Post-operative comparison between standard gradient compression dressing vs. NonCompressive Bioactive Garment on pain, swelling and range of motion following total knee arthroplasty.

NCT04751942

08-09-2021

PROTOCOL TITLE:

Post-operative comparison between standard gradient compression dressing vs. NonCompressive Bioactive Garment on pain, swelling and range of motion following total knee arthroplasty.

PRINCIPAL INVESTIGATOR:

Rachael Kilkenny

216-545-4938

rachael.kilkenny@uhhospitals.org

Objectives

This prospective study will evaluate pain, swelling, ROM as well as narcotic use in postoperative total knee arthroplasty patients using novel Non-Compressive Bioactive Garment (NCBG) versus current standard of care gradient compression stocking (Thrombo-EmbolicDeterrent or TED hose). If NCBG proves to be more effective in these outcome areas, it will provide a new and comfortable way to reduce patient pain and swelling immediately following surgery.

Background

Total knee arthroplasty (TKA) is one of the most popular surgical procedures today. It is designed and proven to effectively reduce pain caused by end-stage osteoarthritis. Despite its achievements, up to 25% of patients remain dissatisfied after the procedure due to lingering pain, amongst other complaints. Post-operative swelling of the knee and leg is thought to be a contributor to this persistent pain.

Traditionally, a standard gradient compression stocking is applied to the knee and leg after surgery to reduce this pain and swelling. However, due to ineffectiveness or patient noncompliance, compression stockings are often not entirely successful at preventing edema. The recently developed NCPS is a lower extremity garment comprised of a technical fabric that is thought to be able to prevent edema and reduce pain all in a comfortable, user-friendly manner. The purpose of this study is to determine if the NCPS is effective at improving post-operative pain, swelling, ROM and analgesic use associated with TKA.

Pain and prolonged recovery time associated with post-operative swelling are two factors that contribute to patient dissatisfaction following TKA. Swelling of the knee following TKA is caused by intraarticular bleeding and inflammation of the periarticular tissues, which can lead to a decrease in functional performance including pain and delayed rehabilitation. In a study by

Noble et al, 1/3 of dissatisfied patients reported that their knees swelled at least once per week, leading to pain and discomfort[1] . Decreased quadriceps strength following knee surgery has been shown to prolong recovery[1-8] . Fahrer et al showed that knee effusions inhibited reflex neurons and altered kinetics and muscle activity in quadriceps, which ultimately causes decreased strength[2] . Holm et al later showed us that knee swelling played a part in post-operative quadriceps strength following TKA[3] . Ultimately, if post-operative swelling can effectively be reduced, patient recovery could be expedited and patient satisfaction could be improved.

Compression stockings have been utilized to attempt to reduce post-operative swelling. Compression works to prevent swelling by reducing the hydrostatic pressure in the leg. Reducing hydrostatic pressure prevents the capillaries from oozing and allows blood to move freely from the superficial to the deep venous system, subsequently allowing excess fluid to flow away from the interstitial space[9] .

More recently, the use of gradient compression stocking following TKA has come into question for its efficacy. While the application of external pressure from these gradient compression stocking is beneficial for a period, they are often unable to exert a sufficient amount of pressure long enough to prevent painful edema for an extended amount of time. A study by Bowling et al showed that these garments showed sufficient compression during the first few hours after surgery, but the pressure they applied dropped with time and required daily measurements and refitting to maintain appropriate and therapeutic compression[10] . This poses a problem not only medically, but financially as well. These compression stockings lose their fit so quickly, new ones must be prescribed frequently, leading to costly bills for the patient. It's clear that compression stockings are not as effective as once thought when it comes to controlling pain and swelling post-operatively.

A potential solution to the problems posed by traditional compression stocking is the NCPG. The garment is comprised of a semi-conductive material ground to nanoparticles that are embedded into the fibers, formed into a three-dimensional woven fabric for optimized comfort. Instead of relying on compression, NCPS utilizes the body's own thermal energy to generate infrared energy. The infrared energy generated is reflected back at the body and modifies cellular activity at the level of the mitochondria through a process known as photobiomodulation[14-15] . This process of photobiomodulation is hypothesized to improve swelling and tissue healing by increasing the activity of mitochondria and the availability of cellular energy in the form of ATP.

This study seeks to determine if NCPS use of infrared energy is more successful at reducing pain and swelling following TKA than traditional gradient compression dressing

Inclusion and Exclusion Criteria

	Inclusion Criteria
1.	Age range: from 18 to 89
2.	Primary unilateral Total Knee Replacement - Cruciate retaining and Posterior stabilized designs

	Exclusion Criteria
1.	Leg circumference > 23 in.
2.	Allergy to silicone/polyester
4.	Current, previous DVT
5.	Primary Inflammatory Type arthritis (i.e. rheumatoid arthritis)
6.	Inability to follow standardized post op and rehab protocols
7.	Lymphedema
8.	History of Vascular Bypass Surgery on Operative Limb ie) Fem-Pop or Fem-Fem
9.	Chronic Narcotic Use History
10.	Anticoagulation therapy (coumadin, rivaroxaban, apixaban)

Number of Research Participants

We will enroll 100 subjects throughout all sites involved in the study.

