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CLINICAL STUDIES

Shorter Recovery Time in Concussed Elite Ice Hockey Players by Early Head-and-Neck Cooling: A Clinical Trial

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Abstract

A sports-related concussion (SRC) is most commonly sustained in contact sports, and is defined as a mild traumatic brain injury. An exercise-induced elevation of core body temperature is associated with increased brain temperature that may accelerate secondary injury processes following SRC, and exacerbate the brain injury. In a recent pilot study, acute head-neck cooling of 29 concussed ice hockey players resulted in shorter time to return-to-play. Here, we extended the clinical trial to include players of 19 male elite Swedish ice hockey teams over five seasons (2016-2021). In the intervention teams, acute head-neck cooling was implemented using a head cap for ≥45 min in addition to the standard SRC management used in controls. The primary endpoint was time from SRC until return-to-play (RTP). Sixty-one SRCs were included in the intervention group and 71 SRCs in the control group. The number of previous SRCs was 2 (median and interquartile range [IQR]: 1.0-2.0) and 1 (IQR 1.0-2.0) in the intervention and control groups, respectively; $p = 0.293$. Median time to initiate head-neck cooling was 10 min (IQR 7-15; range 5-30 min) and median duration of cooling was 45 min (IQR 45-50; range 45-70 min). The median time to RTP was 9 days in the intervention group (IQR 7.0-13.5 days) and 13 days in the control group (IQR 9-30; $p < 0.001$). The proportion of players out from play for more than the expected recovery time of 14 days was 24.7% in the intervention group, and 43.7% in controls ($p < 0.05$). Study limitations include that: 1) allocation to cooling or control management was at the discretion of the medical staff of each team, decided prior to each season, and not by strict randomization; 2) no sham cap was used and evaluations could not be performed by blinded assessors; and 3) it could not be established with certainty that injury severity was similar between groups. While the results should thus be interpreted with caution, early head-neck cooling, with the aim of attenuating cerebral hyperthermia, may reduce post-SRC symptoms and lead to earlier return-to-play in elite ice hockey players.

Keywords: clinical trial; cooling; ice hockey; return-to-play; sport related concussion

Introduction

Sports-related concussions (SRC) are one of the most common injuries in contact sports such as ice hockey, American football, soccer, and rugby.[1,2] The incidence has increased over the last decades in many sports, not least in ice hockey.[1,2] Most athletes recover within the first post-injury weeks, although the proportion of those with prolonged recovery beyond the normal time-range may be up to 30% in ice hockey.[3,4] Athletes with a history of SRCs and persisting post-concussion symptoms

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often end their careers, show a reduced quality of life, and may never recover completely.[5] Depression, neurodegenerative disorders including dementias and chronic traumatic encephalopathy (CTE), and long-term cognitive problems have all been linked to repeated SRCs.[6] While these health concerns are increasingly recognized, current treatment options for SRC are limited. In the acute setting, only initial rest and subsequent adoption of the gradual return-to-play (RTP) protocol have been implemented in many sports.[3,4] However, when aerobic exercise was started within 72 h post-SRC in adolescents, recovery was faster and the incidence of persistent post-concussive symptoms lower,[7] suggesting that a short duration of early rest could be sufficient.

Physical exertion is associated with increased body metabolism and temperature,[8-10] and a rise in body temperature also results in an increased brain temperature.[11] Thus, while an SRC is defined as a mild traumatic brain injury (mTBI) induced during sports activity,[12] an SRC carries the unique feature of the brain injury being sustained at elevated brain temperature. In experimental mTBI, elevated brain temperature leads to increased brain metabolism and exacerbated neuronal injury in rodents,[13] plausibly by acceleration of secondary brain injury cascades.[14,15] For severe clinical TBI, systemic hypothermia is associated with several complications and has not been shown to improve outcome.[16-18] A positive effect of hypothermia in those patients whose target temperature is achieved within a short post-injury time-window has been suggested, and some centers still use hypothermia as a second or third tier therapy for intracranial hypertension, although this is not a widely accepted therapy.[19,20] In contrast, aggressive reduction of hyperthermia to normothermia is an accepted and commonly adopted strategy across a range of acute brain injury disorders.[21] SRC in ice hockey is a major health problem. Since ice hockey is an extremely strenuous activity, players have markedly elevated body temperature during practice or game play.[22] In a recent pilot study on elite ice hockey players, we found that selective head-neck cooling, induced early post-SRC, reduced the time to RTP.[23] While that study included only a small number of concussed players, we could observe that a minimum 45-min duration of cooling was associated with the best results. In the present report, we extended the study of Swedish elite ice hockey players to include five seasons, testing the hypothesis that head-neck cooling initiated ≤1 h post-SRC, with the aim of rapidly reaching brain normothermia, maintained for ≥45 min is beneficial following SRC. Intervention was performed with the PolarCap® System, a selective head-neck cooling system using a silicone-based head cap. The primary endpoints of this clinical study were time to RTP and the proportion of players with extended absence from play.

