Combined cryotherapy and intermittent dynamic compression compared with conventional ice and static compression in post-operative anterior cruciate ligament reconstructions: A randomised controlled trial

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1. Background:

Anterior cruciate ligament (ACL) injury is common in the athletic population. Analyses of population-based data have indicated that the incidence of ACL reconstructions in Australia is amongst the highest in the world and continues to rise [1]. The ACL plays an important role in knee joint proprioception, and is also important in the passive restraint to anterior tibial translation and rotation. There is widespread evidence correlating ACL injury with secondary meniscal damage and altered knee biomechanics, which ultimately results in an increased risk of post-traumatic osteoarthritis [2]. Following injury, early ACL reconstruction has been found to be more cost effective, both directly and from a societal perspective measured by quality-adjusted life years, than delayed surgical reconstruction [3]. Furthermore, ACL reconstruction has demonstrated an association with better quality of life compared with those patients with an ACL-deficient knee, irrespective of whether they undergo delayed reconstruction, which reflects the burden of the injury [4].

Following ACL reconstructive surgery, patients are encouraged to engage in rehabilitation programs that rebuild muscle strength, proprioceptive control and regain joint mobility, all with the aim of returning the individual to their pre-injury level of activity [5]. The primary goal of the healthcare team is to facilitate the quickest, and most effective return to pre-injury activity while mitigating the risk of re-injury. Of course, one of the primary issues that limit the active rehabilitation of the patient is the early pain and swelling that comes with orthopaedic knee surgery. Therefore, cryotherapy is incorporated routinely in to post-reconstruction rehabilitation programs with evidence demonstrating reduced post-operative pain in the first week, without significant adverse effects [6,7]. Cryotherapy has also been found to significantly improve quadriceps strength when used immediately before exercising; hypothesized to be due to resolution of a phenomenon known as arthrogenic muscle inhibition, in which aberrant sensory information from an injured joint's mechanoreceptors reduces the recruitment of motor units in periarticular muscles [8].

While elastic wraps and ice-packs are used most commonly in the application of post-operative cryotherapy, the Game Ready (CoolSystems Inc.) GrPro® 2.1 system offers a novel method of administering constant cryotherapy, at a consistent temperature, with intermittent pneumatic compression. In their case-control study of 39 patients, Murgier and Cassard showed that the Game Ready system reduced analgesic consumption and increased post-operative range of motion compared with a device that offered cryotherapy with static compression only [9]. Waterman and colleagues randomized patients undergoing ACL reconstruction to receive either the combined compression and cryotherapy or traditional ice therapy alone and found

significantly improved short term pain relief and reduced narcotic dependence with the combined group [10]. Therefore, the Game Ready device has shown promise but there remains a paucity of data assessing its impact on post-reconstructive ACL rehabilitation.

This study aims to investigate the functional outcomes of applying combined cryotherapy and intermittent dynamic compression, in the form of the Game Ready system, by comparing it to conventional ice and static compression in post-operative ACL patients. Game Ready is hypothesized to improve post-operative pain, reduce post-operative knee effusion, increase range of motion, regain quadriceps strength; and ultimately lead to expedited recovery and return to pre-injury level of activity, and greater patient satisfaction. In doing so, we aim to assess if the implementation of Game Ready, with its associated cost, can be justified with the gain in functional outcomes.

2. Statement of the purpose and aims:

To assess the benefit of combined cryotherapy and intermittent dynamic compression provided by the Game Ready system, compared with conventional ice and static compression, in the rehabilitation of patients following ACL reconstructive surgery. Benefit will be ascertained through the following functional outcomes:

1. Compare post-operative patient-reported pain outcomes in patients following either use of Game Ready post ACL reconstruction or conventional ice and compression.
2. Compare knee girth (i.e. knee effusion/swelling) and range of movement in patients following either use of Game Ready post ACL reconstruction or conventional ice and compression.
3. Compare knee girth and range of movement in patients following either use of Game Ready post ACL reconstruction or conventional ice and compression.
4. Compare quadriceps strength in patients following either use of Game Ready post ACL reconstruction or conventional ice and compression.
5. Compare functional capacity in patients following either use of Game Ready post ACL reconstruction or conventional ice and compression.
6. Compare quality of life in patients following either use of Game Ready post ACL reconstruction or conventional ice and compression.
7. Compare patient satisfaction life in patients following either use of Game Ready post ACL reconstruction or conventional ice and compression.

3. Methodology:

3.1 Study population, informed consent and recruitment

A prospective randomized controlled trial (RCT) will be undertaken to assess the impact of combined cryotherapy and intermittent dynamic compression (the Game Ready system). Conventional ice and static compression, routinely used after orthopaedic knee and ACL reconstructive surgery, will be utilised as the control.

