

ORTHOPAEDIC APPLICATION OF CRYOTHERAPY

A Comprehensive Review of the History, Basic Science, Methods, and Clinical Effectiveness

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Abstract

» Cold therapy, also known as cryotherapy, includes the use of bagged ice, ice packs, compressive cryotherapy devices, or whole-body cryotherapy chambers. Cryotherapy is commonly used in postoperative care for both arthroscopic and open orthopaedic procedures.

» Cryotherapy is associated with an analgesic effect caused by microvasculature alterations that decrease the production of inflammatory mediators, decrease local edema, disrupt the overall inflammatory response, and reduce nerve conduction velocity.

» Postoperative cryotherapy using bagged ice, ice packs, or continuous cryotherapy devices reduced visual analog scale pain scores and analgesic consumption in approximately half of research studies in which these outcomes were compared with no cryotherapy (11 [44%] of 25 studies on pain and 11 [48%] of 23 studies on opioids). However, an effect was less frequently reported for increasing range of motion (3 [19%] of 16) or decreasing swelling (2 [22%] of 9).

» Continuous cryotherapy devices demonstrated the best outcome in orthopaedic patients after knee arthroscopy procedures, compared with all other procedures and body locations, in terms of showing a significant reduction in pain, swelling, and analgesic consumption and increase in range of motion, compared with bagged ice or ice packs.

» There is no consensus as to whether the use of continuous cryotherapy devices leads to superior outcomes when compared with treatment with bagged ice or ice packs. However, complications from cryotherapy, including skin irritation, frostbite, pernio, and peripheral nerve injuries, can be avoided through patient education and reducing the duration of application.

» Future Level-I or II studies are needed to compare both the clinical and cost benefits of continuous cryotherapy devices to bagged ice or ice pack treatment before continuous cryotherapy devices can be recommended as a standard of care in orthopaedic surgery following injury or surgery.

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Cold therapy, also known as cryotherapy, was utilized by ancient Egyptians as early as 3,000 bce to treat inflammation and infection¹. By the 1800s, the analgesic and numbing effects of cryotherapy were well recognized and utilized for anesthesia before operations and amputations². Following the Industrial Revolution, pressurized gas (nitrogen) was used to ablatively treat a variety of skin lesions by exposing localized areas of the dermis to temperatures as low as -196°C , ushering in the era of cryosurgery³. In 1978, Dr. Gabe Mirkin coined the term “RICE,” a mnemonic well known in the sports medicine field for “rest, ice, compression, and elevation.”⁴ This strategy is still commonly recommended today by orthopaedic surgeons in the postoperative setting and continues to evolve with technological advances.

Cryotherapy is the utilization of the anti-inflammatory and analgesic properties of cold temperatures to facilitate healing, decrease inflammation, and minimize pain after injury or surgery⁵⁻⁹. Cryotherapy is commonly recommended following orthopaedic procedures for these desired effects, and despite many advances in postoperative rehabilitation, it remains a mainstay of treatment. For example, a recent systematic review of the joint arthroplasty literature found that 46% of patients

undergoing total knee arthroplasty (TKA) received some form of cryotherapy as a treatment modality in the immediate postoperative period¹⁰.

There is conflicting literature regarding the effectiveness of cryotherapy. Currently, there is no consensus on the overall benefit that cryotherapy provides in clinical orthopaedic practice. Additionally, no best practices exist for achieving optimal clinical results while minimizing cost. This article aims to provide a comprehensive review of the currently available literature regarding cryotherapy benefits and clinical outcomes in orthopaedic surgery. Based on this updated review of the literature, we will provide recommendations for the use of cryotherapy in orthopaedic surgery.

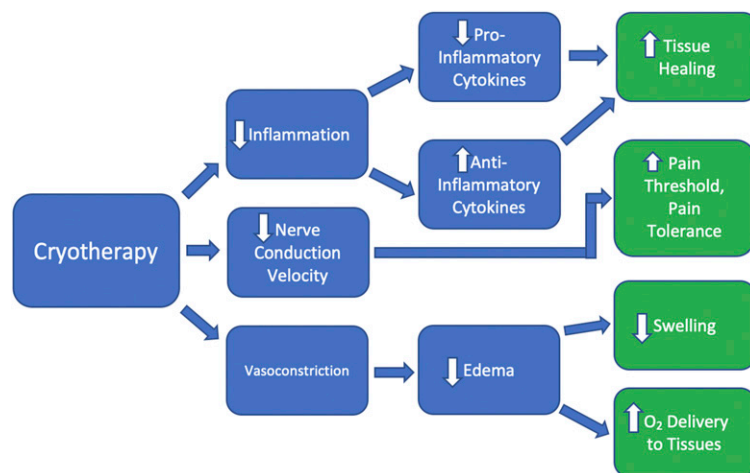
Basic-Science Mechanism of Cryotherapy

Cryotherapy is thought to utilize several different cellular and physiological mechanisms that contribute to its overall effect (Fig. 1). These include reduced inflammation, reduced nerve conduction velocity (NCV), and reduced edema. The anti-inflammatory effects of cryotherapy have been confirmed in a variety of studies that demonstrate a reduction in inflammatory markers, such as C-reactive protein (CRP) and neopterin, following the use of various cryotherapy methods⁵⁻⁷. The anti-

inflammatory effect originates from a variety of biologic pathways, with the overall result being a general shift toward a noninflammatory state that promotes tissue healing rather than tissue destruction.

Several studies identified a notable decrease in pro-inflammatory cytokines such as interleukin-1 beta (IL-1 β), IL-2, IL-3, IL-8, and tumor necrosis factor-alpha (TNF- α) with the use of cryotherapy^{7,11-15}. This reduction in signaling molecules is accompanied by a similar decrease in production of regulatory proteins such as transcription factors that modulate production of other cytokines such as nuclear factor (NF)- κ B, as well as a decrease in the activity of matrix metalloproteinases (MMPs [e.g., MMP-9]), which are responsible for the degradation of extracellular matrix proteins and activation of cytokines¹⁴. Inflammatory markers are primarily secreted by macrophages, and studies have shown that cryotherapy also successfully reduces macrophage infiltration and activation^{5,14}. Histamine, another key inflammatory mediator, was also decreased in patients with rheumatoid arthritis after the administration of whole-body cryotherapy¹⁶. Furthermore, a reduction in the concentration of the inflammatory mediator prostaglandin E₂ (PGE₂) was found in a rat tendon model and confirmed in a recent clinical study that evaluated patients after knee arthroscopy¹⁷. Additionally, a positive correlation was found between the temperature in the knee

Fig. 1
Flowchart outlining the proposed physiological mechanisms of cryotherapy.



and the concentration of PGE₂ in the clinical study¹⁸.

Just as there is a reduction in pro-inflammatory mediators, there is also an increase in several anti-inflammatory mediators after the use of cryotherapy. Several studies have demonstrated an upregulation of anti-inflammatory cytokines, such as IL-10^{11,13,15,19}. This shift to a state of reduced inflammation is accompanied by a marked decrease in the activation of the hypothalamic-pituitary-adrenal (HPA) axis as measured by cortisol in saliva⁵. The HPA axis plays a vital role in the activation of the inflammatory response²⁰.

The use of cryotherapy is also thought to reduce the overall NCV in the affected area²¹. Algafly and George⁸ found that applying ice to the ankle resulted in a substantial decrease in NCV on an electromyogram as well as an increased pain threshold and tolerance as measured by a pressure algometer. This decrease in velocity could be due to delays in the action potential as a result of the low temperature increasing the friction between Ca²⁺ and its cellular gate during the Ca²⁺ and Na⁺ exchange^{8,22}.

Finally, another cryotherapy mechanism of action is local vasocon-

striction caused by a decrease in temperature⁹. This results in a reduction in blood flow to muscles as well as a reduction in hydrostatic pressure within the vessels, which may mitigate the amount of edema at the site of soft-tissue injury^{9,23}. Although it may seem counterintuitive, this decrease in perfusion and hydrostatic pressure is thought to be beneficial because increased intramuscular pressure from edema may diminish O₂ delivery⁹. For example, Yeung et al. concluded that a decrease in muscle tissue oxygenation was mitigated after fatiguing exercise through the use of cold water immersion²⁴.

Cryotherapy Methods

The delivery of cryotherapy following localized injury or surgery has evolved over the past few decades. Despite this evolution, the use of ice bags or packs remains one of the most common and economical cryotherapy methods, with an almost negligible cost. Continuous cryotherapy devices, which feature an external cooling apparatus that circulates chilled water through a joint-specific cuff that the patient wears, can also be used. These devices are capable of cooling at preselected intervals, and

some also feature the ability to provide compression to the joint of interest. These devices offer convenience and customizability as an advantage but can cost hundreds of dollars to buy or rent. Several examples of currently available cryotherapy devices can be found in Figure 2.

While not commonly used in the postoperative setting, whole-body cryotherapy has become a popular athletic recovery technique, especially in the field of sports medicine²⁵. Whole-body cryotherapy has been achieved traditionally through the use of ice baths, but more recently through the use of cold-air chambers. These chambers have seen a substantial increase in popularity in recent years, and work by briefly exposing the body to chilled gas at temperatures as low as -110°C to -140°C in a temperature-controlled cryochamber for 2 to 3 minutes. These chambers cost tens or even hundreds of thousands of dollars to buy, but single sessions can be purchased individually at fitness centers for \$25 to \$75 per session.

Fig. 2

Examples of currently available cryotherapy devices: Aircast Cryo/Cuff IC Cooler Cooling Unit for delivery of continuous cryotherapy (Fig. 2-A, courtesy of DJO Global), Aircast Cryo/Cuff Shoulder, Wrist/Arm, and Knee Cuffs (Fig. 2-B, 2-C, and 2-D, courtesy of DJO Global), and Össur Cold Rush Cold Therapy Unit (Fig. 2-E, © Össur).



TABLE I Summary of 25 Studies Comparing Postoperative Pain Scores for Cryotherapy Versus No Cryotherapy*

Study	Sample Size, Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Outcome Type	Follow-up Time	Results		P Value
		Treatment	Control				Treatment	Control	
TKA									
Desteli ⁴⁵ (2015)	42 vs. 45 (87)	65.4 ± 6.98	65.1 ± 4.06	cTreatment (Waegener)	VAS pain	Day 1	6.1	6.6	>0.05
Gibbons ⁴⁷ (2001)	30 vs. 30 (60)	70 (11:19)	71 (14:16)	Cryo/Cuff IC Cooler (DJO Global)	VAS pain	Days 1, 3, 5, 7, and 9	NR	NR	All >0.05
Holm ⁴⁹ (2012)	10 vs. 10 (20)	66 ± 12 (3:7)	67 ± 12 (7:3)	Bagged ice	VAS pain compared with pre-treatment: at rest	Days 7 and 10	-1.09 ± 1.85	-0.76 ± 1.11	0.48
						Days 7 and 10	-0.08 ± 1.81	-0.48 ± 1.60	0.42
Holmström ⁵⁰ (2005)	23 vs. 17 (40)	68 (14:9)	75 (11:6)	Cryo/Cuff IC Cooler (DJO Global)	VAS pain: at motion and at rest	Days 1-7	NR	NR	All >0.05
Kullenberg ⁵³ (2006)	43 vs. 40 (83)	68.1 ± 6 (18:25)	68.9 ± 6.8 (14:26)	Cryo/Cuff IC Cooler (DJO Global)	VAS pain	Day 1	2.1 ± 1.0	2.2 ± 0.8	>0.05
						Day 3	0.8 ± 0.9	1.2 ± 0.7	>0.05
Kuyucu ⁵⁴ (2015)	27 vs. 33 (60)	67.2 (NR)	68.4 (NR)	Cryo/Cuff IC Cooler (DJO Global)	VAS pain	Day 1	3.6	2.7	<0.05†
						Day 3	3.3	2.5	<0.05†
						Day 5	3.3	3.0	<0.05†
Levy ⁵⁸ (1993)	40 vs 40 (80)	74 (7:33)	73 (8:32)	Cryo/Cuff IC Cooler (DJO Global)	VAS pain	Day 1	7.4 ± 2.7	7.8 ± 2.7	>0.05
						Day 2	5.9 ± 2.4	7.4 ± 1.5	<0.01†
						Day 3	5.6 ± 1.6	6.9 ± 1.9	<0.05†
Mors ⁵⁹ (2002)	30 vs. 30 (30 patients total, as all received bilateral TKA)	NR	NR	Custom-made cooling coil device	VAS pain	Hours 1, 2, and 8, days 2, 3, 4, and 6	4.2 ± 0.74 (overall mean of all days)	6.3 ± 1.3 (overall mean of all days)	<0.001†
Radkowski ⁶¹ (2007)	28 vs. 36 (64)	63.7 ± 10.4 (15:13)	66.9 ± 10.4 (23:13)	Thermo-Tek Solid State Recirculating Chiller (Thermo-Tek)	VAS pain: worst score of day	Day 1	6.0	5.5	>0.05
						Day 3	7.1	6.3	>0.05
						Day 30	6.2	6.5	>0.05
Smith ²⁹ (2002)	44 vs. 40 (84)	72.1 ± 7.8 (21:23)	72.0 ± 7.1 (21:19)	Unspecified cryotherapy pad	VAS pain	Day 1	4.3 ± 1.8	4.2 ± 2	0.32
						Day 2	4.3 ± 2	4.8 ± 1.9	0.72
						Day 3	4.2 ± 1.8	3.5 ± 1.9	0.67
Webb ⁶⁶ (1998)	24 vs. 25 (49)	69.4 (NR)	70.6 (NR)	Aircast Cryo/Cuff (DJO Global)	VAS pain	Day 1	4.5	5.8	<0.05†
Wittig-Wells ⁶⁸ (2015)	29 vs. 29 (29 total patients, due to crossover study design)	64 ± 9.3 (11:18) for combined groups	64 ± 9.3 (11:18) for combined groups	Bagged ice	VAS pain	NR	6.9 ± 1.3	6.7 ± 1.5	>0.05
Knee arthroscopy									
Barber ⁴² (1998)	51 vs. 49 (100)	34 (34:17)	34 (40:9)	Aircast Cryo/Cuff (DJO Global)	VAS pain	Hour 1 Hour 2 Hour 8 Day 2 Day 3 Day 4 Day 5 Day 6 Overall group mean	3.71 3.61 4.1 5.61 5.04 4.55 4.29 4.33	4.63 3.75 5.22 5.88 5.37 4.63 4.65 4.39	0.06
Brandsson ⁴³ (1996)	20 vs. 10 (30)	NR	NR	Cryo/Cuff IC Cooler (DJO Global)	VAS pain	Hours 1, 2, 4, and 6, days 1 and 2	NR	NR	All <0.05†