Methods

Ethics

All research described herein was approved by the regional ethics committee in Lund, Sweden (decision number Dnr 2015/658) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all study participants prior to inclusion into the study. This study was registered at ClinicalTrials.gov (NCT04701125) after the study began.

Study participants

There are two elite ice hockey leagues for males in Sweden (the Swedish Hockey League, and the 2nd League, the HockeyAllsvenskan), including 28 teams with approximately 25 players (range 24-30 players) enrolled in each team. SRCs, in addition to other injuries, are registered by all teams in the Swedish National Injury Register. All 28 teams were invited to participate, whereof 19 teams agreed. All included players completed a questionnaire about previous SRCs, where the criteria used in this study to diagnose an SRC were explained (*vide infra*), as a baseline before the start of each season. Players age ≥18 years, who were part of the team's season roster and sustained an SRC during practice or game play, were eligible for study inclusion (Fig. 1).

Acute SRC management

The SRC diagnosis was made according to established consensus statements.[3,24] Transient neurological symptoms (e.g., loss of consciousness, memory loss, blurred vision, dizziness, balance problems, and confusion) caused by an external force/trauma to the head, either direct or indirect, were defined as an SRC. If there were presence of red flags (such as seizures, focal neurological deficits, deteriorating level of consciousness, signs of spinal cord injury, other suspicion of serious central nervous system injury) mandating immediate hospital transport, or if cooling treatment was interrupted during the first 45 min, the player was excluded from the study. Evaluation was made by the medically responsible individual (primarily a physician, present at all games, or occasionally a physiotherapist) of each team, who all had undergone systematic and thorough training on early SRC management, the use of the standardized graduated RTP protocols, and stepwise rehabilitation of a concussed player.[25] Any player identified with a suspected or diagnosed SRC was immediately removed from practice or game play.

Study design

All medical teams were thoroughly informed of the study protocol prior to study initiation and prior to each season. Allocation to the treatment or control groups was then at the discretion of the medical staff of each team, decided

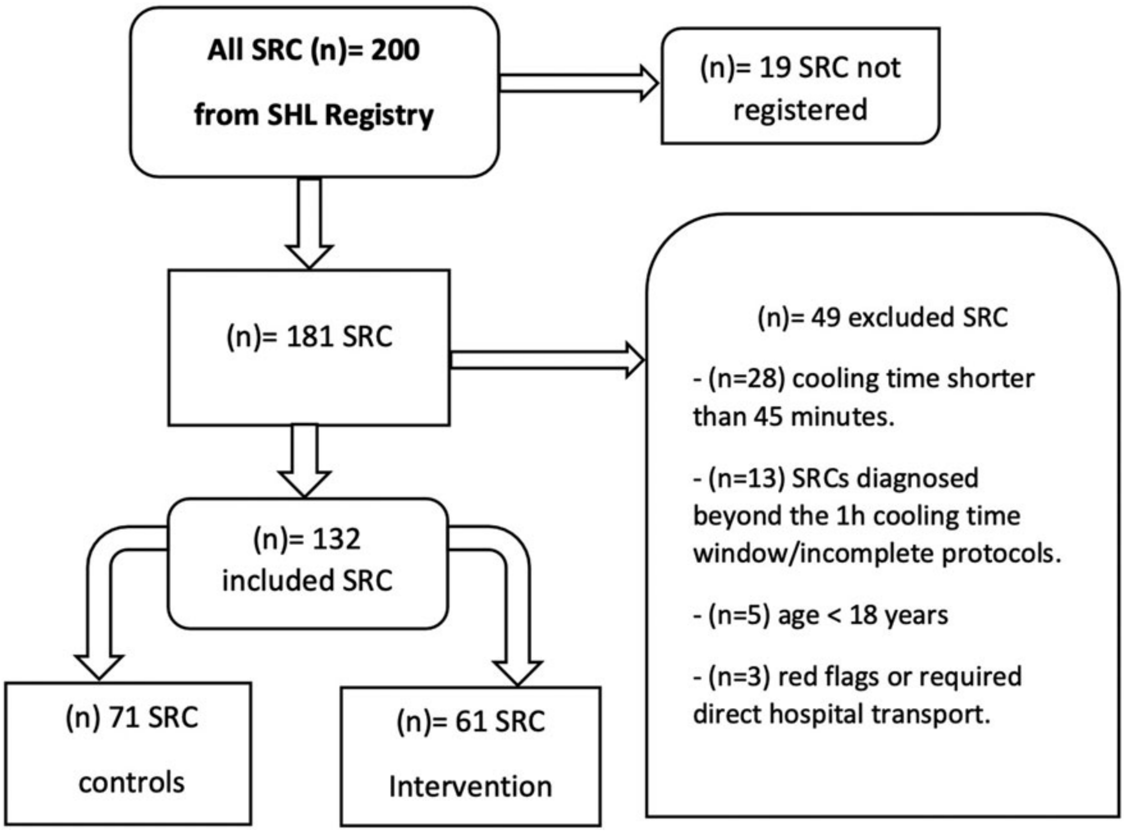

FIG. 1. Consolidated Standards of Reporting Trials (CONSORT) diagram of study set-up and number of included players. SRC, sport related concussion.