The Game Ready system, manufactured by CoolSystems Inc. (Concord, California USA) now trading under Avanos Medical Inc. (Alpharetta, Georgia USA), received approval from the Australian Government Department of Health Therapeutic Goods Administration for clinical use from 13/08/2008.

All patients who are undergoing ACL reconstructive surgery with surgeons from the Perth Orthopaedic and Sports Medicine Centre (West Perth, Western Australia) will be invited to participate in this trial. At this time, patients will provide written informed consent following discussion with the surgeon and reading the Patient Information Sheet (Appendix 1) and will be randomised to one of the two rehabilitation arms of the study (Game Ready or conventional ice with compression).

Inclusion Criteria

- The patient is over 16 years of age.
- A Fellowship-trained Orthopaedic Surgeon deems a patient is suitable for ACL reconstruction following clinical and radiographic examination.
- The patient is undergoing a primary ACL reconstruction.
- Patients with meniscal pathology requiring intervention.
- The patient is not currently being treated for a psychiatric disorder, senile dementia, Alzheimer's disease, presence of alcohol/substance abuse.

Exclusion Criteria

- The individual is unable or unwilling to sign the Patient Informed Consent form, specific to this study, and approved by the Institutional Ethics Review Board.
- Patients with multi-ligament injury
- The individual is unable or unwilling to follow the designated protocol.
- The individual is classified as morbidly obese (>40 BMI).

Withdrawal Criteria

As outlined on the Patient Consent Form, patients will be free to withdraw from the study without prejudice or altered post-operative care.

Ethical approval will be obtained from the Hollywood Private Hospital (HPH) Research Ethics Committee and the patient consent form will be collected prior to surgery.

Sample Size Calculation

For this RCT, a priori power calculation has been determined based on the recommendations of Cohen, which indicates that for an anticipated large effect size (d = 0.80) in the primary outcome variable (VAS – severity of pain 0-10 at 2 weeks post-surgery upon completion of the designated early cryotherpay period), a total of 52 patients (26 in each group) will be required to reveal differences at the 5% significance level, with 80% power. Therefore, 66 patients (33 per group) will allow for a 25% dropout over the trial period.

3.2 Procedures

3.2.1 Consent, Randomization and Surgical Procedures

Patients will be reviewed pre-operatively by the Fellowship-trained Orthopaedic surgeon of their choice at the Perth Orthopaedic and Sports Medicine Centre and undergo the informed consent process specific to their procedure.

Specific to this RCT, the Patient Information Sheet (Appendix 1) and a verbal summary of the study and the expected participation requirements will be presented to the patient. Those patients willing to participate will then complete the Patient Consent Form (Appendix 1). Pre-

operative pain and knee girth measures will be taken for post-operative comparison. Patients will be randomly assigned into either Game Ready or ice and compression group following consent. Concealed allocation will be employed, whereby randomisation will be undertaken by a Research Coordinator using a 'random number generator' (undertaken prior to study recruitment) that will create a random list of numbers (1 = Game Ready, or 2 = Conventional Management).

The surgeon will then perform the arthroscopic-assisted ACL reconstruction as per their routine technique using autologous hamstring grafts from the ipsilateral leg and suspensory tibial and femoral fixation. Post-operative wounds will be closed and covered with water-proof dressings.

3.2.2 Post-operative Procedure

Patients will have their allocated treatment implemented on arrival to the hospital recovery ward. For patients randomized to the Game Ready treatment arm, the GRPro 2.1 machine will be applied; and for patients randomised to the control arm, they will be given a tubigrip (elastic wrap) compression bandage and ice-packs, as per routine management.

The Game Ready setting will be for 20 minutes on low pressure (0-5 days) then medium/high from days 5-14 to be applied 6 times per day with at least a period of one hour off in between each usage. Patients can titrate the temperature of their treatment to their comfort. For the conventional group of ice with compression the same regime of cold/compression frequency and duration will be followed, employing ice-packs for 20 minutes on top of the post-operative compression dressings. From day 1 once the dressings are debulked, tubigrip (an elastic bandage) will be employed over the operated knee as compression and following the same cryotherapy time with the ice of 20 minutes, 6 times per day with at least an hour off time in between for a period of 2 weeks.

Patients will continue their allocated treatment for a total of 14 days, which will coincide with their first post-operative review.

All patients will engage in a standardised post-operative inpatient and outpatient rehabilitation protocols coordinated by physiotherapists, as per routine treatment.

3.2.3 Clinical Assessment

Patients enrolled in the study will have specific variables measured in order to assess whether there is any difference in the two treatment arms (Table 1). Patients will be given a booklet pertaining to outcome measures which will contain questionnaires and charts where they can record pain levels throughout the monitoring period.