Recruitment Methods

Patients will be recruited in the office setting after all non-operative modalities for controlling pain associated with end-stage osteoarthritis of the knee have been exhausted. Patients will then be presented with the option of total knee replacement. After patient has agreed to undergo TKA, patients will then be asked (in a face-to-face setting) if they would like to participate in the study.

Setting

Research procedures will be conducted in the following locations:

- Geauga Medical Center in Chardon, OH
- Beachwood Medical Center, Beachwood, OH

Patients will be identified and recruited at office locations in Geauga and Beachwood, Ohio

Consent Process

Patients will be approached in the office setting after it has been determined that they have failed conservative management of advanced knee arthritis. Patients will be in the surgeons' clinic behind closed doors with the performing surgeon and another member of the research team. Consent will be obtained in the office after scheduling total knee arthroplasty procedure. The consent process is expected to take 30 minutes, but more time is available to ensure that patients have all their questions answered prior to signing the consent form.

Sharing of Results with Research Participants

☒ Results will not be shared with research participants
☒ Results will not be shared with research participants' doctors

Study Design

Prospective randomized control cohort study

Study Procedures

Patients will be enrolled in study prior to surgery, outlined above in the consent process.

At the time of patient enrollment, A trained member of the research team will measure the circumference of the patient's leg at the mid-thigh, mid-knee and mid-calf with the leg in full extension. The patient's range of motion of the operative leg will be measured in flexion and extension. The patient will also fill out a baseline Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Questionnaire. All measurements and questionnaire answers will be recorded on the study data collection sheet and will be transferred to RedCAP. At this time, patient's will be assigned a unique study identifier which will be randomly assigned to the experimental or control group. Unique study identifier numbers will start at "#1" and will go up by one additional number with every patient enrolled in the study. Even numbers will be assigned to the control group and odd numbers will be assigned to the study group, ending with 50 people enrolled in each group.

The patient will then go on to have their primary total knee arthroplasty by standard of care procedure. Both cruciate retaining and posterior stabilized total knee replacement designs will be included in the study. Following closure of the surgical site and placement of a postoperative occlusive dressing, the operative leg will be measured once more for circumference and range of motion, and the values will be recorded on the study data collection sheet and transferred into redcap. The patient will then be placed in their randomized post-operative sleeve/device and will be transferred to the PACU and will receive the standard postoperative treatment.

Pre-operative, intra-operative and post-operative pain protocols will be uniform across performing surgeons and will include pre-operative adductor canal block, intra-operative posterior capsular injection of local anesthetic, and a standardized post-operative medication regimen consisting of:

- Percocet 5/325mg every 6 hours #28 pills
- Ibuprofen 800mg every 8 hours x 14 days
- Carisoprodol 250mg every 8 hours x 14 days
- Gabapentin 300mg every evening x 14 days

- Enteric Coated Aspirin 325mg every 12 hours x 28 days (for DVT prophylaxis)
- Ascorbic Acid 500mg every 12 hours x 14 days
- Colace 100mg every 12 hours for 7 days

On post-operative day one, patient's will be seen and evaluated in their inpatient rooms. Their leg measurements will be taken again with the knee sleeve/compressive gradient dressing pulled down. Measurements will be recorded on the data collection sheet and transferred to RedCAP. Patient's skin will be inspected for any reactions to the sleeve and a standard postoperative examination will be performed to ensure no neurovascular compromise, blood clots, infections or other post-operative complications. The number of oral narcotic pain medications consumed since time of surgery will also be recorded on the data collection sheet and transferred into RedCAP.

Patients will likely be discharged on post-operative day 1. Patients that have not been discharged on post-operative day 1 will not be measured on post-operative day 2.

Sleeves will be worn morning and night for 2 weeks, removing them only for hygiene and washing of the sleeve. After 2 weeks, the patient's will wear the sleeve as much as they can tolerate day and night. At 6 weeks, sleeves will be discontinued all together. Final ROM and Circumference Measurements will be obtained at 12 weeks post-operative mark.

Patients will be asked to fill out the WOMAC questionnaire at the time of consent, postoperative day 1 and at each subsequent post-operative visit.