prior to each season. For the following season, a team could continue with the same allocation, or switch to cooling treatment from being in the control group (or vice versa). The study protocol was distributed to and reviewed by all teams' medical staff at the beginning of the study. Personal information such as age, number of previous concussions, and time to initiation of cooling (in the intervention group) was recorded for each player. As soon as the SRC diagnosis was established, and no exclusion criteria were met, the player was included in the study. Players in the intervention group were treated by selective head-neck cooling within 1h post-SRC using a specifically designed head cap (the PolarCap System) covering the head and the neck, allowing also for cooling of the cervical arteries.

The cooling system has previously been described in detail.[23] In brief, the system consists of a high-powered portable cooling system, using a circulating coolant controlled and maintained at 0°C. The coolant flows through a silicone-based head cap that has an insulating neoprene cover. A concussed player in the intervention group wore the silicone-based head cap along with the neoprene cover placed on his head and neck and was allowed to relax freely (sitting or supine) for the duration of treatment. If cooling treatment could not be started within 1 h post-injury, the SRC was documented but the player was excluded from further analysis. Based on our previously published pilot study, the shortest RTP was observed in players who underwent a minimum of 45 min cooling.[23] Therefore, in the present study, a minimum of 45 min uninterrupted cooling time was a requirement for inclusion of all concussed players.

Time from injury to treatment start, treatment time, and treatment side effects as noted by the player and/or the medical staff were recorded. Players in the control group received standard SRC management with identical treatment *(vide infra)* as those in the intervention group, with the exception of the head-neck cooling. While occasionally used also in the early seasons of the study (data not available), only for the last two seasons of the study was the Symptom Severity Score (SSS) part of the Sports Concussion Assessment Tool-5 (SCAT-5)[26] systematically documented immediately after SRC diagnosis, as well as immediately after the intervention. All concussions in a team were treated similarly (cooling or control treatment) during each season and no crossovers were allowed.

Since it is evident which players are receiving cooling intervention, blinding to treatment was not feasible. The participating teams were given the option to choose either intervention or control management. Based on our pilot study,[23] the Swedish Ice Hockey Medical association recommended the intervention during the last two seasons, adhered to by all teams but one. The teams were for each season either a control team or an intervention team, and some teams were both control and intervention in different seasons; 15 of 19 teams had players in both control and intervention groups throughout the study. All protocols were registered on paper by the teams' medical staff and when a study participant was cleared for RTP, the study protocols were sent by mail for blinding/anonymization of participant identity and later analysis. Protocol assessment and data analysis was done by a researcher (AaH) blinded to the treatment allocation of each participant. After each season, each team was contacted to evaluate the SRC protocol to check for inconsistencies.

Post-SRC management

All SRC players followed the standardized graduated RTP protocol.[3] In brief, following 24-48 h of ''brain rest,'' a gradual, stepwise increase of activity then ensued. The player should not experience additional symptom prior to moving to next step in the protocol, and the minimal time between each step was 24 h. This program has been adopted for many years in Swedish ice hockey and each medical team was trained in, and well experienced with, its use.[27,28] Time until the player was cleared by the medical team to be ready for game play (i.e., RTP) was recorded in the study protocol by the medically responsible person in the team. Assessments of the concussed player were performed daily by the medical team during the first post-injury month, then at a minimum once per week should symptoms persist. The assessment frequency did not change during breaks in the season. Assessments using SCAT-5 as well as the player being able to participate in full physical activity (last step of the RTP protocol; i.e., full practice on ice) were conducted also during seasons breaks since the participating teams continue with regular practices, and thus the RTP reporting was not affected.

Primary and secondary endpoints

The primary endpoint of the study was time (in days) from SRC until return to full practice or game play, the RTP time. The secondary endpoint was the proportion of players out from play during the initial 100 days post-injury. In addition, for the last two seasons of the study, symptom development after injury, prior to and following cooling, was evaluated using the SSS of the SCAT-5.

Statistical analysis

Based on epidemiological evidence and data from the Swedish National Injury Register (seasons 2014-2016), we expected up to 60 SRCs yearly in Swedish elite ice hockey. Based on our previous publication,[23] hypothesizing a similar reduction in RTP duration at a power of 80% and a p value of 0.05, 72 SRCs should be included in each treatment group.

