Effects of cryotherapy on joint position sense and intraarticular blood flow volume in healthy knee joints

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Abstract The purpose of this study was to investigate the influence of cryotherapy on knee joint position sense (JPS) and intraarticular blood flow volume (IBFV) and evaluate their relationships with cooling time as well as with surface temperature and deep temperature. Ten healthy volunteers were examined. This study consisted of a same-subjects repeated-measures design, with the timeframe of cryotherapy application (no therapy [resting control group], 2-min cooling, or 15-min cooling intervention) after exercise being the independent variable, and IBFV, knee JPS, surface temperature, and deep temperature serving as the dependent variables. Dependent variables were examined before 10-min cycle ergometer exercise (baseline), post-exercise, post-cooling, and 15 min later. In the 15-min cooling group, IBFV immediately after cooling and 15 min later were significantly lower than the post-exercise values ($P = 0.048$ and 0.016 , respectively), and knee JPS at 15 min later was significantly lower than the baseline value ($P = 0.037$). By contrast, the 2-min cooling group showed no significant changes in either knee JPS or IBFV. Although both surface and deep temperatures after cooling were significantly lower than baseline ($P = 0.034$ and $P < 0.001$, respectively) in the 2-min cooling group, 15 min later they were significantly higher than post-cooling values ($P = 0.023$ and 0.023 , respectively). These results suggest that 15-min cooling interventions functionally impair the sensitivity of JPS, although cooling is suitable for reduction of IBFV in deep tissue. Cooling interventions lasting less than 2-min did not affect knee JPS; however no reduction of IBFV occurred during this timeframe.

Keywords : cryotherapy, deep temperature knee joint, joint position sense, intraarticular blood flow volume, ultrasonography

Introduction

Cryotherapy is commonly used in sports physical therapy practice to relief pain symptoms, particularly in inflammatory disease, injury, and overuse symptoms^{1,2}. Along with the cryotherapy effects, several authors have focused on the effects of cryotherapy on proprioception³⁻⁵. Evidence concerning the effects of cryotherapy on proprioception, namely on joint position sense (JPS), is limited and ambiguous. A recent study demonstrated that the significant increase observed in the accuracy of positional error of the knee after ice application clearly supports the deleterious effect of cryotherapy on knee JPS⁵. Oliveira et al.⁴ also reported that cryotherapy impairs knee JPS in normal knees. Indeed, several investigators have reported decreased knee JPS after cryotherapy⁴⁻⁶,

whereas other studies have not. Ozmun et al.⁷ reported that ice bag application to the knee had no effect on proprioception. Furthermore, the potential for cryotherapy to degrade JPS is unknown due to a limited number of publications, as noted in a recent systematic review⁸. Thus, the effects of cryotherapy on JPS are not clearly understood.

One important goal of cooling therapy is to reduce inflammation. Blood flow is a key indicator of tissue viability, injury, and inflammation. In animal studies, a high correlation has been observed between synovial partial pressure of oxygen and synovial blood flow in both normal and acutely inflamed rabbit knee joints, suggesting the importance of joint blood flow regulatory mechanisms in supplying oxygen⁹. Utsunomiya et al.¹⁰ reported that 10-min cooling reduced blood flow compared to rest or 2-min cooling. However, they examined blood content in muscle tissue using a spectrophotometer, and did not assess flow in a defined blood vessel located in the joint.

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Thus, few studies have examined the effect of cooling treatment on intraarticular blood flow.

Often athletes return to play soon after using cryotherapy. Likewise, subjects participating in rehabilitation programs also often perform exercise therapy immediately after cryotherapy application⁴⁾. Despite the reported effect of cryotherapy on knee JPS, whether cryotherapy during exercise affects JPS remains unknown. Furthermore, the effects on intraarticular blood flow after exercise and cryotherapy are still obscure. Cryotherapy before or during exercise may result in inadequate peripheral feedback for knee JPS and change hemodynamics in the joint, which may result in knee injury when exercise is resumed. Therefore, the presentation of data concerning knee JPS, intraarticular blood flow, and different cooling timeframes is important to clarify the effectiveness of cryotherapy, not only for athletes but also for therapeutic exercise. The purpose of this study was to investigate the influence of cryotherapy on knee JPS and intraarticular blood flow volume (IBFV) and evaluate their relationships with cooling time as well as with surface temperature and deep temperature.