A range of patient-reported outcome measures (PROMs) will be employed to evaluate patient-perceived pain and function as follows:

Visual Analogue Scale (VAS):

- A Visual Analogue Scale (VAS) will be used to assess patients' pain levels, on a whole number rating scale from 0 (no pain) – 10 (worst pain). Patients will be asked to circle the number that best corresponds to their knee pain level at that time-point.

- The VAS for pain will be assessed initially when the patient has returned to the ward (day 0), and then at 4pm on day 1, 2, 1 week, 2 weeks, 6 weeks, 3 months, 6 months, 12 months and 24 months after surgery.
- We have chosen 4pm as the uniform time of assessment as it is prior to dinner time, when most patients will often be taking their analgesics (in the early post-operative stages).
- While the in-patient VAS recordings (day 0, 1 and 2) will be assisted by the hospital physiotherapy and nursing staff, and the later stage VAS recordings (6, 12 and 24 months) will be facilitated by the research staff at follow-up time-points, patients will also be provided with a set of charts in their study booklet with multiple VAS charts where they can provide their pain scores at the other non-facilitated designated study time-points (2 weeks, 6 weeks and 3 months).
- We will also be recording the amount of PRN analgesia used as in-patients, while analgesia usage following hospital discharge will also be documented.

Knee Injury and Osteoarthritis Outcome Score (KOOS) [11]

- The Knee Injury and Osteoarthritis Outcome Score (KOOS) will also be administered pre-surgery and at 3, 6, 12 and 24 months post-surgery.
- The KOOS is a knee specific questionnaire which includes 42 questions in five individual subscales: Pain, Symptoms, Activities of Daily Living (ADL), Sport and Recreation (Sport/Rec) and Knee Related Quality of Life (QOL). Each of these five subscales is scored from 0 (worst) to 100 (best).

Lysholm Knee Scoring Scale [12]

- Patients' Lysholm scores will be calculated pre-operatively and at 3, 6, 12 and 24 months post-operatively
- The Lysholm is the most widely used score for the evaluation of ACL injury and reconstruction [13]. It consists of 8 functional parameters (limp, using cane/crutch, locking, giving way, pain, swelling, climbing stairs and squatting) that total 100 points in an asymptomatic knee.
- The Lysholm score is sensitive to clinical changes between 3 and 6 months but tends to report higher results compared with other tools, hence the need for the IKDC score [13].

International Knee Documentation Committee (IKDC)[14]

- The IKDC questionnaire will be completed pre-operatively and at 3, 6, 12 and 24 months
- The IKDC scoring system was developed when a group of knee surgeons from America and Europe gathered in 1987 to address the lack of a standardised scoring system[13, 14]. The IKDC form is considered a comprehensive assessment tool with different components that can be considered individually or as a whole: patient demographics and current health, subjective knee evaluation, knee history, surgical documentation, and knee examination.

Patient Satisfaction Questionnaire (PSQ)

- A Patient Satisfaction Questionnaire (PSQ) will be employed to evaluate the patient's level of satisfaction with their surgery overall, as well as their satisfaction with surgery to relieve their pain, improve their ability to perform normal daily and work activities and improve their ability to return to recreational activities.

- The PSQ will also be used to assess their satisfaction with cryotherapy regime for ease of use and application, and perceived satisfaction on swelling control, sleep and mobility.
- A categorical tool was employed: 1 = very satisfied; 2 = somewhat satisfied; 3 = somewhat dissatisfied; 4 = very dissatisfied.

A number of objective measures will also be collected:

Oedema/Swelling:

- Oedema/swelling will be evaluated pre-surgery, and then at day 0, 1 and 2, as well as 2 and 6 weeks post-surgery.
- Knee girth measurements will therefore be taken specifically at the knee joint line and 10cm above the superior aspect of the patella, with the knee flexed to 20 degrees, via a circumferential measurement with a tape measure. This process was undertaken twice for each site and the minimum value was recorded.

Knee Range of Motion:

- Active knee flexion and extension range of motion (ROM) will be measured using a hand-held goniometer, creating an angle made by three anatomical landmarks; the greater trochanter of the femur at the hip, the lateral femoral condyle at the knee and the lateral malleolus at the ankle.
- Knee ROM will be evaluated pre-operatively and at day 0, 1 and 2, 2 and 6 weeks, and at 3, 6, 12 and 24 months after surgery.