Data from protocols were manually entered into a Microsoft Excel (Microsoft Corporation, Washington, USA) spreadsheet. Statistical data was analyzed by SPSS (IBM Corp SPSS; Statistics for Macintosh, Version 27.0. Armonk, NY). Normal distribution was analyzed with Shapiro-Wilks test and histograms, and only age was normally distributed. The number of previous concussions, RTP, time to initiate cooling, cooling time, and SSS were not normally distributed; thus, non-parametric statistics were used and data were presented using median and interquartile range (IQR). A Mann Whitney U test was used to assess differences in concussion history and RTP between groups. A Kaplan-Meier plot was also used to assess the proportion of players in the two groups absent from play over time post-SRC. Correlations between RTP and time to initiate cooling, cooling time, and SSS of the SCAT-5 difference were assessed with Spearman's rank-order correlation test, presented as r score and p-value, where the degrees of freedom are the total number of observations -2. A p value <0.05 was considered statistically significant.

Results

Nineteen elite ice hockey teams were included, 18 in the 1st League (SHL), of which all teams but three reported both intervention and control cases during separate seasons. One team from the 2nd league (HockeyAllsvenskan) reported only intervention cases. The number of teams that participated during the five seasons 2016-17 to 2020-21 were 8, 10, 14, 16, and 16, respectively (Table 1; Fig. 1 and Fig. 2).

In the Swedish Injury Registry, 200 SRCs were reported from these 19 teams over the five seasons 2016-2017 to 2020-2021. Of these, 181 SRCs were included in the present study. SRCs diagnosed beyond the 1-h cooling time window/incomplete protocols ($n=13$), age <18 years ($n=5$), red flags or direct hospital transport ($n=3$), or cooling time shorter than 45 min ($n=28$) resulted in 49 excluded protocols. Thus, 132 SRCs were available for analysis (61 SRCs in control; 71 SRCs in intervention, Fig. 1; Table 1). There were two players who during the five seasons had SRCs in different seasons—they were both in the control (no cooling) group on both occasions.

No significant differences were observed between players in the intervention group and control group regarding age, number of previous SRCs, cooling time or

Table 1. Number of Sports-Related Concussions Included in the Two Groups per Season

	2016-2017	*2017-2018*	*2018-2019*	*2019-2020*	*2020-2021*	*Total*
Intervention	1	10	6	29	15	61
Control	8	5	37	13	9	71
Total	9	15	43	42	24	132

The higher number of players in the intervention (cooling) group in recent seasons is due to a higher number of teams being in the intervention group than in the earlier seasons.

time to treatment (Table 2). The number of reported concussions varied substantially between the teams, where two teams did not report any SRC in any of the included seasons (Fig. 2). The median RTP time for athletes in the intervention group was 9 days (IQR 7.0-13.5 days), which was significantly shorter than in the control group (median 13 days, IQR 9-30 days; $p < 0.001$; Fig. 3A).

The proportion of players having returned to play was consistently higher in the intervention group at 14, 21, 28, 56, and >100 days post-injury. The proportion of players out from play beyond the expected recovery time after an SRC (14 days) was 43.7% in controls and 24.7 % in the intervention group respectively ($p < 0.05$; Fig. 3B). In the control group, seven players were absent from play >100 days, of which five had not returned by 300 days post-SRC, whereas no player in the intervention group was absent from play >100 days post-SRC.

In the intervention group, the median time to initiate cooling was 10 min (IQR 7-15; range 5-30 min), and time to cooling intervention did not correlate with RTP (r = 0.006; $p = 0.964$). The median cooling time was 45 min (IQR 45-50 min; range 45-70 min), and the cooling time did not correlate with RTP (r = -0.06; $p = 0.647$; Fig. 4)

The median SSS of the SCAT-5 prior to cooling was 18.0 (IQR 9-35) and immediately post-cooling 13.6 (IQR 7.5-26.5; $p < 0.001$). There was no correlation between the SSS prior to treatment and RTP ($r = 0.126$; $p = 0.434$; Fig. 5). While there were no significant adverse effects such as neurological deterioration, seizures and emergence of focal neurological deficits from the intervention, 8 reported blurred vision, headache, ''feeling unpleasant,'' fatigue, and/or ''pressure against the head'' during cooling. All players in intervention group reported they would consent to future cooling therapy, if deemed necessary.

Discussion

In this clinical trial, the main finding was that selective head-neck cooling, initiated at a median of 10 min post-injury, reduced return-to-play time in male elite ice hockey players who had sustained an SRC. The intervention was well tolerated, and no significant adverse events of the intervention were noted. In view of the limited treatment options for acute SRC, the present results argue for a beneficial role for attenuation of exercise-induced brain hyperthermia in concussed athletes.

