living.

The Game Ready patients had 4 post-operative interventions (2 manipulations and two DynaSplints). Using the same conservative assumptions above, only 11.7% of the patients in this group were exposed to additional costs of, on average, $4,150 independent of the loss in “normal” activities of daily living.

In addition, the patients in this study utilized physical therapy (PT) differently, where a total average number of PT visits per group was 14 for the Test Group and 17 for the Control Group. That is, Game Ready patients had, on average, 3 FEWER physical therapy visits (avg. charge/visit = $200, or $600/patient savings).

Thus, the Game Ready patients incurred, on average, $2,425 LESS expense than the DuraKold group (independent of loss in “normal” activities of daily living).

	Total # of Patients	Post-Op Interventions Per Group	% of Patients Exposed to Add'l Costs	Estimated Average of Additional Costs	# of Physical Therapy Visits	Estimated Physical Therapy Expense	Estimated total PT and Additional Costs	Estimated total per 100 patients	Estimated Game Ready savings on 100 patients
DuraKold	37	8	22%	$5,975	17	$3,400	$9,375	$938K	
Game Ready	34	4	12%	$4,150	14	$2,800	$6,950	$695K	$242,500

Clinical Study 2: Narcotic Dependence
More recently the results of an independent study (Level of Evidence 1) conducted at Fort Bliss comparing Game Ready to a standard ice pack were reported at the 2011 Annual Meeting of American Academy of Orthopedic Surgeons.

The purpose of this prospective RCT study was to examine the clinical effectiveness of a combined cryotherapy and active compression device versus traditional ice application in the postoperative patient following anterior cruciate ligament (ACL) reconstruction. The study is summarized as follows:

- Group 1 patients were provided with a cryotherapy/compression device (Game Ready), while Group 2 patients were provided a standardized ice pack. Both groups were instructed to use the ice or cryotherapy/active compression device three times per day and return to the clinic at 1, 2, and 6 weeks postoperatively.

- Results showed a significant 27-point decrease in mean visual analog scale (VAS) for Group 1 – Game Ready ($p<0.0001$). Of all patients, 83% of Group

1 discontinued narcotic use by 6 weeks, compared with only 28% of Group 2 -- ice (p=0.0008)

These results indicate that the use of combined cryotherapy and intermittent compression in the postoperative period after ACL reconstruction results in improved, short-term pain relief and a greater likelihood of independence from narcotic use compared with cryotherapy alone.

This is important because the cost of prescription drug addiction represents a combined burden of the direct costs of treatment for the dependence and the more indirect costs associated with the inability to resume the "normal" activities of daily living (return to work) and the extended requirements for PT. Narcotic-dependent patients are typically discontinued from PT and will have to resume therapy once they have achieved independence.

The direct costs in 2010 of narcotic dependence intervention alone ranged from $1,500 for one course of outpatient treatment to $15,000 for a residential 90-day treatment. A report from the Substance Abuse and Mental Health Services Administration (SAMHSA) calculated that the average cost in 2002 for treatment of alcohol or other drug addiction in outpatient facilities was $1,433 per course of treatment.

In August, 2010, the CDC issued recommendations based upon the increasing incidence of prescription drug dependence that included:

- Use opioid medications for acute or chronic pain only after determining that alternative therapies do not deliver adequate pain relief. The lowest effective dose of opioids should be used.
- Do not prescribe long-acting or controlled-release opioids (e.g., OxyContin®, fentanyl patches, and methadone) for acute pain.

Pain Medication and Return to Work

- Over 87% of patients using the Game Ready System say it helped reduce the amount of pain medications they took or enabled them to stop taking pain medications sooner.[7]
- Over 85% of patients using the Game Ready System said it helped them return to work or daily activities sooner.[7]
- Over 90% of patients who had undergone a similar procedure in the past using a cold therapy product other than Game Ready report they had a better recovery with Game Ready.[7]

It is clear that if patients are able to substantially reduce their reliance on chemical pain management by either reducing the amount pain medication they take, or to stop taking pain medication sooner, the risk of addiction is greatly reduced. This in turn avoids a costly cascade of treatment for drug dependence and delayed injury or post-operative rehabilitation.

Conclusion

Thus, the cost analysis for available cryotherapy-based treatment options could be summarized as follows:

- Initial investment of an average of $200/patient with a risk of >50% likelihood of additional rehabilitation costs of $1825-$3000/patient and the potential for still more costs associated with narcotic dependence minimally estimated at $1500/patient – compared to…

- Initial investment of an average of $980/patient with substantially reduced likelihood of these additional costs AND an earlier return to work for a ROI benefit of >$5000.

Product	Cost*	Risk	Therapeutic Benefit	Economic Impact
Ice, DuraKold (& similar)	$10-$65	• Potential for ice burns • Potential for increased post-operative interventions • Minimal edema control (no compression) • Poor patient compliance	• Localized analgesic effect	Risks of additional costs: ↑ >50% likelihood of additional rehabilitation costs of $1825-$3000/patient ↑ Potential for costs associated with narcotic dependence estimated at >$1500/patient
Cryo/Cuff	$150	• Potential for non-freezing tissue injury • Minimal edema control • Poor patient compliance	• Moderate analgesic effect (less than ice)	
Polar Care	$250	• Potential for non-freezing tissue injury • Minimal edema control • Poor patient compliance	• Moderate analgesic effect (less than ice)	
Game Ready	$980 (2 wks)		• Analgesic effect similar to ice** • Improved edema management and improved tissue healing§ • Accelerated recovery	Reduction of additional costs: ↓ Reduced narcotic use and associated costs ($1,500 min) ↓ Earlier return to work ↓ Reduced incidence (and associated cost of ~$3000/pt) of post operative interventions by ~54.2% (compared to DuraKold) ↓ Reduced PT requirements by ~$600/pt (compared to DuraKold) ↓ Substantially reduced likelihood of these additional costs AND an earlier return to work for a ROI benefit of >$5000

* Estimate: actual costs and reimbursement vary
** *Trowbridge Literature Citation*
§ *Literature citing evidence of enhanced healing resulting from active pneumatic compression.*

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