Patients will be seen back at regularly scheduled post-operative visits of 2 weeks, 4 weeks, 6 weeks and 12 weeks. Patients will be given a WOMAC questionnaire to fill out at each visit. They will also give a numerical score for their perceived average pain level since their last visit. Patients will also be asked to bring in their narcotic pain pills to the post-operative appointment so they can be counted. The WOMAC questionnaire, leg circumference, knee range of motion, average pain score and number of remaining narcotic pain pills will be collected on the data collection sheet and transferred to RedCAP. Any complications will also be recorded.

The Reparel leg sleeve is the experimental device being investigated in this study. It is intended to improve swelling in the post-operative knee. Further description of the device is provided in the background section of this protocol

EPIC Electronic Medical Records will be used to collect data about patients during their inpatient, post-operative stay. Ambulatory EMR will be used in the outpatient setting to collect data and track post-operative clinic visits.

Study Timeline

	Pre-Screening	Time of Consent	Post-op	Post-op day 1	2 week post-op	4 week post-op	6 week post-op	12 week Post-op
Total Estimated time of visit	30 minutes	35 Minutes	5 minutes	30 minutes	30 minutes	30 minutes	30 minutes	30 minutes
WOMAC Questionnaire		x		x	x	x	x	x
Leg Circumference measurements		x	x	x	x	x	x	x
Knee Range-of-motion		x	x	x	x	x	x	x
Review of pain scale and narcotic use log				x	x	x	x	x

The enrollment period will be 1 year from the time of the first patient enrolled in the study. The enrollment period may be expanded to allow for the investigators to reach their goal of 100 patients. The total amount of time each patient will be involved in the study will be 12 weeks. Patients will only be required to wear the post-operative sleeve/dressing for 6 weeks post-operatively. Patients will continue to report their narcotic consumption and average pain scores for 12 weeks post-operatively.

Data to be Collected for your study
(AFTER consent and HIPAA Authorization have been obtained)

Mid-thigh, mid-knee, and mid-calf measurements in extension
Range of motion measurements in knee flexion and knee extension
Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)
Visual analog Pain scale
Pain medications consumed
Adverse clinical events including DVT, stroke, PE, surgical site infection, reoperation Name
Medical record number
Patient demographics (age, sex, weight, height, BMI)

Data Analysis Plan

Demographics will be reported using descriptives such as count data and percentages. Differences between groups at baseline (pre-op) will be reported using two-tailed independent ttests for continuous variables, and chi-square or Fisher's Exact tests for categorical data, as appropriate.

The primary outcomes of range of motion, leg circumference, and pain ratings will be compared post-op between conditions using two-tailed independent t-tests. Should clinically relevant

demographics differ significantly between conditions pre-op (baseline), post-op comparisons will instead be conducted using one-way ANCOVAs controlling for differences at pre-op (baseline). These comparisons will additionally be made at multiple additional time-points throughout a 12- week post-op time period.

A priori power analyses were calculated for two-tailed independent t-tests for each primary outcome, using an alpha of .05, power = .80. Each of these are reported and the average of these numbers is used to calculate the final sample size. Clinically significant reductions in pain are defined as a 2-point change with a standard deviation of 2.5 using a 10-point scale; 84 patients were estimated. Clinically significant changes in range of motion are defined as: 10 degrees of difference from a 0-140 degree estimated range of values. Clinically significant changes in leg circumference are defined as: 1 cm difference in leg circumference using a 15-30 estimated range of values. To identify medium effect sizes of .55, 106 patients were estimated. Averaging these values, 99 patients were estimated. To ensure equal numbers of patients in each condition, 100 patients will be recruited for this study.

Risks to Research Participants

Patients will be monitored for allergic reactions and over compression leading to tourniquet effect. There is potential for the experimental garment to not be as effective as the TED hose, which would potentially increase swelling. There is risk of discomfort while wearing the experimental or standard of care garment. Breach of confidentiality is always a concern anytime there is large amounts of patient data being collected, but the risk is being minimized by use of locked storage cabinets for hard copy data and RedCAP for electronic recording of data. There are no perceived psychological, social, legal or economic risks associated with participation in the study. All normal post-operative complications and risks still apply to patients undergoing TKA. Risks associated with the use of the experimental device are expected to be incredibly rare, minor, short lived and completely reversible.

Provisions to Protect the Privacy Interests of Research Participants

Consent will be obtained in a private room at an outpatient clinic facility with solid doors. Consent will be done one-on-one with patients and with another trained members of the research team present in the room.

Potential Benefit to Research Participants

If sleeve is found to be an effective adjunct to decreasing swelling and increase knee ROM, patients will likely have less pain post-operatively and have potential for increased range of motion. If pain is better improved, patients may use less narcotic pain medication which could reduce risk of developing opioid dependence. Patient participation in the study has the potential to benefit society.