continued

TABLE I (continued)

Study	Sample Size, Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Outcome Type	Follow-up Time	Results		P Value
		Treatment	Control				Treatment	Control	
Dervin ⁴⁴ (1998)	40 vs. 38 (78)	30.6 ± 10.2 (27:13)	26.9 ± 6.2 (27:11)	Cryo/Cuff IC Cooler (DJO Global)	VAS pain	Day 1	3.0 ± 1.7	2.5 ± 1.3	>0.05
Edwards ⁴⁶ (1996)	26 vs. 45 (71)	26 (18:8)	27 (32:13)	Cryo/Cuff IC Cooler (DJO Global)	VAS pain	Days 1-3	NR	NR	All >0.05
Lessard ⁵⁷ (1997)	23 vs. 22 (45)	42.0 ± 12.6 (16:7)	44.6 ± 14.9 (15:7)	Cold gel packs	Pain Rating Index Score: total	Days 1-7	8.78 ± 7.08	10.5 ± 6.97	>0.05
					Pain Rating Index Score: Sensory Component	Days 1-7	7.91 ± 6.54	8.59 ± 5.18	>0.05
					Pain Rating Index Score: Affective Component	Days 1-7	0.13 ± 0.34	0.96 ± 1.99	0.03†
					Pain Rating Index Score: Evaluative Dimension	Days 1-7	0.74 ± 0.81	0.91 ± 1.07	>0.05
Ohkoshi ⁶⁰ (1999)	14 vs. 7 (21)	22.1 ± 6.5 (10:11) for combined groups	22.1 ± 6.5 (10:11) for combined groups	Icing System 2000 (Sigmax)	VAS pain	Day 2	76.7 ± 15.1 (5°C group), 34.7 ± 29.8 (10°C group)	6.57 ± 2.05	Significant difference between the 5°C and 10°C groups only†
Whitelaw ⁶⁷ (1995)	56 vs. 46 (102)	39 (36:20)	36 (36:10)	Cryo/Cuff IC Cooler (DJO Global)	VAS pain	Hour 6	6.51	6.59	>0.05
						Hour 12	5.85	6.00	>0.05
						Day 1	4.34	4.98	>0.05
						Day 2	3.82	4.19	>0.05
						Day 3	3.15	3.58	>0.05
THA									
Iwakiri ⁵¹ (2019)	30 vs. 30 (60)	68.1 ± 9.6 (1:29)	67.6 ± 8.9 (1:29)	CF3000 Icing System and Cooling Pad (Sigmax)	VAS pain	Day 4	0.93 ± 1.36	0.12 ± 1.93	0.62
						Day 7	0.71 ± 0.97	1.15 ± 1.73	0.24
						Day 14	0.54 ± 0.94	0.94 ± 1.78	0.29
						Day 28	0.12 ± 0.22	0.33 ± 0.71	0.34
Saito ⁶² (2004)	23 vs. 23 (46)	59.3 ± 11.4	59.0 ± 11.2	Icing System 2000 (Sigmax)	VAS pain	Days 1-4 and days 4-7	NR	NR	All <0.05†
Hip surgery									
Leegwater ⁵⁶ (2017)	64 vs. 61 (125)	80.0 ± 10.9 (15:49)	77.2 ± 10.1 (22:39)	Game Ready (CoolSystems)	VAS pain	Day 1	2.39 ± 1.94	2.61 ± 1.94	0.54
						Day 2	1.98 ± 1.90	1.92 ± 1.82	0.84
						Day 3	1.88 ± 1.94	2.15 ± 1.84	0.42
Open shoulder surgery									
Speer ⁶⁵ (1996)	25 vs. 25 (50)	36.9 (19:6)	39.4 (17:8)	Cryo/Cuff IC Cooler (DJO Global)	VAS pain	Day 1	3.13	5.65	0.001†
						Day 10	3.26	4.66	0.03†
Shoulder arthroscopy									
Singh ⁶⁴ (2001)	32 vs. 37 (69)	NR	NR	Polar Care (Breg)	VAS pain	Day 1	NR	NR	>0.05
						Day 7	NR	NR	>0.05
						Day 14	NR	NR	0.043†
						Day 21	NR	NR	>0.05
Elbow arthrolysis									

continued

TABLE I (continued)

Study	Sample Size, Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Outcome Type	Follow-up Time	Results		P Value	
		Treatment	Control				Treatment	Control		
Yu ⁶⁹ (2015)	31 vs. 28 (51)	37.5 ± 13.3 (17:14)	34.9 ± 10.6 (15:13)	Cryo/Cuff IC Cooler (DJO Global)	VAS pain: at rest and with movement	Day 1	2.7 ± 1.7,	4.7 ± 2.6, 7.7 ± 2.1	<0.05†	
							6.4 ± 1.8			
							Day 2	2.5 ± 1.7,		4.2 ± 2.1, 7.2 ± 1.2
								6.0 ± 1.9		
							Day 3	1.9 ± 1.3,		3.5 ± 1.5, 6.9 ± 1.5
								5.5 ± 2.1		
							Day 4	1.7 ± 1.2,		2.8 ± 1.7, 6.1 ± 1.7
								5.0 ± 1.9		
							Day 5	1.4 ± 1.0,		2.5 ± 1.5, 5.5 ± 1.8
								4.5 ± 1.8		
							Day 6	1.1 ± 1.0,		2.0 ± 1.4, 5.0 ± 1.9
4.0 ± 1.7										
Day 7	1.0 ± 1.0,	1.7 ± 1.2, 4.6 ± 2.0								
	3.7 ± 1.7									
2 weeks	0.5 ± 0.5,	0.8 ± 0.6, 2.8 ± 1.3	>0.05							
	2.4 ± 1.2									
3 months	0.1 ± 0.2,	0.1 ± 0.2, 0.4 ± 0.5	>0.05							
	0.3 ± 0.5									

*Visual analog scale (VAS) pain was reported on a 0-10 scale. NR = not reported. †Significant difference in favor of cryotherapy.

The Role of Compression

Compression is commonly applied simultaneously with cryotherapy (bagged ice, ice packs, or continuous cryotherapy devices) as a component of RICE therapy. Compression is thought to help reduce blood flow and edema in the affected area, and therefore works synergistically with cryotherapy to facilitate healing. Most of the studies have not isolated compression as a variable and instead focused on either the effects of cryotherapy or the combined effects of cryotherapy and compression, making it difficult to draw conclusions regarding the effects of compression alone. However, Waterman et al. focused on the effects of compression by comparing compressive cryotherapy to noncompressive cryotherapy and found that compressive cryotherapy yielded better pain scores at both 2 and 6 weeks postoperatively when compared with preoperative pain scores²⁶. Additionally, a larger number of patients in the compressive cryotherapy group discontinued all narcotic use by 6 weeks compared with the noncompressive group (p = 0.0008). However, there was no significant difference in functional knee scores, edema, or pain scores at 1 week postoperatively

(p > 0.05). In contrast, 3 other studies that compared compressive and non-compressive cryotherapy treatments found no significant difference between the groups in terms of analgesic consumption, pain, range of motion, blood loss, or swelling (p > 0.05)²⁷⁻²⁹.

Whole-Body Cryotherapy: Ice Baths

A vast number of randomized controlled trials (RCTs) have evaluated the effect of whole-body cryotherapy using ice baths on a variety of outcomes. These studies have mixed findings, likely on account of variations in the patient population, cryotherapy delivery method, and outcome of interest. A systematic review and meta-analysis performed by Higgins et al. evaluated cold-water bath immersion on the recovery of trained athletes following athletic activity and found that therapy led to improved neuromuscular function with regard to jumping and sprinting at 24 hours after therapy (p = 0.05), as well as improved perception of fatigue at 72 hours after therapy (p = 0.03)³⁰. However, all other time points from a range of 1 hour to >90 hours post-intervention showed no significant difference when compared with the control therapy (p > 0.05). Additionally, other outcomes of interest, including muscle

soreness, range of motion, and biochemical markers, were found to either show no significant difference or have insufficient data to draw conclusions (p > 0.05).

A large systematic review by Versey et al. evaluated 53 studies with the goal of providing practical recommendations for the application of cold-water immersion therapy and concluded that immersion for 5 to 15 minutes at a temperature of 10°C to 15°C appeared to be most effective at enhancing recovery³¹. However, that systematic review did not include a meta-analysis because of the overwhelmingly large variety of variables and outcomes of interest in the studies evaluated.

Whole-Body Cryotherapy: Cold Air Chambers

From a basic and translational science perspective, there have been fairly consistent and promising results with regard to disruption of inflammatory signaling and the inflammatory cascade with regimented use of whole-body cryotherapy using cold air chambers following exercise and activity^{7,11,15}. Ziemann et al. found improved performance during drills as well as faster recovery in a

TABLE II Summary of 23 Studies Comparing Postoperative Analgesic Consumption with Cryotherapy Versus No Cryotherapy*