Materials and Methods

Subjects. Ten male healthy volunteers (age, 21.2 ± 2.2 years; height, 173.2 ± 4.2 cm; weight, 65.9 ± 4.8 kg) were examined. Each individual was initially screened for any past history, signs, or present symptoms of injury or disability in their knee joints. They had no history of knee injuries and no pathologic conditions affecting the musculoskeletal or neuromuscular systems.

This study consisted of a same-subjects repeated-measures design, with the timeframe of cryotherapy application (no therapy [resting control group], 2-min cooling, or 15-min cooling intervention) after exercise being the independent variable and IBFV, knee JPS, surface temperature, and deep temperature as the dependent variables. The examinations were conducted in a controlled environment with the room temperature maintained at 25°C and performed on separate days. All subjects were informed of the study procedure and purpose, and written informed consent was obtained from all participants prior to participation. This study was conducted in accordance with the guidelines of the Declaration of Helsinki in 1995 and approved by the institutional ethics committee.

Participants were first instructed to wear appropriate clothing to expose the area of the knee. Core Temp (CM-210; Terumo Co., Ltd., Tokyo, Japan) was used to measure surface and deep temperatures by applying disk sensors over the proximal to middle patella and the middle popliteal fossa, respectively. Participants performed incremental exercise tasks for 10 min using a cycle ergometer after 5 min rest. The pedaling rate was set at 60 rpm and was increased by 15 W/min in a ramped fashion over 10 min. During the exercise session, heart rate was moni-

tored to ensure that exercise intensity never exceeded 60% of the maximum heart rate (determined according the formula: $[220 - \text{age}] \times 0.60$). Cryotherapy was performed using a continuous temperature-controlled cryotherapy device with circulating medium, the Icing System CF-3000 (Sigmax, Tokyo, Japan); a 288×330 -mm cooling pad applied to participants' right knee for 2 or 15 min. The temperature of the cooling pad was maintained at 5°C. IBFV, knee JPS, surface temperature, and deep temperature were examined pre-exercise (baseline), post-exercise, post-cooling, and 15 min later ("post-cooling" was not included for the control group).

IBFV. IBFV was measured using ultrasonography (US). IBFV examination was performed by a board-certified sonographer using a 4.0–10.0 MHz micro-convex probe (portable real-time apparatus ProSound $\alpha 7$; Hitachi-Aloka Medical Ltd., Tokyo, Japan). For this test, each subject was seated in the dependent position with both legs lowered. Fundamental B-mode imaging was first used to identify an adequate scanning plane that clearly showed the popliteal artery and middle genicular artery (MGA). Pulse Doppler mode was then used to measure the blood flow volume of the MGA.

Intra- and inter-observer reliabilities were assessed by examining 5 healthy subjects. IBFV measurements were repeated 5 times for each subject, by 2 sonographers. Intra-observer reliability was estimated using intraclass correlation coefficients (ICC; one-way analysis of variance [ANOVA]). Inter-observer reliability was estimated using ICC (two-way ANOVA).

Knee JPS. Knee JPS was evaluated according to the procedure of Skinner et al.¹¹⁾ with modifications. The knee JPS is defined as the ability to actively or passively reproduce an angle that was previously established actively or passively. Knee JPS was measured using a Biodex System 4 (Biodex Medical Systems, Shirley, New York). The Biodex machine extended or flexed the knee at 0.5 degrees per second until the examiner indicated passive motion or a subject changed active motion and stopped the motion with a handheld stop button. Each subject was dressed in shorts and no shoes, seated in a chair, and blindfolded. In this test, an angle was first produced passively in the joint of the subject. The right leg was placed 1 of 5 randomly selected target knee angles between 5° and 75° and held by the examiner for 5 s. The knee was then returned to a neutral position, and finally, the subject was asked to actively reproduce the first angle position. Absolute angle errors values^{12,13)} were obtained for every angle, and then the mean absolute angle error of 5 trials was calculated as the "average absolute angle error".

Statistical analysis. Results are presented as mean $\pm$ standard error of mean (SE), and statistical significance was determined at $P < 0.05$. A two-way factorial ANOVA

test was used to determine differences between temperatures, average absolute angle error, and IBFV (3×3 ; Groups [control, 2-min cooling and 15-min cooling] $\times$ Phase [baseline, post-exercise, and 15 min later]; the average absolute angle error was not determined in the “post-exercise” phase). Tukey’s HSD test was applied to assess differences among multiple comparisons when ANOVA indicated significant difference for a factor. Since the ANOVA was not able to assess the effect of the post-cooling, Mann–Whitney U tests were performed to compare measurements made during each phase in the control, 2-min cooling, and 15-min cooling groups. Pearson correlation coefficients were used to investigate the correlation of IBFV with temperature change. The statistical program used for the calculations was IBM SPSS statistics 19.0 (IBM SPSS, Chicago, IL).