During 110 min of intense ice hockey practice, the core body temperature was found to be markedly elevated by almost 1.0°C (to a mean of 38.4°C, ranging up to 39.1°C).[22] In addition, exercise is known to also increase cerebral metabolism and heat production.[29] Brain and body temperatures are strongly correlated, where brain temperature is higher; in a recent study up to 1.0°C higher in both controls and severe traumatic brain injury

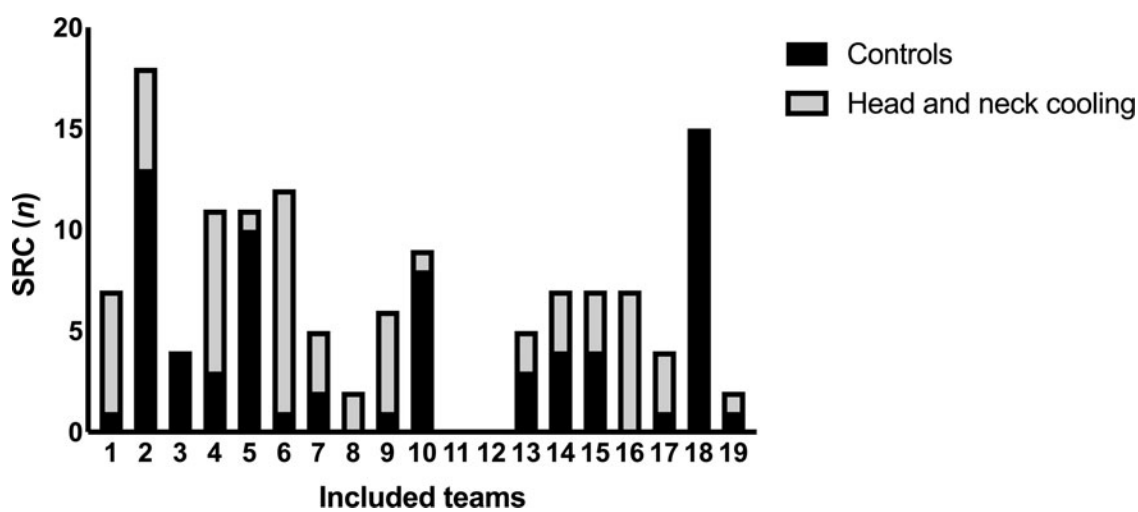

FIG. 2. The number of reported sports-related concussions (SRC) sustained per included team in the two elite leagues—divided into interventions (cooling) and controls.

Table 2. Demographics

	Controls (n = *71)*	*Head and neck cooling* (n = *61)*	p *value*
Age (years), mean (SD)	26.4 (4.6)	26.3 (5.1)	$p = 0.921$
Number of SRC, median (IQR)	2.0 (1.0 - 3.0)	1.0 (1.0 - 2.0)	$p = 0.294$
Cooling time (min), median (IQR)	-	45 (45-50)	N/A
Time to treatment (min), median (IQR)	-	10 (7-15)	N/A

All participants were male. The groups did not differ in age, number of SRCs, cooling time, or time to treatment.

SD, standard deviation; SRC, sports-related concussion; IQR, interquartile range; N/A, not applicable.

patients.[30] Since cerebral venous blood temperature decreases at a slower rate than body temperature, there may be a relatively slow recovery from exercise-induced cerebral hyperthermia.[31] It is well established that increased temperature affects brain metabolism with a 6-10% increased oxygen and glucose consumption for each °C increase in body temperature.[32-34] Since an SRC occurs at time of increased brain temperature, the neurometabolic cascades that may include inflammation and microvascular changes are likely exacerbated,[35] and aggravate the initial brain injury.[15,36] These reports argue for an increased cerebral vulnerability when an SRC is sustained at cerebral hyperthermia, as supported by robust experimental evidence.[37,38]

Local cooling is a widely used method aimed at improving recovery of soft tissue and muscular injuries in the sports setting.[39] In these sport-related musculoskeletal injuries, rapid cooling may reduce microvascular dysfunction, inflammation, and structural impairment although there is a lack of high-quality clinical studies supporting these suggested mechanisms. While the experiences from peripheral, musculoskeletal injuries cannot be directly applied to SRC, we aimed to rapidly lower brain temperature from hyperthermia to normothermia post-SRC by cooling the head and the cervical regions, also targeting the cervical blood vessels. In healthy volunteers performing strenuous exercise using a zero-heat-flux thermometry sensor aimed to measure temperature in superficial cortex, the cooling head cap used in the present study resulted in a more rapid normalization of brain temperature (from 38.5°C to 36.4°C after 45 min).[23] Using other cooling caps, brain temperature was reduced by 1.0-1.5 °C after 30 min and by 1.8 °C within 1 h of cooling initiation,[40-42] similar to what was observed in animal studies.[23,43,44] However, invasive intracerebral monitoring of brain temperature has not been used in human SRC to validate these findings, for obvious reasons. We initiated the cooling as soon as possible post-SRC although the optimal time-window has not yet been established.[45]

In the cardiac arrest setting, cooling initiated by the emergency medical services within 20 min from cardiac arrest tended to improve the chance of favorable neurologic outcome and recovery in patients with initial shockable rhythms.[46] In numerous studies on induced hypothermia in severe TBI,[47-49] no benefit was observed in randomized trials. However, when time to initiate cooling was analyzed, rapid hypothermia may be associated with improved outcome.[50] These data argue for early cooling used in our present study and supported by experimental studies.[50] While these reports argue for a short time-window for head-and neck cooling, this treatment resulted in improved symptom scores also when initiated up to several days following SRC in adolescent athletes.[51,52] There may be differences between the adult players included in the present study, and adolescents.

