The Association Between a Comprehensive Multimodal Pathway And Pain 0-48 Hours After Arthroscopic Rotator Cuff Repair: A Before-and After Study

FUNDER: Research & Education Fund, Department of Anesthesiology, Critical Care & Pain Management

PROTOCOL NO.: 2018-0814

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PROTOCOL SYNOPSIS

Protocol Title:	The Association Between a Comprehensive Multimodal Pathway And Pain 0-48 Hours After Arthroscopic Rotator Cuff Repair: A Before-and After Study
Protocol Number:	2018-0814
Protocol Date:	8/22/2018
Sponsor:	N/A
Principal Investigator:	Jacques T YaDeau, MD PhD
Products:	NA
Objective:	The specific aim is to determine whether a comprehensive pathway that includes a well-defined regional technique and multimodal analgesia (scheduled NSAID, acetaminophen, gabapentin) will reduce the worst pain with movement 0-48 hours after block placement compared to the current standard practice
Study Design:	Before and After Observational Study
Enrollment:	140
Subject Criteria:	Ambulatory rotator cuff patients with participating surgeons. Includes the following concomitant procedures: Arthroscopic SLAP (Superior Labrum Anterior and Posterior) repair Arthroscopic Stabilization Arthroscopic AC (Acromioclavicular) resection Arthroscopic SAD (Sub-Acromial Decompression) Arthroscopic or mini open biceps tenodesis Age 18-80
Study Duration:	September 2018 – January 2020
Data Collection:	• Name • MRN ID • Age • Race • Ethnicity

	• Gender • Height • Weight • BMI • ASA • NRS Pain scores at rest and with movement • PainOUT questionnaire • Nerve Block Success • Use of Multimodal Analgesia • Extent of Surgery • Sleep Interference • Postoperative Complications
Outcome Parameters:	• The primary outcome is the worst NRS pain score with movement from 0 – 48 hours after block placement.
	1. Total opioid use (POD 0, 1, 2, 7, 14) 2. Pain scores at additional timepoints (Preop, POD 0, 1, 2, 7, 14) 3. Patient-oriented pain questionnaire (PainOUT) (POD1, 2) 4. Block duration (POD2, 7) 5. Satisfaction with pain management (POD 7) 6. Patient and physician adherence to the pathway (POD 0, 1, 2, 7, 14)

Statistical Analysis:	Proposed sample size analysis, include the following: Student's t-test, ANOVA, chi-square, regression, etc; Alpha level; Beta or power level; Primary outcome variable estimate (mean +/-s.d. for continuous outcome, frequency/percentage for categorical variable); Number of groups being compared (use 1 for paired analysis within the same subjects); Effect size or change expected between groups; Resulting number per group 1. Proposed analysis (e.g., student's t-test, ANOVA, chi-square, regression, etc.): Multivariable linear regression 2. Interim analysis planned? No 3. Alpha level: 0.05 4. Beta or power level: 80% 5. Primary outcome variable estimate (mean +/- s.d. for continuous outcome, frequency/percentage for categorical variable): Mean ± SD worst NRS pain score with movement 24-48 hours post rotator cuff repair: 7.0 ± 2.1 à 7.0 ± 2.4 (Kahn 2018) 6. Number of groups being compared (use 1 for paired analysis within the same subjects):2 7. Effect size or change expected between groups: 1.3 (Todd 1996) 8. Resulting number per group: 58 9. Total sample size required: 116 + 20% to account for protocol violations and/or missing data = 140 Based on Harrell (2015), a minimum of 15 patients per predictor is suggested for a multivariable linear regression model. 116 patients would provide approximately 19 patients per each of 6 predictors (i.e., before vs. after pathway implementation, preoperative worst NRS pain score with movement over past 24 hours, boney work (yes vs. no), age, sex, and BMI). References Kahn, RL, et al. Perineural Low Dose Dexamethasone Prolongs Inter-Scalene Block Analgesia with Bupivacaine Compared to Systemic Dexamethasone: A Randomized Trial. (Accepted to RAPM) Todd KH, Funk KG, Funk JP, et al. Clinical significance of reported changes in pain severity. Ann Emerg Med 1996; 27(4): 485–489 Harrell, FE. Regression Modeling Strategies, with Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis, second edition ed. New York: Springer, 2015.

1.0 INTRODUCTION

Rotator cuff surgery is mostly performed on an outpatient basis, and many patients still experience moderate to severe pain after surgery, despite the use of regional anesthesia and opioids. Among shoulder surgery patients receiving long-acting nerve blocks, the worst pain typically coincides with recession of peripheral nerve blockade. Interscalene nerve block is an effective regional anesthesia technique that involves injection of local anesthetic near the brachial plexus resulting in excellent postoperative analgesia (Hadzic et al. 2005, Kinnard et al. 1994). As the sensory blockade wears off, however, it is not uncommon for patients to experience moderate to severe pain and report high pain scores after surgery (Cheng et al. 2013, Gadsden et al. 2011). There is also considerable variability in anesthesiologists' practice with regard to regional techniques, intraoperative management, and patient education that can influence postoperative analgesia.