Results

Intra-observer reproducibility was high for US examination (Observer A, ICC = 0.996; Observer B, ICC = 0.998), as was inter-observer reproducibility (ICC = 0.998). An ICC value > 0.9 was considered very good.

Measurements for several parameters according to group and trial phase are shown in Table 1. Significant interactions were observed for the IBFV [$F(4, 36) = 2.7$, $P = 0.044$] and surface [$F(4, 36) = 17.8$, $P < 0.001$] and deep temperatures [$F(4, 36) = 46.4$, $P < 0.001$]. No significant main effects or interactions were observed for average absolute angle error. Despite no significant main effects among the groups, a significant main effect for phase was observed for IBFV in the MGA [$F(2, 18) = 7.2$, $P = 0.005$]. For surface temperatures, significant main effect for the various groups was observed [$F(2, 18) = 6.6$, $P = 0.007$]. For deep temperatures, significant main

Table 1. IBFV, average absolute angle error, and temperature of the subject, before and after cooling intervention

Parameters	Group	Phase				Two-Way ANOVA (F-Value)		
		(Range)	Baseline	Post-Exercise	Post-Cooling	15 min Later	Group	Phase
		(Range)	(0.6 — 15.3)	(1.4 — 17.1)	(0.5 — 8.6)	(0.9 — 12.1)		
IBFV of the	Control		4.7 ± 1.3	6.6 ± 1.0	NA	4.7 ± 0.8	1.0	7.2
MGA, ml/min	2-min cooling		3.5 ± 0.7	5.4 ± 0.7	6.2 ± 0.9	5.6 ± 1.0	$(P = 0.005)$	
	15-min cooling		3.2 ± 0.6	7.0 ± 1.6	3.4 ± 0.7	1.6 ± 0.5	$(P = 0.044)$	
		(Range)	(2.2 — 6.5)	NA	(1.8 — 9.2)	(1.6 — 6.8)		
Average absolute	Control		3.93 ± 0.34	NA	NA	3.65 ± 0.32	0.3	2.1
angle error, °	2-min cooling		3.84 ± 0.37	NA	3.58 ± 0.38	3.66 ± 0.43		
	15-min cooling		3.51 ± 0.32	NA	4.52 ± 0.48	4.74 ± 0.38		
		(Range)	(28.5 — 31.8)	(28.9 — 33.2)	(20.8 — 30.9)	(24.1 — 32.6)		
Surface temperature	Control		29.3 ± 0.5	30.2 ± 0.5	NA	31.3 ± 0.3	6.6	1.3
at the quadriceps	2-min cooling		30.6 ± 0.4	31.6 ± 0.4	29.3 ± 0.4	30.1 ± 0.3	$(P = 0.007)$	
femoris, °C	15-min cooling		30.2 ± 0.5	31.1 ± 0.4	26.1 ± 0.9	28.3 ± 0.8	$(P < 0.001)$	
		(Range)	(33.1 — 35.4)	(31.2 — 35.9)	(24.2 — 32.5)	(28.0 — 34.2)		
Deep temperature	Control		34.0 ± 0.2	33.3 ± 0.3	NA	34.3 ± 0.4	35.7	4.3
at the popliteal,	2-min cooling		33.8 ± 0.2	33.2 ± 0.3	31.3 ± 0.4	32.8 ± 0.3	$(P < 0.001)$	
°C	15-min cooling		34.5 ± 0.3	33.9 ± 0.4	28.5 ± 0.6	30.6 ± 0.5	$(P = 0.031)$	

IBFV, intraarticular blood flow volume; MGA, middle genicular artery; NA, not applicable

effects for the various groups and phases were observed [$F(2, 18) = 35.7, P < 0.001$; $F(2, 18) = 4.3, P = 0.031$].

Fig. 1 shows changes in IBFV value for each phase (baseline, post-exercise, post-cooling, and 15 min later). In the 2-min cooling group, the IBFV significantly increased post-exercise and post-cooling compared with baseline ($P = 0.039$ and $P = 0.048$, respectively). In the 15-min cooling group, the IBFV significantly increased post-exercise compared with baseline ($P = 0.049$) and significantly decreased both post-cooling and 15 min later compared with post-exercise ($P = 0.048$ and $P = 0.016$,

respectively).

Fig. 2 shows changes in average absolute angle error for each phase (baseline, post-cooling, and 15 min later). In the 15-min cooling group, the average absolute angle error significantly increased 15 min later compared with baseline ($P = 0.037$).