We based our minimum 45-min duration on our pilot study,[23] where shorter cooling time was associated with a prolonged RTP, findings which need confirmation in future studies. Previous studies used 30-min cooling showing efficacy on clinical symptoms and on cerebral blood flow using functional magnetic resonance imaging.[51,52] While there have been safety concerns such as infectious and coagulation complications with hypothermia in the severe TBI setting,[45,53] we emphasize that the target of our present study is to rapidly achieve brain normothermia, not hypothermia. In summary, these reports and our argue that the head-and neck cooling protocol is safe in SRC.

In the present study, we have no imaging or biomarker data to support the more rapid resolution of symptoms enabling a shorter RTP time observed in players receiving head-neck cooling. However, it appears unlikely that merely a placebo effect explains the resolution of symptoms at such prolonged time-points following SRC as was observed here. Further, cerebral blood flow was improved by head cooling in SRC athletes,[52] arguing that head-neck cooling can influence cerebral physiology.

Despite the best of our efforts, there were some missing protocols of players registered as SRC in the national ice hockey injury registry although not in the present study. Some of these 19 SRC may have been eligible for inclusion. There was also a large variation in reported concussion between the teams and it appears unlikely that some teams did not have a single SRC over five seasons. There is no reason, however, to assume a systemic bias in those SRCs not reported that would markedly influence the present results. Further, SCAT-5 protocols were systematically used only during the last 2 years of the study, when a majority of teams were in the intervention group. Thus, we cannot exclude the possibility that the immediate symptoms—a well-known risk factor for prolonged recovery[54]—were different between the control and intervention groups.