Study	Sample Size Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Outcome Type	Follow-up Time	Results		P Value
		Treatment	Control				Treatment	Control	
TKA									
Gibbons ⁴⁷ (2001)	30 vs. 30 (60)	70 (11:19)	71 (14:16)	Cryo/Cuff IC Cooler (DJO Global)	Mean no. of doses of co-dydramol normalized to patient body weight	Day 10	44	40	>0.05
Healy ⁴⁸ (1994)	50 vs. 55 (105)	NR	NR	Aircast Cryo/Cuff (DJO Global)	Mean narcotic requirements for both unilateral and bilateral procedures (MME)	Days 1-3	96.6, 143.4	100.0, 115.7	>0.05
						Days 4-7	66.3, 52.0	59.5, 79.6	>0.05
Holmström ⁵⁰ (2005)	23 vs. 17 (40)	68 (14:9)	75 (15:6)	Cryo/Cuff IC Cooler (DJO Global)	Mean morphine usage (mg)	Day 1	13.4	20.8	0.03†
						Days 2-7	NR	NR	> 0.05
Kullenberg ⁵³ (2006)	43 vs. 40 (83)	68.1 ± 6 (18:25)	68.9 ± 6.8 (14:26)	Cryo/Cuff IC Cooler (DJO Global)	Mean morphine usage (mg morphine per kg per 24 hr)	Day 1	0.37 ± 0.11	0.43 ± 0.05	>0.05
Levy ⁵⁸ (1993)	40 vs 40 (80)	74 (7:33)	73 (8:32)	Cryo/Cuff IC Cooler (DJO Global)	Mean normalized injectable morphine (mg/kg)	Day 2	0.53 ± 0.2	0.69 ± 0.3	<0.05†
Morsj ⁵⁹ (2002)	30 vs. 30 (30)	NR	NR	Custom-made cooling coil device	Mean analgesic consumption (no. of pills/day)	Day 1-6	1.9 ± 0.73	2.8 ± 0.63	<0.01†
Radkowski ⁶¹ (2007)	28 vs. 36 (64)	63.7 ± 10.4 (15:13)	66.9 ± 10.4 (23:13)	Thermo-Tek Solid State Recirculating Chiller (Thermo-Tek)	Postop. opioid consumption (% of patients who did not require additional opioid analgesics)	Day 1	7.1	5.6	0.981
						Day 3	46.4	25	0.111
Scarcella ⁶³ (1995)	12 vs. 12 (24)	69 (NR)	67 (NR)	Hot/Ice Blanket (Thermo Temp)	Mean normalized meperidine usage (mg/kg)	Total through discharge	4.75	4.75	>0.05
Smith ²⁹ (2002)	44 vs. 40 (84)	72.1 ± 7.8 (21:23)	72.0 ± 7.1 (21:19)	Unspecified cryotherapy pad	Mean normalized opioid consumption (mg/kg)	Day 2	0.422 ± 0.31	0.32 ± 0.29	0.245
Webb ⁶⁶ (1998)	24 vs. 25 (49)	69.4 (NR)	70.6 (NR)	Aircast Cryo/Cuff (DJO Global)	Mean normalized opioid dosage required (mg/kg over 48 hours)	Days 1 and 2	0.57	0.71	<0.01†
Knee arthroscopy									

continued

TABLE II (continued)

Study	Sample Size Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Outcome Type	Follow-up Time	Results		P Value	
		Treatment	Control				Treatment	Control		
Barber ⁴² (1998)	51 vs. 49 (100)	34 (34:17)	34 (40:9)	Aircast Cryo/Cuff (DJO Global)	Mean Vicodin consumption (no. of pills/day)	Day 1	0.86	1.94	0.013†	
						Day 2	1.49	2.85		
						Day 3	2.06	2.88		
						Day 4	1.90	3.35		
						Day 5	2.12	3.31		
						Day 6	2.47	2.6		
						Day 7	1.73	1.82		
						Overall group Mean				
						Mean Percocet consumption (no. of pills/day)	Day 1	1.41		1.94
							Day 2	3.29		3.22
							Day 3	3.24		2.43
							Day 4	1.92		1.37
							Day 5	1.22		1.00
							Day 6	0.91		0.97
Day 7	1.06	0.51								
Overall group mean			>0.05							
Brandsson ⁴³ (1996)	20 vs. 10 (30)	NR	NR	Cryo/Cuff IC Cooler (DJO Global)	Mean morphine usage (mg)	Days 1 and 2	NR	NR	<0.05*	
					Mean codeine usage (mg)	Days 1 and 2	NR	NR	<0.05*	
Dervin ⁴⁴ (1998)	40 vs. 38 (78)	30.6 ± 10.2 (27:13)	26.9 ± 6.2 (27:11)	Cryo/Cuff IC Cooler (DJO Global)	Mean normalized morphine usage (mg/kg)	Total postop.	0.37 ± 0.23	0.35 ± 0.21	>0.05	
					Mean codeine usage (no. of 30-mg tablets)	Total postop.	3.86 ± 2.72	3.44 ± 2.1	>0.05	
Edwards ⁴⁶ (1996)	26 vs. 45 (71)	26 (18:8)	27 (32:13)	Cryo/Cuff IC Cooler (DJO Global)	Normalized mean analgesic (morphine, codeine, acetaminophen) usage (mg/kg)	Total through discharge	0.65, 4.14, 73.82	0.60, 3.91, 85.2 (room-temp. cuff)	>0.05	
							0.65, 4.31, 70.6 (no cuff)	>0.05		
Konrath ⁵² (1996)	27 vs. 23 (50)	27	23	Polar Care (Breg)	Normalized mean pain medication required (mg/kg)	At discharge	0.59	0.52	>0.05	
	23 vs. 27 (50)	26	26	Ice bag	Normalized mean pain medication required (mg/kg)	At discharge	0.60	0.52	>0.05	

continued

TABLE II (continued)

Study	Sample Size Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Outcome Type	Follow-up Time	Results		P Value
		Treatment	Control				Treatment	Control	
Ohkoshi ⁶⁰ (1999)	14 vs. 7 (21)	22.1 ± 6.5 (10:11) for combined groups	22.1 ± 6.5 (10:11) for combined groups	Icing System 2000 (Sigmax)	Mean analgesic required (number of doses)	Days 1 and 2	1.25 ± 0.4 (5°C cuff) 0.7 ± 0.8 (10°C cuff)	1.5 ± 1.0	>0.05 <0.05*
Whitelaw ⁶⁷ (1995)	56 vs. 46 (102)	39 (36:20)	36 (36:10)	Cryo/Cuff IC Cooler (DJO Global)	Mean pain medication required (doses/day)	Day 1 Day 2 Day 3 Mean	4.23 3.21 2.7	5 4.22 3.12	>0.05 >0.05 >0.05 <0.05*
THA									
Iwakiri ⁵¹ (2019)	30 vs. 30 (60)	68.1 ± 9.6 (1:29)	67.6 ± 8.9 (1:29)	CF3000 Icing System and Cooling Pad (Sigmax)	Mean amount of diclofenac sodium suppository (mg)	Through day 21	31.7 ± 60.9	72.2 ± 79.5	0.07
Leegwater ⁵⁵ (2012)	15 vs. 15 (30)	66 (8:7)	68 (4:11)	Game Ready (CoolSystems)	Mean analgesic usage (MME)	Total postop.	84.7 + 43.6	100 + 73.5	0.593
Saito ⁶² (2004)	23 vs. 23 (46)	59.3 ± 11.4 (NR)	59.0 ± 11.2 (NR)	Icing System 2000 (Sigmax)	Mean dose of mepivacaine hydrochloride (mg)	Through day 7	295 ± 99	489 ± 160	<0.001*
					Mean dose of diclofenac sodium (mg)	Through day 7	58 ± 54	60 ± 50	0.529
Scarcella ⁶³ (1995)	12 vs. 12 (24)	69 (NR)	67 (NR)	Hot/Ice Blanket (Thermo Temp)	Mean normalized meperidine usage (mg/kg)	Total through discharge	4.14	4.44	>0.05
Hip (multiple procedures)									
Leegwater ⁵⁶ (2017)	64 vs. 61 (125)	80.0 ± 10.9 (15:49)	77.2 ± 10.1 (22:39)	Game Ready (CoolSystems)	Incidence of analgesic usage (%)	Day 1 Day 2 Day 3	60 32 18	68 26 26	0.35 0.18 0.09
Elbow arthrolysis									
Yu ⁶⁹ (2015)	31 vs. 28 (51)	37.5 ± 13.3 (17:14)	34.9 ± 10.6 (15:13)	Cryo/Cuff IC Cooler (DJO Global)	Mean dose of sufentanil (µg)	Days 1 and 2	86.5 ± 18.0	93.1 ± 13.2	0.002*

*MME = morphine milligram equivalents, and NR = not reported. †Significant difference in favor of cryotherapy.

population of professional tennis players who received cryotherapy using cold air chambers compared with no cryotherapy¹⁵. In addition, whole-body cryotherapy has been found to alter bone metabolism in favor of healing by inducing higher levels of osteoprotegerin³². A systematic review by Costello

et al. evaluated 4 studies to determine the effects of cold air exposure on muscle soreness in exercising adults³³. The authors found less muscle pain 1 hour after therapy involving cold air exposure compared with controls, but not at any other time points up to 72 hours, and described the evidence from the studies

that were evaluated as “very low quality.”³³ Another systematic review, by Bleakley et al., evaluated 10 studies to determine the overall effectiveness of cold air exposure and determined that it may improve short-term subjective measures of soreness and recovery, but overall appears to provide little benefit with

TABLE III Summary of 16 Studies Comparing Postoperative Range of Motion with Cryotherapy Versus No Cryotherapy*

Study	Sample Size Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Outcome	Follow-up Time	Results		P Value
		Treatment	Control				Treatment	Control	
TKA									
Gibbons ⁴⁷ (2001)	30 vs. 30 (60)	70 (11:19)	71 (14:16)	Cryo/Cuff IC Cooler (DJO Global)	Full knee ROM (°)	Day 10	5 to 82	3 to 78	>0.05
Healy ⁴⁸ (1994)	50 vs. 55 (105)	NR	NR	Aircast Cryo/Cuff (DJO Global)	Mean max. knee ROM (°)	Days 2-4	80	88	>0.05
						Days 7-14	93	97	>0.05
						Weeks 4-6	111	108	>0.05
Holmström ⁵⁰ (2005)	23 vs. 17 (40)	68 (14:9)	75 (11:6)	Cryo/Cuff IC Cooler (DJO Global)	Mean active ROM (°)	Week 1	10-84	13-80	>0.05
						Week 6	5-112	9-108	>0.05
						Week 1	4-87	6-84	>0.05
						Week 6	2-116	3-111	>0.05
Kullenberg ⁵³ (2006)	43 vs. 40 (83)	68.1 ± 6 (18:25)	68.9 ± 6.8 (14:26)	Cryo/Cuff IC Cooler (DJO Global)	Mean max. knee ROM (°)	Day 1	50.4 ± 8	51.4 ± 11.1	>0.05
						At discharge	75.1 ± 10.5	62.9 ± 12.8	0.0019†
						Week 3	98.9 ± 9.4	87.6 ± 7.8	0.0045†
Levy ⁵⁸ (1993)	40 vs. 40 (80)	74 (7:33)	73 (8:32)	Cryo/Cuff IC Cooler (DJO Global)	Mean total knee ROM (°)	Day 7	53 ± 13	44 ± 15	<0.05†
						Day 14	77 ± 13	5 ± 14	<0.01†
Morsi ⁵⁹ (2002)	30 vs. 30 (30)	NR	NR	Custom-made cooling coil device	Mean total knee ROM (°)	Week 1	68 ± 14.8	54 ± 11.04	<0.01†
						Week 6	NR	NR	>0.05
Webb ⁶⁶ (1998)	24 vs. 25 (49)	69.4 (NR)	70.6 (NR)	Aircast Cryo/Cuff (DJO Global)	Mean total knee ROM (°)	Day 5, week 6, month 3	NR	NR	All >0.05
Scarcella ⁶³ (1995)	12 vs. 12 (24)	69 (NR)	67 (NR)	Hot/Ice Blanket (Thermo Temp)	Mean total knee ROM (°)	At discharge	72.5 ± 15.8	76.8 ± 10.5	>0.05
						Mean gain in knee ROM (°/day)	At discharge	5.5 ± 3.4	4.3 ± 2.8
Smith ²⁹ (2002)	44 vs. 40 (84)	72.1 ± 7.8 (21:23)	72.0 ± 7.1 (21:19)	Unspecified cryotherapy pad	Mean max. knee flexion (°)	Day 1	81.3 ± 11.8	83.6 ± 12.9	0.384
						Day 2	84.9 ± 13.4	86.6 ± 12.3	0.95
Knee arthroscopy									
Barber ⁴² (1998)	51 vs. 49 (100)	34 (34:17)	34 (40:9)	Aircast Cryo/Cuff (DJO Global)	Mean max. knee flexion (°)	Day 7	88	77	0.06
Edwards ⁴⁶ (1996)	26 vs. 45 (71)	26 (18:8)	27 (32:13)	Cryo/Cuff IC Cooler (DJO Global)	Mean max. knee ROM (°)	Day 2	78	76 (room temp. cuff), 72 (no cuff)	All >0.05
Konrath ⁵² (1996)	27 vs. 23 (50)	27 (11:8)	25 (13:10)	Polar Care (Breg)	Mean total knee ROM (°)	Before discharge	61 (cuff)	57	>0.05
				Ice bag	Mean total knee ROM (°)	Before discharge	60 (ice bag)	57	>0.05
Ohkoshi ⁶⁰ (1999)	14 vs. 7 (21)	22.1 ± 6.5 (10:11) for combined groups	22.1 ± 6.5 (10:11) for combined groups	Icing System 2000 (Sigmax)	Days to 120° flexion	NR	12.7 ± 2.2 (5° C cuff)	16.7 ± 5.1	>0.05
							12.9 ± 3.2 (10°C cuff)		>0.05
Whitelaw ⁶⁷ (1995)	56 vs. 46 (102)	39 (36:20)	36 (36:10)	Cryo/Cuff IC Cooler (DJO Global)	Mean total knee ROM, min. and max. values (°)	NR	5.4 to 121.9	4.2 to 123.6	>0.05
Lessard ⁵⁷ (1997)	23 vs. 22 (45)	42.0 ± 12.6 (16:7)	44.6 ± 14.9 (15:7)	Cold gel packs	Mean total knee ROM (°)	Day 7	122.1 ± 14.6	114.4 ± 24.4	>0.05
Elbow arthrolysis									
Yu ⁶⁹ (2015)	31 vs. 28 (51)	37.5 ± 13.3 (17:14)	34.9 ± 10.6 (15:13)	Cryo/Cuff IC Cooler (DJO Global)	Total elbow ROM in flexion-extension (°)	Day 1	103.7 ± 14.6	102.0 ± 15.6	0.341
						Day 3	118.6 ± 14.5	118.0 ± 11.2	0.412
						Day 7	125.0 ± 13.2	123.4 ± 10.8	0.632

*ROM = range of motion, and NR = not reported. †Significant difference in favor of cryotherapy.