Functional Hop Capacity:

- All patients will undertake a previously validated 4-hop test battery in the following order: 1) the single hop for distance, 2) the 6m timed hop, 3) the triple hop for distance, and 4) the triple crossover hop for distance, at 6, 12 and 24 months post-surgery.
- Patients will be provided verbal descriptions of each test and will be permitted 2-3 warm-up hops on each limb prior to initiating the hop test battery. Each of the four hop tests are initiated on the unaffected limb, and then alternated between the unaffected and operated limbs until the required number of valid test trials is obtained.
- To avoid fatigue, patients will be given as much time as required between trials; though this time will not be standardised and will be based on the individual patient's readiness to proceed.

Peak Strength:

- Peak knee extensor and flexor strength will be assessed in patients at 6, 12 and 24 months post-surgery, using an isokinetic dynamometer.
- Peak concentric knee extension and flexion strength will be measured through a range of 0-90˚ of knee flexion, at a single isokinetic angular velocity of 90°/s.
- Patients will be informed that each trial will consist of four repetitions on the same leg: three low intensity repetitions of knee extension and flexion, immediately followed by one maximal test effort which is recorded.
- Standardised verbal encouragement will be provided across all trials. Each test will be initiated on the unaffected leg, and then alternated between the unaffected and operated limb until three valid trials on each limb are completed. Patients will be given adequate rest in between trials to minimise fatigue.

The knee girth, ROM, strength and functional measurements will be recorded by the physiotherapist and added to a password protected word document that only the research team will have access to. Pre- and post-operative clinical assessments will be undertaken by a blinded therapist and at a variety of locations given the equipment required and patient ease, which will include the hospital (i.e. Hollywood Private Hospital), the Perth Orthopaedic and Sports Medicine Centre, Beatty Park Physiotherapy and the HFRC Rehabilitation Clinic.

Table 1. Timeline of patient evaluation throughout the study.

Measure	Pre-surgery Assessment	Post-operative Clinical Assessments						
		In-patient			Out-patient			
		Day 0	Day 1	Day 2	Week 1	Week 2	Week 6	3, 6, 12 and 24 months
VAS (Pain)	x	x	x	x	x	x	x	x
Analgesia Usage		x	x	x	x	x	x	
Swelling	x	x	x	x	x	x	x	
KOOS	x							x
IKDC	x							x
Lysholm	x							x
Satisfaction						x	x	x
Knee ROM	x	x	x	x		x	x	x
Functional Hop Capacity								x
Knee Strength								x

3.3 Adverse Events

For this study, an adverse event has been defined as a clinical sign, symptom or condition that is causally related to the surgery and/or subsequent rehabilitation intervention. Irrespective of the severity of adverse event, all events will be documented accordingly, along with relevant treatment(s), within the individual's patient file and within the study database. Information on adverse events will be collected at each post-operative visit. Specific information will be solicited from participants at each study visit and via physical examination to capture adverse events associated with study treatment.
Adverse events will be graded as follows:

- Mild (Grade 1): Transient or mild discomfort; no limitation in activity; no intervention or therapy required.

- Moderate (Grade 2): Mild to moderate limitation in activity; some assistance may be needed; no or minimal medical intervention/therapy required.
- Severe (Grade 3): Marked limitation in activity; some assistance usually required; medical intervention/therapy required; hospitalisation possible.
- Extreme (Grade 4): Extreme limitation in activity; significant assistance required; significant medical intervention/therapy required; hospitalisation or hospice care probable; potentially life-threatening.

All adverse events deemed to be severe or extreme will be reported accordingly to the relevant ethics board, and treated accordingly.

3.4 Interim analysis

While we do not anticipate an adverse event as a direct result of the intervention proposed in this study, periodic interim analysis will be undertaken on the study data to ensure patients are not adversely affected. This will be made with particular reference to adverse events and episodes of re-injury/re-tear. Interim analysis will be undertaken by investigation team every three months and/or specifically after the report of an adverse event deemed attributable to the rehabilitation intervention.

3.5 Data handling, statistical analysis and reporting of results

Paper records will be kept under lock and key in a metal filling cabinet at the Perth Orthopaedic & Sports Medicine Centre. Computer records will be stored in the assessor database and will be password protected. No patient names will be saved in the computerised records as all patients will be assigned a number which their results will be recorded under. The patients consulting surgeon and the study investigators will only have access to hand written and electronic records. Records will be kept for 15 years after which, paper records will be shredded and computer records will be permanently deleted including back-up copies. The result of the research will be made available through medical journals or meetings, but all patient information will be de-identified and no private information will be identified outside the investigator office.

Statistical analysis will be performed using SPSS software (SPSS, Version 11.5, SPSS Inc., USA). A series of repeated measures ANCOVAs will be used to investigate clinical outcomes between the two patient groups. A Tukeys post-hoc statistic will be used to determine time-points at which the two groups differ, given any significant main effects.

Relevant results will be reported at the state meeting of the Western Australian Orthopaedic Association and results published in peer reviewed journals.

4. References

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