Pain control after surgery has a number of important implications. Adequate analgesia improves patient satisfaction and facilitates the process of rehabilitation. On the other hand, uncontrolled pain is a common cause of distress and unplanned emergency department and urgent care visits (Navarro et al. 2018). Furthermore, patients with poorly controlled acute pain are at risk for developing chronic pain.

Clinical pathways are based on the concept of a multimodal approach to improving recovery after surgery (Kehlet et al. 1997). These pathways emphasize the importance of patient education and using multiple approaches to treating postoperative pain rather than relying on a single modality or technique of analgesia (White et al. 2005). These principles have been applied for total shoulder arthroplasty and demonstrated low pain scores after surgery (Goon et al. 2014). The aim of this study is to evaluate pain outcomes with arthroscopic rotator cuff surgery after implementing a clinical pathway that incorporates patient education, long-acting nerve block, and preemptive multimodal analgesia. Worst pain is chosen as the primary outcome because it is a well-validated endpoint for evaluating a pain-reduction treatment effect (Atkinson et al. 2010, Mendoza et al. 2006), and it has been used in prior investigations (Vandepitte et al. 2017).

Atkinson T, Mendoza T, et al. The Brief Pain Inventory and its "Pain at its Worst in the last 24 Hours" Item: Clinical Trial Endpoint Considerations. Pain Med. 2010 March; 11(3): 337-346

Cheng J, Kahn R, YaDeau JT, et al. The fibromyalgia survey score correlates with preoperative pain phenotypes but does not predict pain outcomes after shoulder arthroscopy. Clin J Pain. 2016 August; 32(8):689-94.
Gadsden J, Hadzic A, Gandhi K, et al. The effect of mixing 1.5% mepivacaine and 0.5% bupivacaine on duration of analgesia and latency of block onset in ultrasound-guided interscalene block. Anesth Analg. 2011; 112:471-6.
Goon Ak, Dines DM, Craig EV, et al. A clinical pathway for total shoulder arthroplasty – a pilot study. HSS J. 2014 July; 10(2):100-6

Hadzic A,Williams BA, Karaca PE, et al. For outpatient rotator cuff surgery, nerve block anesthesia provides superior same-day recovery over general anesthesia. Anesthesiology. 2005; 102: 1001-1007.

Kehlet, H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br. J Anaesth 1997; 78(5):606-17.

Kinnard P, Truchon R, St-Pierre A, Montreuil J. Interscalene block for pain relief after shoulder surgery. A prospective randomized study. Clin Orthop Relat Res. 1994; 304: 22-24.

Mendoza T, Mayne T, et al. Reliability and validity of a modified Brief Pain Inventory short form in patients with osteoarthritis. Eur J Pain. 2006 May; 10(4): 353-61

Navarro RA, Lin CC, Foroohar A, et al. Unplanned emergency department or urgent care visits after outpatient rotator cuff repair: potential for avoidance. J Shoulder Elbow Surg. 2018 Jan; pii: S1058-2746(17)30830-3. doi: 10.1016/j.jse.2017.12.011. [Epub ahead of print]

Vandepitte C, Kuroda M, et al. Addition of Liposome Bupivacaine to Bupivacaine HCl Versus Bupivacaine HCl Alone for Interscalene Brachial Plexus Block in Patients Having Major Shoulder Surgery. Reg Anesth Pain Med. 2017 May/Jun; 42(3): 334-341

White PF. The changing role of non-opioid analgesic techniques in the management of postoperative pain. Anesth Analg. 2005; 101: S5-S22.

2.0 PRODUCT DESCRIPTION

N/A

3.0 OBJECTIVE OF CLINICAL STUDY

The specific aim is to determine whether a comprehensive pathway that includes a well-defined regional technique and multi-modal analgesia (scheduled NSAID, acetaminophen, gabapentin) will reduce the worst pain with movement0-48 hours after block placement compared to the current standard practice.

4.0 STUDY HYPOTHESES

Use of a comprehensive multimodal pathway will reduce the worst pain with movement after arthroscopic rotator cuff surgery (0 to 48 hours after block placement) compared to the current standard practice.

5.0 STUDY DESIGN

5.1 Study Duration

9/2018-1/2020

5.2 Endpoints

5.2.1 Primary Endpoint

The primary outcome is the worst NRS pain score with movement from 0 – 48 hours after block placement.