TABLE IV Summary of 9 Studies Comparing Postoperative Swelling with Cryotherapy Versus No Cryotherapy*

Study	Sample Size Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Outcome Type	Follow-up Time	Results		P Value
		Treatment	Control				Treatment	Control	
TKA									
Healy ⁴⁸ (1994)	50 vs. 55 (105)	NR	NR	Aircast Cryo/ Cuff (DJO Global)	Mean increase from baseline in circumference of thigh at mid-patella and dis- tal aspect of thigh (cm)	Between days 2-4 Between days 7-14 Between weeks 4-6	2.3, 2.2 0.3, 0.6 0.8, 1.0	2.0, 2.0 0.7, 0.6 0.6, 1.0	>0.05 >0.05 >0.05
Holmström ⁵⁰ (2005)	23 vs. 17 (40)	68 (14:9)	75 (15:6)	Cryo/Cuff IC Cooler (DJO Global)	Change in knee diameter compared with baseline (cm)	Day 7 Week 6	2.0 NR	2.9 NR	>0.05 >0.05
Smith ²⁹ (2002)	44 vs. 40 (84)	72.1 ± 7.8 (21:23)	72.0 ± 7.1 (21:19)	Unspecified cryotherapy pad	Knee swelling (cm)	Hour 24 Hour 48	43.8 ± 3.3 43.9 ± 2.6	43.9 ± 3.6 44.5 ± 3.8	0.84 0.51
Webb ⁶⁶ (1998)	24 vs. 25 (49)	69.4 (NR)	70.6 (NR)	Aircast Cryo/ Cuff (DJO Global)	Knee circumference 2 cm proximal to patella (cm)	Day 5, week 6, month 3	NR	NR	All >0.05
Knee arthroscopy									
Barber ⁴² (1998)	51 vs. 49 (100)	34 (34:17)	34 (40:9)	Aircast Cryo/ Cuff (DJO Global)	Swelling (unspecified units)	Day 7	NR	NR	0.76
Lessard ⁵⁷ (1997)	23 vs. 22 (45)	42.0 ± 12.6 (16:7)	44.6 ± 14.9 (15:7)	Cold gel packs	Circumference of knee 3 cm proximal to patellar base (cm)	Day 7	39.2 ± 3.29	40.4 ± 3.37	>0.05
Whitelaw ⁶⁷ (1995)	56 vs. 46 (102)	39 (36:20)	36 (36:10)	Cryo/Cuff IC Cooler (DJO Global)	Mean circumference of knee at superior pole of patella (cm)	NR	40.5	38.2	>0.05
THA									
Iwakiri ⁵¹ (2019)	30 vs. 30 (60)	68.1 ± 9.6 (1:29)	67.6 ± 8.9 (1:29)	CF3000 Icing System and Cooling Pad (Sigmax)	Thigh circumference 5 cm proximal to superior patellar border (ratio of postop.:preop. values)	Day 4 Day 7 Day 14 Day 28	1.04 ± 0.04 1.06 ± 0.05 1.02 ± 0.05 0.95 ± 0.27	1.07 ± 0.06 1.05 ± 0.06 1.01 ± 0.03 1.01 ± 0.03	0.045† 0.27 0.16 0.25
Open shoulder surgery									
Speer ⁶⁵ (1996)	25 vs. 25 (50)	36.9 (19:6)	39.4 (17:8)	Cryo/Cuff IC Cooler (DJO Global)	Visual analog scale asking patients to rate swelling in shoulder (0- 10)	Day 10	0.98	2.59	0.002†

*NR = not reported. †Significant difference in favor of cryotherapy.

regard to functional recovery; the authors therefore concluded that athletes can achieve comparable results with cheaper therapies such as a local ice pack³⁴.

Beyond pain management and acute postoperative care, whole-body cryotherapy using either ice baths or cold air chambers has also been studied extensively as a tool to aid athletes in their recovery. Some studies found neither cold water immersion nor whole-body cryotherapy to be more effective than a placebo intervention at improving functional recovery or muscle soreness after various exercises^{33,35-39}. However, other

studies found cold water therapy to be more helpful in reducing delayed-onset muscle soreness and enhancing recovery from muscle damage after exercise^{5,40,41}. Future high-level studies will be necessary to determine the exact benefits of ice-bath and cryotherapy chamber treatment.

Cryotherapy Outcomes in the Literature

Methodology

A literature search was performed using PubMed. Broad search terms related to cryotherapy were used, including “cryo-

therapy,” “cold therapy,” “ice therapy,” “continuous cryotherapy,” “compressive cryotherapy,” and “orthopaedic.” After screening for relevant RCTs, 29 studies were identified that directly compared cryotherapy of any form to no cryotherapy following orthopaedic procedures, while 15 studies were identified that compared continuous cryotherapy devices to either bagged ice or ice pack treatment.

Cryotherapy Versus No Cryotherapy

After a review of the current literature, 29 studies were identified that compared

TABLE V Summary of 14 RCTs Comparing Postoperative Pain Scores with Continuous Cryotherapy Devices Versus Bagged Ice or Ice Pack Treatment*

Study	Sample Size Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Outcome Type	Follow- Up Time	Results		P Value
		Treatment	Control				Treatment	Control	
TKA									
Bech ⁷³ (2015)	37 vs. 34 (71)	70.4 ± 1.8 (17:20)	71.5 ± 1.8 (19:15)	DonJoy Iceman (DonJoy Canada)	VAS pain	Day 2	3.8 ± 0.25	3.6 ± 0.27	0.67
Demoulin ⁷⁴ (2012)	22 vs. 22 (44)	Males: 71.7 ± 5.6 (9 total), females: 70.9 ± 8.8 (13 total)	Males: 67.2 ± 11.9 (9 total), females: 68.8 ± 9.5 (13 total)	Aircast Cryo/ Cuff (DJO Global)	VAS pain	Day 7	NR	NR	All >0.05
Schinsky ⁷⁸ (2016)	49 vs. 51 (100)	64.7 (20:29)	65.3 (24:27)	Unspecified continuous cryotherapy device	VAS pain	At discharge Week 3 Week 6	4.82 ± 2.10 2.68 ± 1.68 2.36 ± 2.03	4.85 ± 2.14 2.96 ± 2.20 2.26 ± 2.44	0.97 0.82 0.01†
Sadoghi ⁷⁷ (2018)	46 vs. 51 (97)	70.4 (14:32)	71.7 (15:36)	cTreatment (Waegener)	VAS pain	Day 2 Day 4 Day 6	3.7 ± 2.1 NR NR	4.6 ± 2.1 NR NR	0.03† >0.05 >0.05
Su ⁸⁰ (2012)	103 vs. 84 (187)	NR	NR	GameReady (CoolSystems)	VAS pain difference compared with preop. value	Week 2 Week 6	-0.9 -2.34	-1.35 -2.21	>0.05 >0.05
Thienpont ⁸¹ (2014)	50 vs. 50 (100)	67.5 ± 10.5 (15:35)	68.5 ± 10 (10:40)	cTreatment (Waegener)	VAS pain	Day 2	4.0 ± 3.0	3.5 ± 2.5	0.18
Knee arthroscopy									
Barber ⁴² (1998)	51 vs. 49 (100)	34 (34:17)	34 (40:9)	Aircast Cryo/ Cuff (DJO Global)	VAS pain	Hour 1 Hour 2 Hour 8 Day 2 Day 3 Day 4 Day 5 Day 6	3.71 3.61 4.10 5.61 5.04 4.55 4.29 4.33	4.51 4.06 5.49 7.32 5.91 5.03 4.88 4.45	>0.05 >0.05 0.02† 0.01† >0.05 >0.05 >0.05 >0.05
Ruffilli ⁷⁶ (2015)	23 vs. 24 (47)	32.2 ± 6.7 (14:9)	31.4 ± 8.1 (15:9)	Hilotherm (Hilotherm)	VAS pain	Day 1	.09 ± 0.8	2.4 ± 1.7	<0.0001†
Schröder ⁷⁹ (1994)	21 vs. 23 (44)	24.8 ± 5.6 (15:6)	24.2 ± 4.5 (18:5)	Cryo/Cuff IC Cooler (DJO Global)	VAS pain	Day 1 Day 2 Day 3 Day 6 Week 2 Week 4	NR NR NR NR NR NR	NR NR NR NR NR NR	>0.05 >0.05 >0.05 <0.05† >0.05 >0.05
Waterman ²⁶ (2012)	18 vs. 18 (36)	28.7 (15:3)	30.9 (15:3)	GameReady (CoolSystems)	VAS pain difference compared with preop. score	Week 1 Week 2 Week 6	2.22 1.57 .47	1.06 4.11 2.68	0.07 0.002† <0.001†
Woolf ⁸² (2008)	24 vs. 29 (53)	NR	NR	Polar Care 500 (Breg)	VAS pain	Day 2 Day 5 Day 8 Day 11 Day 14	5.28 4.46 4.44 3.32 2.30	5.90 4.30 3.80 2.92 3.20	>0.05 >0.05 >0.05 >0.05 >0.05
Shoulder arthroplasty									

continued

TABLE V (continued)

Study	Sample Size Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Outcome Type	Follow- Up Time	Results		P Value	
		Treatment	Control				Treatment	Control		
Noyes ⁷⁵ (2018)	20 vs. 20 (40)	NR	NR	Polar Care Shoulder Cuff (Breg)	VAS pain	Day 1	4.2 ± 3.0	4.3 ± 3.1	0.989	
						Day 3	4.8 ± 2.7	4.7 ± 3.2	0.944	
						Week 1	2.9 ± 1.8	3.3 ± 2.5	0.593	
						Week 2	2.5 ± 2.1	2.7 ± 1.8	0.742	
Shoulder arthroscopy	Kraeutler ²⁸ (2015)	25 vs. 21 (46)	55.4 (NR)	55.8 (NR)	GameReady Shoulder Wrap (CoolSystems)	VAS pain	Day 0	4.5	4.1	0.67
Days 1-7							NR	NR	All days >0.05	
Wrist arthroscopy	Meyer- Marcotty ²⁷ (2011)	25 vs. 27 (52)	NR	NR	Cryo/Cuff Wrist Cuff (DJO Global)	VAS pain	Days 1-21	NR	NR	<0.05 for days 1 and 2†, >0.05 for all other days

*Visual analog scale (VAS) pain reported on a 0-10 scale. NR = not reported. †Significant difference in favor of continuous cryotherapy devices. ‡Significant difference in favor of simple ice treatment.

cryotherapy using either bagged ice, ice packs, or continuous cryotherapy devices to no cryotherapy in the postoperative setting (Tables I through IV)^{29,42-69}. Postoperative pain scores, analgesic consumption, range of motion, and swelling were summarized from these studies, and the results of the studies included in this review were also stratified by surgical procedure. The majority of studies evaluated the role of postoperative cryotherapy compared with no cryotherapy for knee arthroplasty and knee arthroscopy. The results of these RCTs were generally mixed, but all showed either an equal or superior benefit of cryotherapy use compared with no cryotherapy. Additionally, none of the studies identified any complications that were specifically caused by cryotherapy treatment. Although the available literature is limited in the hip, shoulder, elbow, and wrist, current studies have shown promising results in favor of cryotherapy. However, the limited number of studies in these areas and their heterogenous patient populations and cryotherapy methods make it difficult to draw meaningful conclusions,

especially when combined with the small sample sizes used in many of the studies.