Fig. 3 shows changes in surface temperature for each phase (baseline, post-exercise, post-cooling, and 15 min later). In the control group, the surface temperature significantly increased 15 min later compared with baseline ($P = 0.004$). In the 2-min cooling group, the surface

Fig. 1 Changes in intraarticular blood flow volume at baseline, post-exercise, post-cooling, and 15 min later. * $P < 0.05$ vs. baseline in the same group. † $P < 0.05$, vs. post-exercise in the same group.

Fig. 2 Changes in average absolute angle error at baseline, post-cooling, and 15 min later. * $P < 0.05$ vs. baseline in the same group.

temperature significantly decreased post-cooling compared with baseline and post-exercise ($P = 0.034$ and $P < 0.001$, respectively) and significantly increased 15 min later compared with post-cooling ($P = 0.023$). In the 15-min cooling group, the surface temperature significantly decreased post-cooling compared with baseline and post-exercise ($P = 0.027$ and $P = 0.004$, respectively) and remained significantly decreased 15 min later compared with baseline and post-exercise ($P = 0.048$ and $P = 0.006$, respectively).

Fig. 4 shows changes in deep temperature for each

phase (baseline, post-exercise, post-cooling, and 15 min later). In the control group, the deep temperature significantly increased 15 min later compared with post-exercise ($P = 0.031$). In the 2-min cooling group, the deep temperature significantly decreased post-cooling compared with baseline and post-exercise (both $P < 0.001$) and significantly increased 15 min later compared with post-cooling ($P = 0.023$). In the 15-min cooling group, the deep temperature significantly decreased post-cooling and 15 min later compared with baseline and post-exercise ($P < 0.001$).

The results of the correlation between IBFV and tem-

Fig. 3 Changes in surface temperature at baseline, post-exercise, post-cooling, and 15 min later. * $P < 0.05$, and ** $P < 0.01$ vs. baseline in the same group. † $P < 0.05$, and †† $P < 0.01$ vs. post-exercise in the same group. ‡ $P < 0.05$ vs. post-cooling in the same group.

Fig. 4 Changes in deep temperature at baseline, post-exercise, post-cooling, and 15 min later. *** $P < 0.001$ vs. baseline in the same group. † $P < 0.05$, †† $P < 0.01$, and ††† $P < 0.001$ vs. post-exercise in the same group. ‡ $P < 0.05$ vs. post-cooling in the same group.

perature difference (determined according the formula: baseline - each phase), revealed significant correlations between IBFV and deep temperature difference ($r = 0.342$, $P < 0.001$) and between IBFV and surface temperature difference ($r = 0.215$, $P = 0.029$). However, no significant correlations were observed between average absolute angle error and temperature or IBFV (data not shown).

Discussion

This study examined the influence of cryotherapy on JPS and IBFV in the knee joint. The results of this study showed a significant increase in IBFV after exercise. Furthermore, our results showed a significant decrease in IBFV after cooling intervention related to decreased temperatures, and significant differences were observed in knee JPS 15 min post-cooling compared to baseline.

Several researchers have reported that cryotherapy impairs knee JPS in normal knees^{4,6}. Oliveria et al.⁴ reported that 20 min of cryotherapy using an ice bag over the anterior thigh muscles or over the knee joint impaired knee JPS. The authors emphasized the implications of these findings for rehabilitation programs that use exercise immediately after cryotherapy and for athletes when returning to practice following cryotherapy, as impaired proprioceptive acuity may increase the risk of injury during exercise, and our 15-min cooling results support their opinion. Our findings are also in agreement with previous studies that examined the effects of cryotherapy on knee JPS^{4,6}. Meanwhile, in the 2-min cooling intervention, no significant differences in knee JPS were observed post-cooling compared to baseline, and 15 min after cooling, results were comparable to baseline. Uchio et al.⁶ explained the effects of cryotherapy on knee JPS neurophysiologically through a reduction and eventual blocking of nerve conduction velocity (NCV). Our results indicate that cooling intervention lasting less than 2 min has no effect on reducing NCV; therefore this cooling timeframe does not affect knee JPS. However, a recent study showed average NCV reductions of 33% and 17% when the skin temperature was reduced to 10°C and 15°C, respectively, which relates to a 0.4 m/s decrease in NCV for each 1°C drop in skin temperature¹⁴. Although the present study demonstrated a significant reduction of the surface temperature after 15 min cooling, the change was not sufficient to cause a reduction in NCV as described above. Chesterton et al.¹⁵ found differences in skin temperature response, with frozen peas lowering mean skin temperature to 10.8°C after 20 min compared with 14.4°C with a frozen gel pack. Uchio et al.⁶ evaluated the effect of cryotherapy using a cooling device (circulating medium at 4°C) that resembled our results. In their study, the mean surface temperature after 15 min cooling and temperature difference were 23.2°C and 3.5°C, which is similar to our results of 26.1°C and 4.1°C. Thus, the authors hypothesize that impaired knee JPS may occur due to decreased

NCV, which may also occur due to other factors such as changed muscle properties and reduced muscle spindle activity^{16,17}.