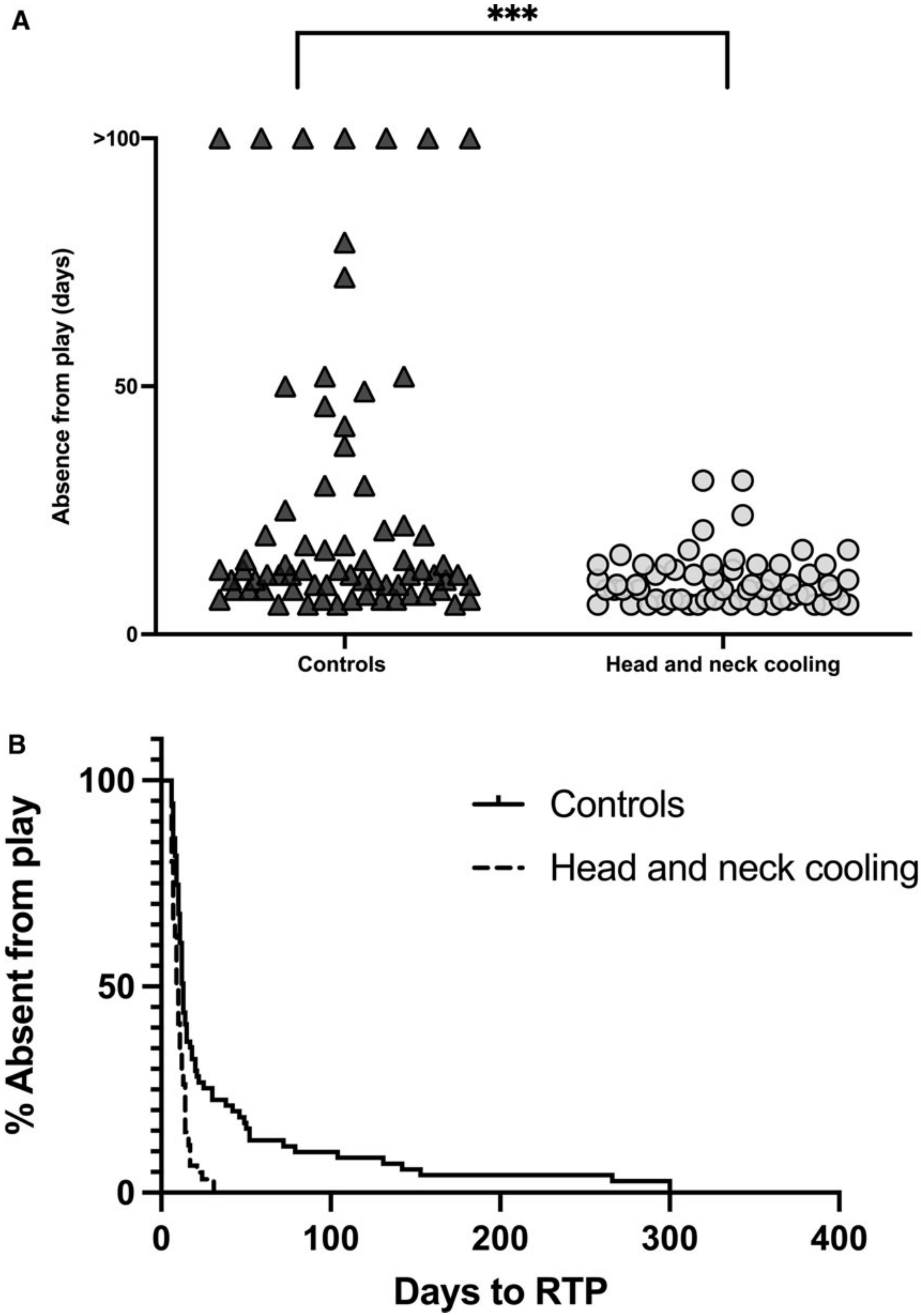

FIG. 3. Return to play. **(A)** The individual players' absence from play (days) following sports-related concussion in elite ice hockey. The median time in days for the intervention (selective head-neck cooling) and control (standard management) groups to return-to-play (RTP) was 9 days (interquartile range [IQR] 7-13.5 days) and 13 days (IQR 9-30 days). Five of the seven controls who were absent from play >100 days, had not returned to play at 300 days post–sports-related concussion. ***$p < 0.001$. **(B)** Kaplan-Meier plot showing that less players in the intervention (cooling) group were absent from play (shorter RTP) than in the control group throughout the study period. The proportion of players out for more than 14 days was consistently higher in the control group ($p < 0.05$).

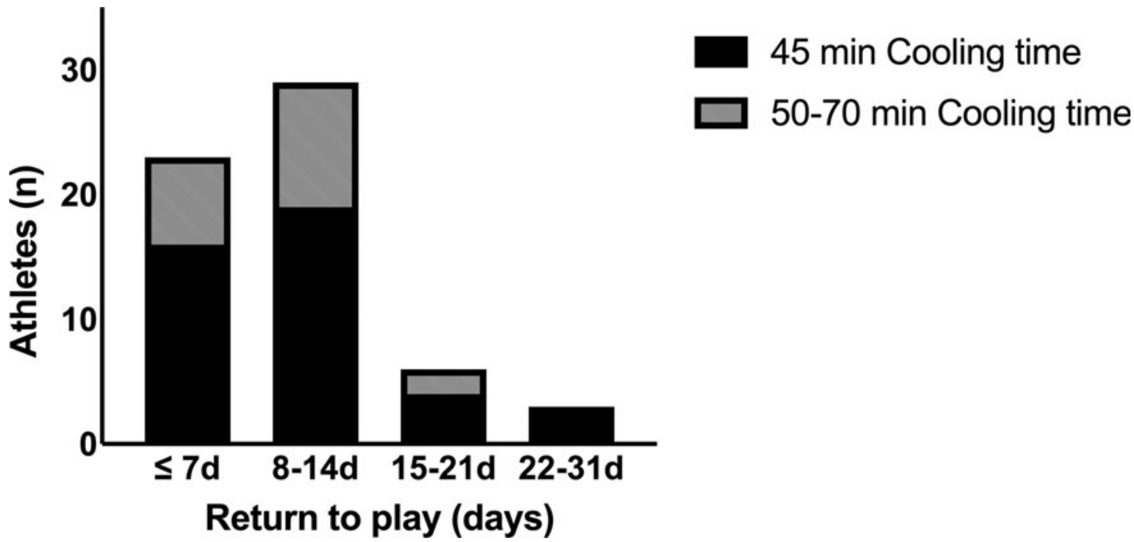

FIG. 4. Cooling time and return to play. The duration of head-neck cooling, divided into the minimum 45 min or longer (50-70 min) cooling time, did not correlate with the return-to-play time, shown as number of days until return-to-play.