The results seen after lower-extremity surgery—for both arthroplasty and arthroscopic procedures—suggest that cryotherapy may be helpful to aid in recovery, depending on the patient population, but the studies offer mixed results. For example, Kullenberg et al. found that compressive cryotherapy tended to improve pain, range of motion, and the length of hospital stay after TKA compared with no cryotherapy, although these results were not statistically significant⁵³. Morsi found similar results suggesting that the use of a continuous cryotherapy device after TKA improved range of motion, blood loss, pain scores, and wound-healing and decreased pain medication usage⁵⁹. However, Gibbons et al. compared compressive cryotherapy to a Robert Jones bandage after TKA and found no difference between the 2 groups with the exception of reduced blood loss in the compressive cryotherapy group⁴⁷.

The results were similar after hip surgery. Saito et al. concluded that administration of a continuous cryotherapy device after total hip arthro-

plasty (THA) improved pain and reduced pain medication use, while Iwakiri et al. found that continuous cryotherapy devices significantly reduced local swelling^{51,62}. In contrast, Leegwater et al. found that compressive cryotherapy did not contribute any added value in the acute postoperative recovery phase after hip fracture surgery⁵⁶.

One pertinent question regarding all forms of cryotherapy is the amount of tissue penetration achieved, and thus whether the reduction in temperature is reaching subcutaneous and deeper tissues. Several studies have sought to answer this question, and while cryotherapy provides an obvious temperature reduction in cutaneous tissues, some studies suggest that this effect may not be reaching subcutaneous tissues. An RCT used temperature probes to determine the reduction in temperature achieved by local cryotherapy using a continuous cryotherapy device in the glenohumeral joint and subacromial space following shoulder arthroscopy⁷⁰. The authors found that surface-applied cryotherapy did not penetrate the glenohumeral joint or the subacromial

TABLE VI Summary of 12 Studies Comparing Postoperative Analgesic Consumption with Continuous Cryotherapy Devices Versus Bagged Ice or Ice Pack Treatment*

Study	Sample Size Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Variable	Follow- up Time	Results		P Value		
		Treatment	Control				Treatment	Control			
TKA											
Bech ⁷³ (2015)	37 vs. 34 (71)	70.4 ± 1.8 (17:20)	71.5 ± 1.8 (19:15)	DonJoy Iceman (DonJoy Canada)	Mean opioid usage (mg)	Between hours 24- 48	49.9 ± 5.8	42.3 ± 4.9	0.33		
Schinsky ⁷⁸ (2016)	49 vs. 51 (100)	64.7 (20:29)	65.3 (24:27)	Unspecified continuous cryotherapy device	Doses of analgesic usage in the previous 24 hr (no. of doses)	At discharge	2.54 ± 1.17	2.38 ± 1.03	0.63		
						Week 3	2.23 ± 1.51	2.50 ± 1.54	0.83		
						Week 6	2.21 ± 1.91	2.23 ± 2.06	0.94		
Sadoghi ⁷⁷ (2018)	46 vs. 51 (97)	70.4 (14:32)	71.7 (15:36)	cTreatment (Waegener)	Total hydromorphone usage (mg)	Day 6	10.23 ± 5.05	12.11 ± 7.97	>0.05		
Su ⁸⁰ (2012)	103 vs. 84 (187)	NR	NR	GameReady (CoolSystems)	MME usage from weeks 0-2 (mg)	Week 2	509	680	<0.05†		
						Week 6	NR	NR	>0.05		
Thienpont ⁸¹ (2014)	50 vs. 50 (100)	67.5 ± 10.5 (15:35)	68.5 ± 10 (10: 40)	cTreatment (Waegener)	Morphine usage (mg)	Day 2	38 ± 27	38.5 ± 26	0.925		
					Tramadol usage (mg)	Day 2	282 ± 240	317 ± 416	0.61		
Knee arthroscopy											
Barber ⁴² (1998)	51 vs. 49 (100)	34 (34:17)	34 (40:9)	Aircast Cryo/ Cuff (DJO Global)	Vicodin usage (mg/ day)	Day 1	0.86	2.26	<0.001†		
						Day 2	1.49	2.7	0.04†		
						Day 3	2.06	2.74	>0.05		
						Day 4	1.9	1.51	>0.05		
						Day 5	2.12	1.51	>0.05		
						Day 6	2.47	1.4	>0.05		
Konrath ⁵² (1996)	27 vs. 23 (50)	27 (11:8)	26 (13:10)	Polar Care (Breg)	Total pain medication usage, normalized to body weight (mg/kg)	At discharge	0.59	0.60	>0.05		
Ruffilli ⁷⁶ (2015)	23 vs. 24 (47)	32.2 ± 6.7 (14:9)	31.4 ± 8.1 (15:9)	Hilotherm (Hilotherm)	Tramadol usage	Day 1	NR	NR	>0.05		
Schröder ⁷⁹ (1994)	21 vs. 23 (44)	24.8 ± 5.6 (15:6)	24.2 ± 4.5 (18:5)	Cryo/Cuff IC Cooler (DJO Global)	Bupivacaine usage (mg/kg)	At discharge	NR	NR	>0.05		
						Tramadol (mg/kg)	At discharge	NR	NR	>0.05	
							Tilidine (mg/kg)	At discharge	NR	NR	<0.05†
							Pethidine (mg/kg)	At discharge	NR	NR	>0.05
							Pitiramide (mg/kg)	At discharge	NR	NR	<0.05†
Waterman ²⁶ (2012)	18 vs. 18 (36)	28.7 (15:3)	30.9 (15:3)	GameReady (CoolSystems)	No. of patients no longer using analgesics	Week 6	15 of 18	5 of 18	0.0008†		
Shoulder arthroplasty											
Noyes ⁷⁵ (2018)	20 vs. 20 (40)	NR	NR	Polar Care Shoulder Cuff (Breg)	Total MME narcotic consumption	Day 1	43.0 ± 36.7	38.0 ± 42.9	0.382		
						Day 3	149.0 ± 106.5	116.3 ± 108.9	0.601		
						Day 7	308.1 ± 234.0	228 ± 258.3	0.319		
						Day 14	430.8 ± 384.2	347.5 ± 493.4	0.348		
Shoulder arthroscopy											
Kraeutler ²⁸ (2015)	25 vs. 21 (46)	55.4	55.8	GameReady Shoulder Wrap (CoolSystems)	MME dose of opioid analgesics	Day 7	201	154	>0.05		

*MME = morphine milligram equivalents, and NR = not reported. †Significant difference in favor of continuous cryotherapy devices.

TABLE VII Summary of 11 Studies Comparing Postoperative Range of Motion with Continuous Cryotherapy Devices Versus Bagged Ice or Ice Pack Treatment*

Study	Sample Size Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Outcome Type	Follow-up Time	Results		P Value
		Treatment	Control				Treatment	Control	
TKA									
Bech ⁷³ (2015)	37 vs. 34 (71)	70.4 ± 1.8 (17:20)	71.5 ± 1.8 (19:15)	DonJoy Iceman (DonJoy Canada)	Passive ROM (°)	Day 2	54.0 ± 2.4	59.8 ± 3.1	0.14
Demoulin ⁷⁴ (2012)	22 vs. 22 (44)	Males: 71.7 ± 5.6 (9 total), females: 70.9 ± 8.8 (13 total)	Males: 67.2 ± 11.9 (9 total), females: 68.8 ± 9.5 (13 total)	Aircast Cryo/Cuff (DJO Global)	Mean max. active and passive flexion (°)	Week 1	NR	NR	>0.05
					Mean max. active and passive extension (°)	Week 1	NR	NR	>0.05
Sadoghi ⁷⁷ (2018)	46 vs. 51 (97)	70.4 (14:32)	71.7 (15:36)	cTreatment (Waegener)	Mean total knee flexion (°)	Day 2	56 ± 11	51 ± 16	0.089
						Day 4	NR	NR	>0.05
						Day 6	86 ± 7	80 ± 14	0.021†
Schinsky ⁷⁸ (2016)	49 vs. 51 (100)	64.7 (20:29)	65.3 (24:27)	Unspecified continuous cryotherapy device	Mean ROM in flexion (°)	At discharge	75.9 ± 15.7	79.5 ± 11.7	0.18
					Mean ROM in extension (°)	At discharge	8.32 ± 6.95	6.00 ± 7.94	0.86
Su ⁸⁰ (2012)	103 vs. 84 (187)	NR	NR	GameReady (CoolSystems)	Difference in max. knee flexion compared with preop. value (°)	Week 2	-33	-28.7	>0.05
						Week 6	-9.5	-8.6	>0.05
					Difference in max. knee extension compared with preop. value (°)	Week 2	1.5	1.6	>0.05
						Week 6	-1.7	-1.5	>0.05
Thienpont ⁸¹ (2014)	50 vs. 50 (100)	67.5 ± 10.5 (15:35)	68.5 ± 10 (10:40)	cTreatment (Waegener)	Mean active flexion (°)	Day 4	88.5 ± 12.5	92 ± 20	0.30
						Week 6	114 ± 12	120 ± 14	0.02‡
					Mean active extension (°)	Day 4	-1.5 ± 2.5	-1.5 ± 4	0.88
						Week 6	-0.5 ± 0.7	-0.6 ± 0.8	0.51
Knee arthroscopy									
Barber ⁴² (1998)	51 vs. 49 (100)	34 (34:17)	34 (40:9)	Aircast Cryo/Cuff (DJO Global)	Mean max. knee flexion (°)	Day 7	88	77	0.03†
					No. of patients who failed to achieve full knee extension	Day 7	27 of 52	26 of 35	>0.05
Konrath ⁵² (1996)	27 vs. 23 (50)	27 (11:8)	26 (13:10)	Polar Care (Breg)	Mean total knee ROM (°)	Before discharge	61	60	>0.05

continued

TABLE VII (continued)

Study	Sample Size Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Outcome Type	Follow-up Time	Results		P Value
		Treatment	Control				Treatment	Control	
Ruffilli ⁷⁶ (2015)	23 vs. 24 (47)	32.2 ± 6.7 (14:9)	31.4 ± 8.1 (15:9)	Hilotherm (Hilotherm)	Mean max. knee flexion (°)	Day 1	74.8 ± 22.3	43.3 ± 24.7	<0.0001†
Schröder ⁷⁹ (1994)	21 vs. 23 (44)	24.8 ± 5.6 (15:6)	24.2 ± 4.5 (18:5)	Cryo/Cuff IC Cooler (DJO Global)	Max. knee flexion (°)	Day 1, 2, 3, and 6, weeks 2 and 4	NR	NR	<0.05 for all days†
					Knee extension deficit (°)	Day 1, 2, 3, and 6, weeks 2 and 4	NR	NR	<0.05 for day 28 only†
Wrist arthroscopy Meyer-Marcotty ²⁷ (2011)	25 vs. 27 (52)	NR	NR	Cryo/Cuff Wrist Cuff (DJO Global)	Global ROM (°)	Days 1 and 8, week 3	NR	NR	All >0.05

*ROM = range of motion, and NR = not reported. †Significant difference in favor of continuous cryotherapy devices. ‡Significant difference in favor of simple ice treatment.

space. In contrast, Osbahr et al. performed a similar study at the shoulder and found significant decreases in subacromial and glenohumeral temperatures at various time points from 4 to 23 hours after initiation of cryotherapy using a continuous cryotherapy device ($p < 0.05$)⁷¹.

The variation in outcomes that is seen in the literature could be caused by several factors such as the level of tissue penetration, method of cryotherapy, time of application, and types of outcome measures that were used in each study. If the cold temperature does not reach the intended area, then the temperature-dependent mechanisms discussed earlier in the section on basic-science mechanisms would not be relevant. The degree of tissue penetration achieved by cryotherapy as well as the ideal joint temperature to be achieved are areas that will require further study. However, it is important to note that cryotherapy did not result in inferior outcomes in any of studies presented in Tables I through IV when compared with no cryotherapy treatment, and there were also no cryotherapy-specific complications in any of the areas identified.