Various modalities, including hot and cold therapies, are often used in sports medicine to treat symptoms associated with local inflammation, which is a response to tissue trauma. Previous research has suggested that application of modalities produces changes in pain perception, metabolism, temperature, and blood flow. Recently, several studies have reported a significant reduction in local blood flow volume using cryotherapy¹⁸⁻²⁰. However, intraarticular vascular changes are not well understood, because the majority of research involving vascular changes has used plethysmography in the muscle. Indeed, few reports concerning the effect of cryotherapy on intraarticular blood flow volume using US have been conducted. Thus, another purpose of our investigation was to examine changes in IBFV in the knee during cold therapy using US. The present results confirmed that cryotherapy in the knee produced reductions in IBFV.

In the knee, the middle genicular artery is a branch of the popliteal artery in the popliteal fossa²¹. We thus assumed that MGA supplies blood to the knee joint. Recent advancements in high-resolution diagnostic US have revealed minute aspects of blood flow at synovial joints²². Additionally, US can dynamically assess small changes in blood flow and is an effective imaging modality for evaluating the musculoskeletal area^{22,23}. For the last few years, real-time virtual sonography (RVS) has been available in high-end US equipment. RVS is a novel fusion imaging technology that can accurately fuse real-time US images of computed tomography or magnetic resonance imaging volume data, displaying them side-by-side on the same monitor. Therefore, the authors conducted a preliminary examination using RVS to confirm the position of the MGA before beginning this study (Fig. 5).

In an experimental animal study, Najafipour and Ferrell⁹ demonstrated a significant reduction in the efficacy of the sympathetic nervous system in regulating blood flow to an inflamed joint, one possible explanation for the significantly higher blood flow observed in this condition. Another previous study demonstrated that application of a cooling and compression device after knee arthroscopy significantly lowered the temperature in the knee postoperatively, and that the synovial prostaglandin E2 (PGE2) concentration was correlated with temperature²⁴. Because PGE2 is a marker of pain and inflammation, these authors concluded that postoperative local cooling and compression appeared to have a positive anti-inflammatory effect. Our results showed that IBFV was substantially reduced after a 15-min cooling intervention in association with decreased deep temperatures; thus, these findings suggest that the intraarticular circulation volume is influenced by deep temperature. Meanwhile, increased IBFV, indicating reactive vasodilatation, was not observed after the 15-min cooling intervention or 15 min later, although several

Fig. 5 Real-time virtual sonography images of the right knee joint. A. Longitudinal plane. B. Transverse plane. MRI image (left) and ultrasonographic image using Doppler mode (right) of the same slice. P, posterior; A, anterior; D, distal; Pr, proximal; F, femur; T, tibia; PA, popliteal artery; white arrow, middle genicular artery.

authors have reported that cooling intervention induces vasodilatation. This discrepancy may be explained by temperature variation or by insufficient cooling time. Further study with cold interventions $<5^{\circ}\text{C}$ or for longer than a 15-min period are needed for confirmation.

Our study has several limitations. First, it did not include patients with knee injuries and inflammation; hence, it did not evaluate the potential enhancement of blood flow induced by inflammation in the knee joint. Second, this study did not examine multiple arteries. It only examined flow in one artery; the knee joint has abundant anastomosis. To validate our findings, further studies are warranted with a larger number of participants and broader sampling of the vasa vasorum of the knee joints. Further investigation is needed to confirm whether IBFV is related to position sense.

In conclusion, the results of this study showed a significant decrease in IBFV and knee JPS after a 15-min cooling intervention along with decreased deep temperature, but no significant effects from a 2-min cooling intervention. Our results indicate that 15-min cooling is only suitable to induce an anti-inflammatory effect in the deep tissue after a competition, because it may induce functional impairments in JPS. By contrast, a 2-min cooling intervention does not appear to affect knee JPS; however no reduction of intraarticular blood flow occurs during this timeframe.

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