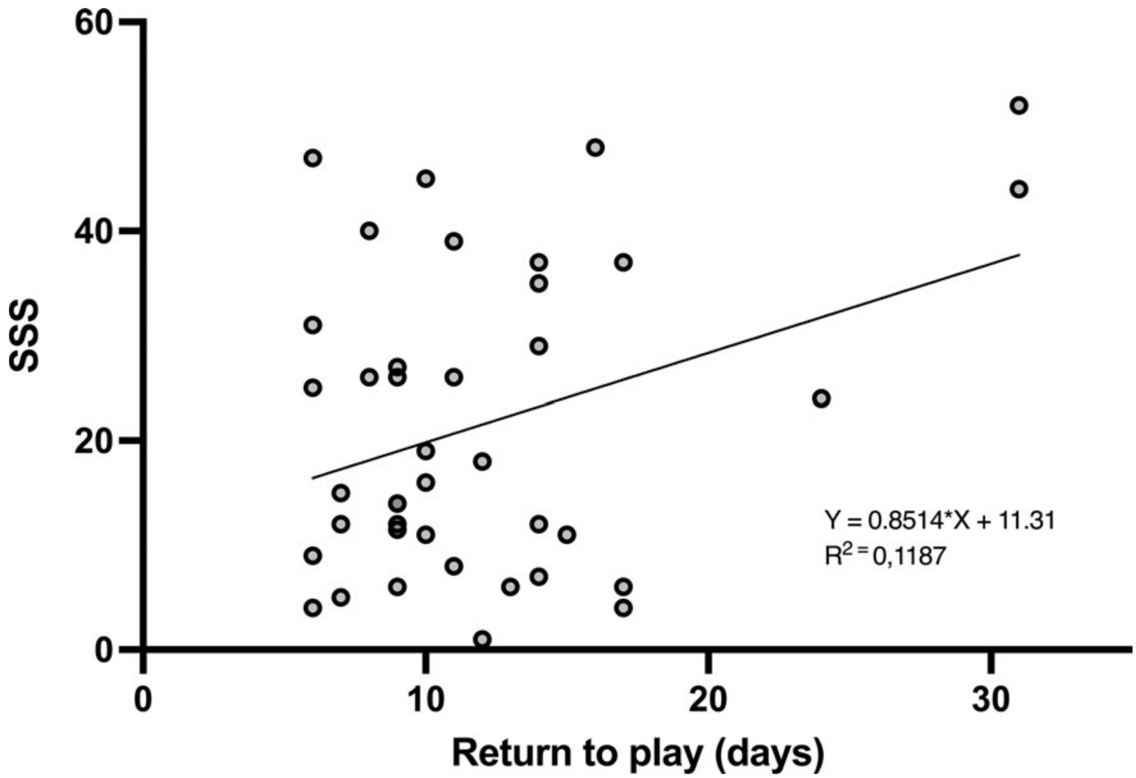

FIG. 5. Symptom severity score and return to play. There was no correlation between the Symptom Severity Score (SSS) immediately following sports-related concussion, a well-established risk factor for duration of symptoms, prior to cooling intervention (SSS prior) and return-to-play in the intervention (cooling) group.

We argue against a bias between the groups, however, based on several lines of reasoning. First, the diagnostic criteria and treatment protocol used were the same in all teams over the seasons. Secondly, while the treating physicians who made the return-to-play evaluation were not blinded to intervention group, the assessment should not be influenced by treatment status since each player in a team either received the cooling treatment or the routine, control management. Third, 15 of the 19 teams reported both control and intervention players and a systemic bias within the same team but between seasons is unlikely. Finally, the SSS in the intervention group prior to cooling intervention was rather high, suggesting that without intervention a long recovery time would be expected.

No strict randomization between individual players in the same team was used. Instead, the allocation to intervention or control was decided by the teams prior to each season and applied on a team level. The arguments for this between- team allocation were that the treating physician performing the assessments for return-to-play could not be blinded to the treatment status (control or cooling) of each player, and that a bias towards treating with cooling the concussed player in the team could not be excluded. In addition, the use of a ''sham cap''—wearing the cap without the cooling turned on-—was considered, although in view of the strong cooling effect on the head it is obvious to the player if the cooling system is turned on or not and the cooling intervention could thus not be blinded.

Finally, in Swedish ice hockey, a large number of elite players have had to end their careers due to persistent symptoms following SRCs[5] and there are increasing concerns among players of the health risks associated with SRCs. Based on discussions with team leaders, there was a concern that a concussed player would not accept being randomized to control treatment (i.e., no cooling) knowing that a potentially beneficial therapy was available. Thus, there was a strong argument made that a between-player randomization could have resulted in poor compliance to the study protocol. Regardless, that treatments could not be allocated randomly, that the assessments were performed by team members not blinded to the treatment status of each participant (no sham treatment was used), and that it could not be confirmed with absolute certainty that injury severity was similar in both treatment groups are remaining limitations of our study. Thus, the present data, while promising, should be interpreted with caution.

Conclusion

The results of this clinical trial suggest beneficial effects of head-neck cooling, applied as early as possible post-SRC and continuing for a minimum of 45 min. In players receiving the cooling intervention, shortened RTP and a reduced proportion of long-term absence in elite ice hockey players following SRC was observed. In addition, players did not experience any significant adverse side effects associated with the cooling intervention. An acute, selective head-neck cooling intervention aimed at achieving brain normothermia may be a safe and effective treatment option in athletes to reduce symptoms and shorten return-to-play time following SRC.

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Author Contributions

The authors confirm contribution to the paper as follows: conception and study design (YT), collection or acquisition of data (AaH, MFB, AG), statistical analysis (AaH, AG), interpretation of results (AaH, YT, NM), drafting the manuscript work (AaH, YT, NM) and producing the figures (AaH, NM). All authors have revised the manuscript and approved the final version of the manuscript.

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Author Disclosure Statement

Niklas Marklund and Yelverton Tegner are scientific advisors for PolarCool, AB., Lund, Sweden. Mohammad Fazel Bakhsheshi is a BrainCool AB employee as scientific manager.

For the remaining authors, no competing financial interests exist.

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