Continuous Cryotherapy Devices Versus Bagged Ice or Ice Packs

Overall, there were 15 RCTs that directly compared continuous cryo-

therapy devices to the use of bagged ice or ice packs^{26-28,52,72-82}. Once again, the majority of these studies were conducted to evaluate effectiveness in TKA and knee arthroscopy. Results after shoulder arthroplasty, shoulder arthroscopy, and wrist arthroscopy were also evaluated. In the studies evaluated, continuous cryotherapy was found to be superior to bagged ice or ice pack therapy in 6 (43%) of 14 studies in terms of pain scores, 4 (33%) of 12 in terms of analgesic consumption, 4 (36%) of 11 in terms of range of motion, and 2 (22%) of 9 in terms of swelling (Tables V through VIII). In contrast, 2 studies found bagged ice or ice pack treatment to be superior to continuous cryotherapy devices, 1 in terms of pain scores and another in terms of range of motion^{78,81}.

Out of all procedures studied, continuous cryotherapy after knee arthroscopy appeared to most consistently have favorable results, with the majority of studies demonstrating a significant reduction in pain, swelling, and analgesic consumption and increase in range of motion compared with bagged ice or ice packs (Table IX). Of these studies, only 1 of 6 received funding from an industry partner⁴². The results were more mixed in the knee arthroplasty literature. The majority of studies

found no significant reduction in postoperative pain or swelling or improvement in range of motion with continuous cryotherapy compared with bagged ice or ice packs ($p > 0.05$).

Although the studies were limited, continuous cryotherapy does not appear to have a benefit for shoulder surgery compared with bagged ice or ice pack therapy. There was no benefit in any of the postoperative measures in the 2 RCTs that evaluated the shoulder. These results explain why insurance companies often do not cover the costs associated with continuous cryotherapy devices. Continuous cryotherapy may offer convenience as an advantage, with 1 study showing that patients were likely to use continuous cryotherapy devices more often than bagged ice treatment in the postoperative setting⁵⁵. However, based on the results of this review, that may not translate into clinical results. Further Level-I and II studies are needed to better understand the advantage that continuous cryotherapy devices may have in comparison with bagged ice or ice packs according to the surgery type.

Potential Side Effects

Cryotherapy offers a relatively low risk profile within the orthopaedic and athletic community. Many of the

TABLE VIII Summary of 9 Studies Comparing Postoperative Swelling with Continuous Cryotherapy Devices Versus Bagged Ice or Ice Pack Treatment*

Study	Sample Size Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Variable	Follow-up Time	Results		P Value
		Treatment	Control				Treatment	Control	
TKA									
Demoulin ⁷⁴ (2012)	22 vs. 22 (44)	Males: 71.7 ± 5.6 (9 total), females: 70.9 ± 8.8 (13 total)	Males: 67.2 ± 11.9 (9 total), females: 68.8 ± 9.5 (13 total)	Aircast Cryo/Cuff (DJO Global)	Circumference of knee at joint line, 10 cm above joint line, and 5 cm below joint line (cm)	Day 7	NR	NR	All >0.05
Sadoghi ⁷⁷ (2018)	46 vs. 51 (97)	70.4 (14:32)	71.7 (15:36)	cTreatment (Waegener)	Mean circumference of knee, mid-patella, 7 cm proximal to patellar base, and 7 cm distal to patellar apex (cm)	Day 6	NR	NR	All >0.05
Schinsky ⁷⁸ (2016)	49 vs. 51 (100)	64.7 (20:29)	65.3 (24:27)	Unspecified continuous cryotherapy device	Difference in circumference of knee 3 cm above mid-patella compared with baseline (cm)	Postop. Week 3 Week 6	2.56 ± 5.37 1.83 ± 4.70 0.94 ± 4.56	2.83 ± 5.28 2.69 ± 5.25 1.56 ± 4.32	0.41 0.22 0.28
Su ⁸⁰ (2012)	103 vs. 84 (187)	NR	NR	GameReady (CoolSystems)	Knee girth	Weeks 2 and 6	NR	NR	All >0.05
Thienpont ⁸¹ (2014)	50 vs. 50 (100)	67.5 ± 10.5 (15:35)	68.5 ± 10 (10:40)	cTreatment (Waegener)	Knee circumference (cm)	Week 6	45 ± 4.5	45.5 ± 5.1	0.60
Knee arthroscopy									
Ruffilli ⁷⁶ (2015)	23 vs. 24 (47)	32.2 ± 6.7 (14:9)	31.4 ± 8.1 (15:9)	Hilotherm (Hilotherm)	Circumference of knee at patellar apex, compared with preop. (cm)	Day 1	NR	NR	0.01†
					Circumference of knee 10 cm proximal to the superior patellar pole, compared with preop. (cm)	Day 1	NR	NR	0.001†
					Circumference of knee 15 cm distal to the superior patellar pole, compared with preop. (cm)	Day 1	NR	NR	>0.05
Schröder ⁷⁹ (1994)	21 vs. 23 (44)	24.8 ± 5.6 (15:6)	24.2 ± 4.5 (18:5)	Cryo/Cuff IC Cooler (DJO Global)	Change in circumference of knee compared with baseline for superior patellar pole, mid-patella, and max. calf girth (cm)	Day 1 Day 2 Day 3 Day 6 Day 14 Day 28	NR NR NR NR NR NR	NR NR NR NR NR NR	>0.05 <0.05 at calf only <0.05 at superior patella, calf <0.05 at superior patella, calf <0.05 at calf only <0.05 at calf only
<i>continued</i>									

TABLE VIII (continued)

Study	Sample Size Treatment Vs. Control (Total)	Mean Age (No. Male: Female)		Cryotherapy Method	Variable	Follow-up Time	Results		P Value
		Treatment	Control				Treatment	Control	
Waterman ²⁶ (2012)	18 vs. 18 (36)	28.7 (15:3)	30.9 (15:3)	GameReady (CoolSystems)	Knee circumference at proximal, central, and distal portions of patella (cm)	Week 1	44.1, 41.4, 38.1	44.0, 41.9, 39.3	>0.05
						Week 2	42.9, 40.3, 37.4	41.8, 40.1, 37.9	>0.05
						Week 6	41.4, 39.7, 36.8	41.3, 40.0, 37.6	>0.05
Wrist arthroscopy Meyer-Marcotty ²⁷ (2011)	25 vs. 27 (52)	NR	NR	Cryo/Cuff Wrist Cuff (DJO Global)	Change in wrist volume compared with preop. value (mL)	Day 1	967 ± 24 to 932 ± 34	890 ± 36 to 912 ± 38	>0.05
						Day 21	967 ± 24 to 954 ± 25	890 ± 36 to 905 ± 33	>0.05

*NR = not reported. †Significant difference in favor of continuous cryotherapy devices.

complications related to cryotherapy are secondary to poor patient understanding or prolonged duration of use. Currently, most of the literature pertaining to adverse outcomes involves case reports.

The most publicized and frequently acknowledged complications of cryotherapy are cutaneous reactions. Frostbite damages tissue by direct cellular damage from alterations in osmotic gradient and progressive dermal ischemia^{83,84}. Fingers and toes are especially prone to frostbite injuries due to limited blood supply and minimal collateral circulation. Case reports have documented frostbite following an extended duration of cryotherapy to digits following injury or operative procedures^{85,86}. In addition to the distal aspects of extremities, the knee is a susceptible region for developing skin complications. Dundon et al. reported on 2 patients who developed skin necrosis over the patella after using cryotherapy for an extended period of time following knee arthroplasty⁸⁷. King et al. described 2 patients who underwent arthroscopic knee surgery and developed pernio secondary to use of a continuous cryotherapy device in the acute postoperative period⁸⁸. These complications can often be easily prevented by avoiding direct skin contact with the cryotherapy

device, limiting the time of usage, and providing appropriate patient counseling.

Cryotherapy has also been linked with peripheral nerve injuries. Malone et al. reported 6 cases of peripheral nerve injuries in athletes following direct cryotherapy. The peripheral nerve injuries included 3 peroneal nerves, 2 lateral femoral cutaneous nerves, and 1 supraclavicular nerve. All athletes returned to baseline neurologic function⁸⁹. This again highlights the importance of appropriate counseling and monitoring of orthopaedic patients receiving cryotherapy.

The greatest risk of complications has been associated with the use of whole-body cryotherapy in nitrogen gas chambers²⁵. The extreme temperatures of these chambers place patients at higher risks for complications, and the recommended exposure duration is only 2 to 3 minutes to optimize benefit and minimize risk⁹⁰. There is concern for nitrogen asphyxiation and loss of consciousness secondary to inhalation of the nitrogen gas, and there is 1 documented complication of global amnesia following a whole-body cryotherapy session^{90,91}.

Cost-Benefit Analysis of Cryotherapy

An extensive review of the literature demonstrated that 44% of studies

showed improvement in pain scores with the use of cryotherapy compared with no cryotherapy. In terms of reduction in pain medication consumption, 48% of the studies reported a decrease in pain medication in the cryotherapy group. While the cost reduction in pain medication may or may not justify the additional cost of more advanced methods of cryotherapy application, including continuous flow combined with compression, the reduction in narcotic medication has a societal benefit in helping to curb unwanted diversion into the community. More efficacious and reliable cryotherapy application may make narcotic-free surgery a more realistic goal.

The least expensive cryotherapy method is a single bag of ice for localized pain control, while joint-specific continuous cryotherapy devices represent more expensive options. The cost of these devices can range between \$65 and >\$250 depending on the hospital contract and on the patient's insurance, which may or may not cover the cost of these devices. The rental cost of units providing continuous cryotherapy with compression can vary substantially between \$100 and \$700 per week, which may not be covered by insurance. To our knowledge, there is no study in the literature evaluating the cost-

TABLE IX Summary of the Clinical Effectiveness of All Studies Evaluating Postoperative Pain Scores, Analgesic Consumption, Range of Motion, and Swelling

Variable	Joint (Procedure)	No. of Studies			Total
		Cryotherapy Superior to No Cryotherapy	No Difference	Cryotherapy Inferior to No Cryotherapy	
Cryotherapy of any form vs. no cryotherapy					
Pain score	Knee (arthroplasty)	4 (33%)	8 (67%)	–	12
	Knee (arthroscopy)	3 (43%)	4 (57%)	–	7
	Hip	1 (33%)	2 (67%)	–	3
	Shoulder	2 (100%)	–	–	2
	Elbow	1 (100%)	–	–	1
	Total	11 (44%)	14 (56%)	–	25
	Analgesic consumption	Knee (arthroplasty)	4 (40%)	6 (60%)	–
Knee (arthroscopy)		4 (57%)	3 (43%)	–	7
Hip		2 (40%)	3 (60%)	–	5
Elbow		1 (100%)	–	–	1
Total		11 (48%)	12 (52%)	–	23
Range of motion	Knee (arthroplasty)	3 (33%)	6 (67%)	–	9
	Knee (arthroscopy)	–	6 (100%)	–	6
	Elbow	–	1 (100%)	–	1
	Total	3 (19%)	13 (81%)	–	16
Swelling	Knee (arthroplasty)	–	4 (100%)	–	4
	Knee (arthroscopy)	–	3 (100%)	–	3
	Hip	1 (100%)	–	–	1
	Shoulder	1 (100%)	–	–	1
	Total	2 (22%)	7 (78%)	–	9
Overall total					
29					
Continuous cryotherapy devices vs. simple ice treatment					
Pain score	Knee (arthroplasty)	1 (17%)	4 (67%)	1 (17%)	6
	Knee (arthroscopy)	4 (80%)	1 (20%)	–	5
	Shoulder	–	2 (100%)	–	2
	Wrist	1 (100%)	–	–	1
	Total	6 (43%)	7 (50%)	1 (7%)	14
Analgesic consumption	Knee (arthroplasty)	1 (20%)	4 (80%)	–	5
	Knee (arthroscopy)	3 (60%)	2 (40%)	–	5
	Shoulder	–	2 (100%)	–	2
	Total	4 (33%)	8 (67%)	–	12
Range of motion	Knee (arthroplasty)	1 (17%)	4 (67%)	1 (17%)	6
	Knee (arthroscopy)	3 (75%)	1 (25%)	–	4
	Wrist	–	1 (100%)	–	1
	Total	4 (36%)	6 (55%)	1 (9%)	11
Swelling	Knee (arthroplasty)	–	5 (100%)	–	5
	Knee (arthroscopy)	2 (67%)	1 (33%)	–	3
	Wrist	–	1 (100%)	–	1
	Total	2 (22%)	7 (78%)	–	9
Overall total					
15					

effectiveness of using continuous cryotherapy devices with or without compression after surgery. Theoretically, if we can reduce both pain and pain medication consumption after surgery and help to prevent opioid addiction in patients undergoing elective orthopaedic procedures, then that could justify the cost of providing routine continuous cryotherapy treatment for all orthopaedic patients after surgery. However, we do not currently have any evidence to support this statement. Also, if we can reduce postoperative stiffness and physical therapy visits after surgery with cryotherapy, then that could justify the cost as well. In this review of the literature, only 3 (19%) of 16 studies demonstrated improved range of motion after surgery with cryotherapy, whereas the majority of the studies (13 [81%] of 16) showed no difference. Considering the theoretical cost-effectiveness of cryotherapy protocols compared with other strategies, providers may have a value-based incentive to utilize continuous cryotherapy more often for postoperative management, given the reduction in both pain scores (11 [44%] of the 25 studies reviewed) and pain medication consumption (11 [48%] of the 23 studies reviewed). Future high-level prospective studies are needed to reveal the exact cost and benefit of using cryotherapy as a standard of care.