Withdrawal of Research Participants

Patients are able to withdraw from the study at any point in time. If this occurs we will use the data we have recorded if possible and the patient will be included in the withdrawn numbers of the study.

Alternatives to Participation

Patients are still free to undergo TKA without needing to participate in the study using the SOC gradient compression dressing

Costs to Research Participants

There is no additional cost to the patient. The standard TKA procedure and all associated costs will be billable to the patient's insurance company. The experimental knee sleeve will be provided to the patient at no cost. The standard of care gradient compressive dressing will be billed to the patient's insurance. Patients will be responsible for payment of provided services in the event of insurance denial. The Non-Compressive Bioactive Garment will be provided at no cost by Challenger Health, LLC (dba Reparel).

Research Participant Compensation

Patients will not be compensated for their participation in the study.

Provisions to Monitor the Data to Ensure the Safety of Research Participants

The data will be monitored every 10 patients to assess for completeness, accuracy and adherence to the protocol. We will also be monitoring for any obvious safety concerns that may arise.

Dr. Jonathan Macknin, MD will be the designated Independent Medical Monitor who will review halting rules, advise the study team on safety oversight, evaluate adverse events and SAEs, review safety reports and protocols deviations related to safety, rights and welfare of patients.

Drugs or Devices

Non-Compressive Bioactive Garment– Reparel leg Sleeve Company Name: Challenger Health, LLC (dba Reparel) FDA Registration Number: 3012651665 Device Listing Number: D269770 Product Classification: Class I Medical Device, 510(k) exempt Product Code: FQL, Stocking/Medical Support

References:

1. Noble PC1, Conditt MA, Cook KF, Mathis KB. The John Insall Award: Patient Expectations Affect Satisfaction with Total Knee Arthroplasty. Clin Orthop Relat Res. 2006 Nov;452:35-43.
2. Fahrer H., Rentsch H.U., Gerber N.J., Beyeler C., Hess C.W., and Grunig B.: Knee effusion and reflex inhibition of the quadriceps. J Bone Joint Surg Br 1988; 70: pp. 635-638
3. Holm, B., Kristensen, M. T., Bencke, J., Husted, H., Kehlet, H., & Bandholm, T. (2010). Loss of knee-extension strength is related to knee swelling after total knee arthroplasty. Archives of Physical Medicine and Rehabilitaion, 91 (11), 1770 – 1776.
4. Spencer J.D., Hayes K.C., and Alexander I.J.: Knee joint effusion and quadriceps reflex inhibition in man. Arch Phys Med Rehabil 1984; 65: pp. 171-177
5. Hopkins J.T.: Knee joint effusion and cryotherapy alter lower chain kinetics and muscle activity. J Athl Train 2006; 41: pp. 177-184
6. Hopkins J.T., Ingersoll C.D., Krause B.A., Edwards J.E., and Cordova M.L.: Effect of knee joint effusion on quadriceps and soleus motoneuron pool excitability. Med Sci Sports Exerc 2001; 33: pp. 123-126
7. McNair P.J., Marshall R.N., and Maguire K.: Swelling of the knee joint: effects of exercise on quadriceps muscle strength. Arch Phys Med Rehabil 1996; 77: pp. 896-899
8. Mizner R.L., Petterson S.C., Stevens J.E., Vandenborne K., and Snyder-Mackler L.: Early quadriceps strength loss after total knee arthroplasty. J Bone Joint Surg Am 2005; 87: pp. 1047- 1053
9. Rong Liu et all.: The Effects of Graduated Compression Stockings on Cutaneous Surface Pressure Along the Path of Main Superficial Veins of Lower Leg. Wounds. 2006;18(6):150-157
10. Bowling K , Ratcliffe C, Townsend J, Kirkpatrick U.: Clinical thromboembolic detterrent stockings application: are thromboembolic detterrent stockings in practice matching manufacturers application guidelines. Phlebology. 2015 Apr;30(3):200-3. doi: 10.1177/0268355514542843. Epub 2014 Jul 2.
11. Munk, S., Jensen, N.J.F., Andersen, I. et al. Knee Surg Sports Traumatol Arthrosc (2013) 21: 388. https://doi.org/10.1007/s00167-012-1963-0
12. Ross M, Worrell TW (1998) Thigh and calf girth following knee injury and surgery. J Orthop Phys Ther 27:9–15
13. 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;21(2):61–6. doi: 10.1097/00006416-200203000-00009
14. De Freitas LF, Hamblin MR. Proposed Mechanisms of Photobiomodulation or Low-Level Light Therapy. IEEE Journal of Selected Topics in Quantum Electronics. 2016;22:7000417.

15. Karu TI. Mitochondrial signaling in mammalian cells activated by red and near-IR radiation. Photochem Photobiol. 2008;84:1091–1099