Conclusions

In summary, cryotherapy is commonly used in conjunction with orthopaedic care and includes the use of bagged ice, ice packs, or continuous cryotherapy devices with or without compression. Cryotherapy has been linked with microvasculature alterations that decrease production of inflammatory mediators, disrupt the overall inflammatory response, decrease edema, as well as decrease NCV. The reduction in cytokines as well as the decreased NCV are thought to underlie the analgesic effect of cryotherapy. Mixed results from outcome studies provide no clear consensus on the advantages of postoperative continuous cryotherapy devices, with or without compression,

compared with bagged ice or ice pack use. However, the risk of complications from cryotherapy, which include skin irritation, frostbite, pernio, and peripheral nerve injuries, is minimal. Whole-body cryotherapy remains an unproven methodology with higher costs and potentially greater risks. Future high-quality Level-I or II studies are needed to determine the value of continuous cryotherapy devices with and without compression before they can be recommended as a standard of care in orthopaedic surgery following both injury and surgery.

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References

1. Maranda E, Simmons BJ, Romanelli P. Cryotherapy-as ancient as the pharaohs. *JAMA Dermatol*. 2016 Jun 1;152(6):730.
2. Wang H, Olivero W, Wang D, Lanzino G. Cold as a therapeutic agent. *Acta Neurochir (Wien)*. 2006 May;148(5):565-70; discussion 569-70. Epub 2006 Feb 17.
3. Freiman A, Bouganim N. History of cryotherapy. *Dermatol Online J*. 2005 Aug 1;11(2):9.
4. Mirkin G, Hoffman M. The sports medicine book. Little Brown; 1978.
5. Lindsay A, Carr S, Cross S, Petersen C, Lewis JG, Gieseg SP. The physiological response to cold-

water immersion following a mixed martial arts training session. *Appl Physiol Nutr Metab*. 2017 May;42(5):529-36. Epub 2017 Jan 17.

6. Kang JI, Jeong DK, Choi H. Effects of microcurrent and cryotherapy on C-reactive protein levels and muscle tone of patients with rotator cuff reconstruction. *J Phys Ther Sci*. 2018 Jan;30(1):37-41. Epub 2018 Jan 27.

7. Pournot H, Bieuzen F, Louis J, Mounier R, Fillard JR, Barbiche E, Hausswirth C. Time-course of changes in inflammatory response after whole-body cryotherapy multi exposures following severe exercise. *PLoS One*. 2011;6(7):e22748. Epub 2011 Jul 28.

8. Algaflly AA, George KP. The effect of cryotherapy on nerve conduction velocity, pain threshold and pain tolerance. *Br J Sports Med*. 2007 Jun;41(6):365-9; discussion 369. Epub 2007 Jan 15.

9. White GE, Wells GD. Cold-water immersion and other forms of cryotherapy: physiological changes potentially affecting recovery from high-intensity exercise. *Extrem Physiol Med*. 2013 Sep 1;2(1):26.

10. Mayer M, Naylor J, Harris I, Badge H, Adie S, Mills K, Descallar J. Evidence base and practice variation in acute care processes for knee and hip arthroplasty surgeries. *PLoS One*. 2017 Jul 19;12(7):e0180090.

11. Ziemann E, Olek RA, Grzywacz T, Kaczor JJ, Antosiewicz J, Skrobot W, Kujach S, Laskowski R. Whole-body cryostimulation as an effective way of reducing exercise-induced inflammation and blood cholesterol in young men. *Eur Cytokine Netw*. 2014 Mar 1;25(1):14-23.

12. Szygula Z, Lubkowska A, Giemza C, Skrzek A, Bryczkowska I, Dołęgowska B. Hematological parameters, and hematopoietic growth factors: EPO and IL-3 in response to whole-body cryostimulation (WBC) in military academy students. *PLoS One*. 2014 Apr 2;9(4):e93096.

13. Banfi G, Lombardi G, Colombini A, Melegati G. Whole-body cryotherapy in athletes. *Sports Med*. 2010 Jun 1;40(6):509-17.

14. Vieira Ramos G, Pinheiro CM, Messa SP, Delfino GB, Marqueti RdeC, Salvini TdeF, Durigan JL. Cryotherapy reduces inflammatory response without altering muscle regeneration process and extracellular matrix remodeling of rat muscle. *Sci Rep*. 2016 Jan 4;6:18525.

15. Ziemann E, Olek RA, Kujach S, Grzywacz T, Antosiewicz J, Garszka T, Laskowski R. Five-day whole-body cryostimulation, blood inflammatory markers, and performance in high-ranking professional tennis players. *J Athl Train*. 2012 Nov-Dec;47(6):664-72.

16. Wojtecka-Lukasik E, Ksiezopolska-Orlowska K, Gaszewska E, Krasowicz-Towalska O, Rzdokiewicz P, Maslinska D, Szukiewicz D, Maslinski S. Cryotherapy decreases histamine levels in the blood of patients with rheumatoid arthritis. *Inflamm Res*. 2010 Mar;59(Suppl 2):S253-5.

17. Zhang J, Pan T, Wang JH. Cryotherapy suppresses tendon inflammation in an animal model. *J Orthop Translat*. 2014 Apr;2(2):75-81. Epub 2014 Feb 20.

18. Stålmán A, Berglund L, Dungenberg E, Arner P, Felländer-Tsai L. Temperature-sensitive release of prostaglandin E₂ and diminished energy requirements in synovial tissue with postoperative cryotherapy: a prospective randomized study after knee arthroscopy. *J Bone Joint Surg Am*. 2011 Nov 2;93(21):1961-8.

19. Lubkowska A, Szygula Z, Chlubek D, Banfi G. The effect of prolonged whole-body

- cryostimulation treatment with different amounts of sessions on chosen pro- and anti-inflammatory cytokines levels in healthy men. *Scand J Clin Lab Invest*. 2011 Sep;71(5):419-25. Epub 2011 May 16.
- 20.** Leonard BE. The HPA and immune axes in stress: the involvement of the serotonergic system. *Eur Psychiatry*. 2005 Oct;20(Suppl 3):S302-6.
- 21.** Herrera E, Sandoval MC, Camargo DM, Salvini TF. Motor and sensory nerve conduction are affected differently by ice pack, ice massage, and cold water immersion. *Phys Ther*. 2010 Apr;90(4):581-91. Epub 2010 Feb 25.
- 22.** Reid G, Babes A, Pluteanu F. A cold- and menthol-activated current in rat dorsal root ganglion neurones: properties and role in cold transduction. *J Physiol*. 2002 Dec 1;545(2):595-614.
- 23.** Yanagisawa O, Kudo H, Takahashi N, Yoshioka H. Magnetic resonance imaging evaluation of cooling on blood flow and oedema in skeletal muscles after exercise. *Eur J Appl Physiol*. 2004 May;91(5-6):737-40. Epub 2004 Mar 13.
- 24.** Yeung SS, Ting KH, Hon M, Fung NY, Choi MM, Cheng JC, Yeung EW. Effects of cold water immersion on muscle oxygenation during repeated bouts of fatiguing exercise: a randomized controlled study. *Medicine (Baltimore)*. 2016 Jan;95(1):e2455.
- 25.** Patel K, Bakshi N, Freehill MT, Awan TM. Whole-body cryotherapy in sports medicine. *Curr Sports Med Rep*. 2019 Apr;18(4):136-40.
- 26.** Waterman B, Walker JJ, Swaims C, Shortt M, Todd MS, Machen SM, Owens BD. The efficacy of combined cryotherapy and compression compared with cryotherapy alone following anterior cruciate ligament reconstruction. *J Knee Surg*. 2012 May;25(2):155-60.
- 27.** Meyer-Marcotty M, Jungling O, Vaske B, Vogt PM, Knobloch K. Standardized combined cryotherapy and compression using Cryo/Cuff after wrist arthroscopy. *Knee Surg Sports Traumatol Arthrosc*. 2011 Feb;19(2):314-9. Epub 2010 Oct 7.
- 28.** Kraeutler MJ, Reynolds KA, Long C, McCarty EC. Compressive cryotherapy versus ice-a prospective, randomized study on postoperative pain in patients undergoing arthroscopic rotator cuff repair or subacromial decompression. *J Shoulder Elbow Surg*. 2015 Jun;24(6):854-9. Epub 2015 Mar 29.
- 29.** Smith J, Stevens J, Taylor M, Tibbey J. A randomized, controlled trial comparing compression bandaging and cold therapy in postoperative total knee replacement surgery. *Orthop Nurs*. 2002 Mar-Apr;21(2):61-6.
- 30.** Higgins TR, Greene DA, Baker MK. Effects of cold water immersion and contrast water therapy for recovery from team sport: a systematic review and meta-analysis. *J Strength Cond Res*. 2017 May;31(5):1443-60.
- 31.** Versey NG, Halson SL, Dawson BT. Water immersion recovery for athletes: effect on exercise performance and practical recommendations. *Sports Med*. 2013 Nov;43(11):1101-30.
- 32.** Galliera E, Dogliotti G, Melegati G, Corsi Romanelli MM, Cabitza P, Banfi G. Bone remodelling biomarkers after whole body cryotherapy (WBC) in elite rugby players. *Injury*. 2013 Aug;44(8):1117-21. Epub 2012 Sep 21.
- 33.** Costello JT, Baker PR, Minett GM, Bieuzen F, Stewart IB, Bleakley C. Whole-body cryotherapy (extreme cold air exposure) for preventing and treating muscle soreness after exercise in adults. *Cochrane Database Syst Rev*. 2015 Sep 18;9:CD010789.
- 34.** Bleakley CM, Bieuzen F, Davison GW, Costello JT. Whole-body cryotherapy: empirical evidence and theoretical perspectives. *Open Access J Sports Med*. 2014 Mar 10;5:25-36.
- 35.** Wilson LJ, Dimitriou L, Hills FA, Gondek MB, Cockburn E. Whole body cryotherapy, cold water immersion, or a placebo following resistance exercise: a case of mind over matter? *Eur J Appl Physiol*. 2019 Jan;119(1):135-47. Epub 2018 Oct 11.
- 36.** Wilson LJ, Cockburn E, Paice K, Sinclair S, Faki T, Hills FA, Gondek MB, Wood A, Dimitriou L. Recovery following a marathon: a comparison of cold water immersion, whole body cryotherapy and a placebo control. *Eur J Appl Physiol*. 2018 Jan;118(1):153-63. Epub 2017 Nov 10.
- 37.** Peake JM, Roberts LA, Figueiredo VC, Egner I, Krog S, Aas SN, Suzuki K, Markworth JF, Coombes JS, Cameron-Smith D, Raastad T. The effects of cold water immersion and active recovery on inflammation and cell stress responses in human skeletal muscle after resistance exercise. *J Physiol*. 2017 Feb 1;595(3):695-711. Epub 2016 Nov 13.
- 38.** Broatch JR, Petersen A, Bishop DJ. Postexercise cold water immersion benefits are not greater than the placebo effect. *Med Sci Sports Exerc*. 2014 Nov;46(11):2139-47.
- 39.** Goodall S, Howatson G. The effects of multiple cold water immersions on indices of muscle damage. *J Sports Sci Med*. 2008 Jun 1;7(2):235-41.
- 40.** Bailey DM, Erith SJ, Griffin PJ, Dowson A, Brewer DS, Gant N, Williams C. Influence of cold-water immersion on indices of muscle damage following prolonged intermittent shuttle running. *J Sports Sci*. 2007 Sep;25(11):1163-70.
- 41.** Ferreira-Junior JB, Bottaro M, Vieira A, Siqueira AF, Vieira CA, Durigan JL, Cadore EL, Coelho LG, Simões HG, Bembem MG. One session of partial-body cryotherapy (-110 °C) improves muscle damage recovery. *Scand J Med Sci Sports*. 2015 Oct;25(5):e524-30. Epub 2014 Dec 30.
- 42.** Barber FA, McGuire DA, Click S. Continuous-flow cold therapy for outpatient anterior cruciate ligament reconstruction. *Arthroscopy*. 1998 Mar;14(2):130-5.
- 43.** Brandsson S, Rydgren B, Hedner T, Eriksson BI, Lundin O, Swärd L, Karlsson J. Postoperative analgesic effects of an external cooling system and intra-articular bupivacaine/morphine after arthroscopic cruciate ligament surgery. *Knee Surg Sports Traumatol Arthrosc*. 1996;4(4):200-5.
- 44.** Dervin GF, Taylor DE, Keene GC. Effects of cold and compression dressings on early postoperative outcomes for the arthroscopic anterior cruciate ligament reconstruction patient. *J Orthop Sports Phys Ther*. 1998 Jun;27(6):403-6.
- 45.** Desteli EE, Imren Y, Aydın N. Effect of both preoperative and postoperative cryocutaneous treatment on hemostasis and postoperative pain following total knee arthroplasty. *Int J Clin Exp Med*. 2015 Oct 15;8(10):19150-5.
- 46.** Edwards DJ, Rimmer M, Keene GC. The use of cold therapy in the postoperative management of patients undergoing arthroscopic anterior cruciate ligament reconstruction. *Am J Sports Med*. 1996 Mar-Apr;24(2):193-5.
- 47.** Gibbons CE, Solan MC, Ricketts DM, Patterson M. Cryotherapy compared with Robert Jones bandage after total knee replacement: a prospective randomized trial. *Int Orthop*. 2001;25(4):250-2.
- 48.** Healy WL, Seidman J, Pfeiffer BA, Brown DG. Cold compressive dressing after total knee arthroplasty. *Clin Orthop Relat Res*. 1994 Feb;299:143-6.
- 49.** Holm B, Husted H, Kehlet H, Bandholm T. Effect of knee joint icing on knee extension strength and knee pain early after total knee arthroplasty: a randomized cross-over study. *Clin Rehabil*. 2012 Aug;26(8):716-23. Epub 2012 Jan 19.
- 50.** Holmström A, Härdin BC. Cryo/Cuff compared to epidural anesthesia after knee unicompartmental arthroplasty: a prospective, randomized and controlled study of 60 patients with a 6-week follow-up. *J Arthroplasty*. 2005 Apr;20(3):316-21.
- 51.** Iwakiri K, Kobayashi A, Takeuchi Y, Kimura Y, Ohata Y, Nakamura H. Efficacy of continuous local cryotherapy following total hip arthroplasty. *SICOT J*. 2019;5:13. Epub 2019 May 3.
- 52.** Konrath GA, Lock T, Goitz HT, Scheidler J. The use of cold therapy after anterior cruciate ligament reconstruction. A prospective, randomized study and literature review. *Am J Sports Med*. 1996 Sep-Oct;24(5):629-33.
- 53.** Kullenberg B, Ylipää S, Söderlund K, Resch S. Postoperative cryotherapy after total knee arthroplasty: a prospective study of 86 patients. *J Arthroplasty*. 2006 Dec;21(8):1175-9.
- 54.** Kuyucu E, Bülbül M, Kara A, Koçyiğit F, Erdil M. Is cold therapy really efficient after knee arthroplasty? *Ann Med Surg (Lond)*. 2015 Nov 11;4(4):475-8.
- 55.** Leegwater NC, Willems JH, Brohet R, Nolte PA. Cryocompression therapy after elective arthroplasty of the hip. *Hip Int*. 2012 Sep-Oct;22(5):527-33.
- 56.** Leegwater NC, Bloemers FW, de Korte N, Heetveld MJ, Kalisvaart KJ, Schönhuth CP, Pijnenburg BACM, Burger BJ, Ponsen KJ, Maier AB, van Royen BJ, Nolte PA. Postoperative continuous-flow cryocompression therapy in the acute recovery phase of hip fracture surgery-a randomized controlled clinical trial. *Injury*. 2017 Dec;48(12):2754-61. Epub 2017 Oct 10.
- 57.** Lessard LA, Scudds RA, Amendola A, Vaz MD. The efficacy of cryotherapy following arthroscopic knee surgery. *J Orthop Sports Phys Ther*. 1997 Jul;26(1):14-22.
- 58.** Levy AS, Marmar E. The role of cold compression dressings in the postoperative treatment of total knee arthroplasty. *Clin Orthop Relat Res*. 1993 Dec;297:174-8.
- 59.** Morsi E. Continuous-flow cold therapy after total knee arthroplasty. *J Arthroplasty*. 2002 Sep;17(6):718-22.
- 60.** Ohkoshi Y, Ohkoshi M, Nagasaki S, Ono A, Hashimoto T, Yamane S. The effect of cryotherapy on intraarticular temperature and postoperative care after anterior cruciate ligament reconstruction. *Am J Sports Med*. 1999 May-Jun;27(3):357-62.
- 61.** Radkowski CA, Pietrobon R, Vail TP, Nunley JA 2nd, Jain NB, Easley ME. Cryotherapy temperature differences after total knee arthroplasty: a prospective randomized trial. *J Surg Orthop Adv*. 2007 Summer;16(2):67-72.

- 62.** Saito N, Horiuchi H, Kobayashi S, Nawata M, Takaoka K. Continuous local cooling for pain relief following total hip arthroplasty. *J Arthroplasty*. 2004 Apr;19(3):334-7.
- 63.** Scarcella JB, Cohn BT. The effect of cold therapy on the postoperative course of total hip and knee arthroplasty patients. *Am J Orthop (Belle Mead NJ)*. 1995 Nov;24(11):847-52.
- 64.** Singh H, Osbahr DC, Holovac TF, Cawley PW, Speer KP. The efficacy of continuous cryotherapy on the postoperative shoulder: a prospective, randomized investigation. *J Shoulder Elbow Surg*. 2001 Nov-Dec;10(6):522-5.
- 65.** Speer KP, Warren RF, Horowitz L. The efficacy of cryotherapy in the postoperative shoulder. *J Shoulder Elbow Surg*. 1996 Jan-Feb;5(1):62-8.
- 66.** Webb JM, Williams D, Ivory JP, Day S, Williamson DM. The use of cold compression dressings after total knee replacement: a randomized controlled trial. *Orthopedics*. 1998 Jan;21(1):59-61.
- 67.** Whitelaw GP, DeMuth KA, Demos HA, Schepis A, Jacques E. The use of the Cryo/Cuff versus ice and elastic wrap in the postoperative care of knee arthroscopy patients. *Am J Knee Surg*. 1995 Winter;8(1):28-30; discussion 30-1.
- 68.** Wittig-Wells D, Johnson I, Samms-McPherson J, Thankachan S, Titus B, Jacob A, Higgins M. Does the use of a brief cryotherapy intervention with analgesic administration improve pain management after total knee arthroplasty? *Orthop Nurs*. 2015 May-Jun;34(3):148-53.
- 69.** Yu SY, Chen S, Yan HD, Fan CY. Effect of cryotherapy after elbow arthrolysis: a prospective, single-blinded, randomized controlled study. *Arch Phys Med Rehabil*. 2015 Jan;96(1):1-6. Epub 2014 Sep 4.
- 70.** Levy AS, Kelly B, Lintner S, Speer K. Penetration of cryotherapy in treatment after shoulder arthroscopy. *Arthroscopy*. 1997 Aug;13(4):461-4.
- 71.** Osbahr DC, Cawley PW, Speer KP. The effect of continuous cryotherapy on glenohumeral joint and subacromial space temperatures in the postoperative shoulder. *Arthroscopy*. 2002 Sep;18(7):748-54.
- 72.** Barber FA. A comparison of crushed ice and continuous flow cold therapy. *Am J Knee Surg*. 2000 Spring;13(2):97-101; discussion 102.
- 73.** Bech M, Moorhen J, Cho M, Lavergne MR, Stothers K, Hoens AM. Device or ice: the effect of consistent cooling using a device compared with intermittent cooling using an ice bag after total knee arthroplasty. *Phys other Can*. 2015 Winter;67(1):48-55.
- 74.** Demoulin C, Brouwers M, Darot S, Gillet P, Crielaard JM, Vanderthommen M. Comparison of gaseous cryotherapy with more traditional forms of cryotherapy following total knee arthroplasty. *Ann Phys Rehabil Med*. 2012 May;55(4):229-40. Epub 2012 Apr 5.
- 75.** Noyes MP, Denard PJ. Continuous cryotherapy vs ice following total shoulder arthroplasty: a randomized control trial. *Am J Orthop (Belle Mead NJ)*. 2018 Jun;47(6).
- 76.** Ruffilli A, Buda R, Castagnini F, Di Nicolantonio D, Evangelisti G, Giannini S, Faldini C. Temperature-controlled continuous cold flow device versus traditional icing regimen following anterior cruciate ligament reconstruction: a prospective randomized comparative trial. *Arch Orthop Trauma Surg*. 2015 Oct;135(10):1405-10. Epub 2015 Jul 4.
- 77.** Sadoghi P, Hasenhütl S, Gruber G, Leitner L, Leithner A, Rumpold-Seitlinger G, Kastner N, Poolman RW, Glehr M. Impact of a new cryotherapy device on early rehabilitation after primary total knee arthroplasty (TKA): a prospective randomised controlled trial. *Int Orthop*. 2018 Jun;42(6):1265-73. Epub 2018 Jan 22.
- 78.** Schinsky MF, McCune C, Bonomi J. Multifaceted comparison of two cryotherapy devices used after total knee arthroplasty: cryotherapy device comparison. *Orthop Nurs*. 2016 Sep-Oct;35(5):309-16.
- 79.** Schröder D, Pässler HH. Combination of cold and compression after knee surgery. A prospective randomized study. *Knee Surg Sports Traumatol Arthrosc*. 1994;2(3):158-65.
- 80.** Su EP, Perna M, Boettner F, Mayman DJ, Gerlinger T, Barsoum W, Randolph J, Lee G. A prospective, multi-center, randomised trial to evaluate the efficacy of a cryopneumatic device on total knee arthroplasty recovery. *J Bone Joint Surg Br*. 2012 Nov;94(11)(Suppl A):153-6.
- 81.** Thienpont E. Does advanced cryotherapy reduce pain and narcotic consumption after knee arthroplasty? *Clin Orthop Relat Res*. 2014 Nov;472(11):3417-23. Epub 2014 Jul 25.
- 82.** Woolf SK, Barfield WR, Merrill KD, McBryde AM Jr. Comparison of a continuous temperature-controlled cryotherapy device to a simple icing regimen following outpatient knee arthroscopy. *J Knee Surg*. 2008 Jan;21(1):15-9.
- 83.** Hutchison RL. Frostbite of the hand. *J Hand Surg Am*. 2014 Sep;39(9):1863-8.
- 84.** McAdams TR, Swenson DR, Miller RA. Frostbite: an orthopedic perspective. *Am J Orthop (Belle Mead NJ)*. 1999 Jan;28(1):21-6.
- 85.** Rivlin M, King M, Kruse R, Ilyas AM. Frostbite in an adolescent football player: a case report. *J Athl Train*. 2014 Jan-Feb;49(1):97-101. Epub 2013 Oct 23.
- 86.** Brown WC, Hahn DB. Frostbite of the feet after cryotherapy: a report of two cases. *J Foot Ankle Surg*. 2009 Sep-Oct;48(5):577-80. Epub 2009 Jul 16.
- 87.** Dundon JM, Rymer MC, Johnson RM. Total patellar skin loss from cryotherapy after total knee arthroplasty. *J Arthroplasty*. 2013 Feb;28(2):376.e5-7. Epub 2012 Jun 30.
- 88.** King JM, Plotner AN, Adams BB. Perniosis induced by a cold-therapy system. *Arch Dermatol*. 2012 Sep;148(9):1101-2.
- 89.** Malone TR, Engelhardt DL, Kirkpatrick JS, Bassett FH. Nerve injury in athletes caused by cryotherapy. *J Athl Train*. 1992;27(3):235-7.
- 90.** Lombardi G, Lanteri P, Porcelli S, Mauri C, Colombini A, Grasso D, Zani V, Bonomi FG, Melegati G, Banfi G. Hematological profile and martial status in rugby players during whole body cryostimulation. *PLoS One*. 2013;8(2):e55803. Epub 2013 Feb 1.
- 91.** Carrard J, Lambert AC, Genné D. Transient global amnesia following a whole-body cryotherapy session. *BMJ Case Rep*. 2017 Oct 13; 2017:bcr-2017-221431.