5.2.2 Secondary Endpoints

1. Total opioid use (POD 0, 1, 2, 7, 14)
2. Pain scores at additional timepoints (Preop, POD 0, 1, 2, 7, 14)
3. Patient-oriented pain questionnaire (PainOUT) (POD1, 2)
4. Block duration (POD2, 7)
5. Satisfaction with pain management (POD 7)
6. Patient and physician adherence to the pathway (POD 0, 1, 2, 7, 14)

5.3 Study Sites

Hospital for Special Surgery – Main Campus

6.0 STUDY POPULATION

6.1 Number of Subjects

140

6.2 Inclusion Criteria

Ambulatory rotator cuff patients with participating surgeons; Age 18-80

Includes the following concomitant procedures:
Arthroscopic SLAP (Superior Labrum Anterior and Posterior) repair
Arthroscopic Stabilization
Arthroscopic AC (Acromioclavicular) resection
Arthroscopic SAD (Sub-Acromial Decompression)
Arthroscopic or mini open biceps tenodesis

6.3 Exclusion Criteria

Subjects will be excluded from the study if they:

- chronic pain history (defined as use of opioids > 3 months or current gabapentinoids for pain)
- open surgery (but sub pectoralis mini open biceps tenodesis is not excluded)
- revision surgery
- kidney disease (GFR < 60 ml/min/1.73 m2 for 3 months or more)
- liver disease (transaminitis, cirrhosis, hepatitis, hypoalbuminemia, coagulopathy)
- planned avoidance of regional anesthesia
- any contraindication to or patient refusal of any component in the pathway
- Non-English speakers

6.4 Randomization

The study does not involve randomization.

7.0 PROCEDURES

7.1 Surgical Procedure

Ambulatory rotator cuff patients with participating surgeons;

Includes the following concomitant procedures:
Arthroscopic SLAP (Superior Labrum Anterior and Posterior) repair
Arthroscopic Stabilization
Arthroscopic AC (Acromioclavicular) resection
Arthroscopic SAD (Sub-Acromial Decompression)
Arthroscopic or mini open biceps tenodesis

7.1.1 Investigational Product Application

N/A

7.2 Data Collection

Data will be collected by an investigator or research assistant. Sources of data include medical records and patient physical assessments conducted by study personnel. Data will be recorded and managed using REDCap electronic data capture tools hosted at the Clinical and Translational Science Center (CTSC) at Weill Cornell Medical College. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. Connection to REDCap occurs via the hospital's encrypted cable and wireless networks, and data will be entered through a password-protected computer terminal or iPad.

7.3 Schedule of Assessments

Study Visit #	Surveys / Questionnaires	Surgery	Anesthesia	Pain Management	Phone Contacts
Day of Surgery	RES	SOC	SOC	SOC	
Day 1 after surgery	RES			SOC	RES
Day 2 after surgery	RES			SOC	RES
Day 7 after surgery	RES			SOC	RES
Day 14 after surgery	RES			SOC	RES

RES= Research Procedures

SOC= Standard of care (care you would receive if you were not participating in this study)

8.0 STATISTICAL ANALYSIS

Proposed sample size analysis, include the following:
Student's t-test, ANOVA, chi-square, regression, etc; Alpha level; Beta or power level; Primary outcome variable estimate (mean +/-s.d. for continuous outcome, frequency/percentage for categorical variable); Number of groups being compared (use 1 for paired analysis within the same subjects); Effect size or change expected between groups; Resulting number per group

1. Proposed analysis (e.g., student's t-test, ANOVA, chi-square, regression, etc.): Multivariable linear regression
2. Interim analysis planned? No
3. Alpha level: 0.05
4. Beta or power level: 80%
5. Primary outcome variable estimate (mean +/- s.d. for continuous outcome, frequency/percentage for categorical variable): Mean ± SD worst NRS pain score with movement 24-48 hours post rotator cuff repair: 7.0 ± 2.1 à 7.0 ± 2.4 (Kahn 2018)
6. Number of groups being compared (use 1 for paired analysis within the same subjects):2
7. Effect size or change expected between groups: 1.3 (Todd 1996)
8. Resulting number per group: 58
9. Total sample size required: 116 + 20% to account for protocol violations and/or missing data = 140

Based on Harrell (2015), a minimum of 15 patients per predictor is suggested for a multivariable linear regression model. 116 patients would provide approximately 19 patients per each of 6 predictors (i.e., before vs. after pathway implementation, preoperative worst NRS pain score with movement over past 24 hours, boney work (yes vs. no), age, sex, and BMI).

References:
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Harrell, FE. Regression Modeling Strategies, with Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis, second edition ed. New York: Springer, 2015.

ADVERSE EVENT ASSESSMENT

All Adverse Events (AEs) will be reported in the final study report. Definitions for Adverse Event (AE) used in this study are listed below and are based on FDA and international guidelines:

8.1 Adverse Event (AE)

Participation in this research involves the potential risk of a break of confidentiality to stored health information. HSS tries to minimize those risks by (i) removing some direct identifiers from stored information (i.e., names, social security numbers,

medical record numbers); (ii) securing, in a separate location, and limiting access to information that would be identifiable; and (iii) limiting access to information stored to HSS investigators.

The likelihood of a breach of confidentiality is minimal.

8.2 Serious Adverse Events (SAE)

N/A

8.3 Subsequent Surgical Interventions Definitions

N/A

8.4 Adverse Event Reporting

All adverse events will be reported to the DSMB and IRB within five working days of the event.

9.0 INVESTIGATOR RESPONSIBILITIES, RECORD AND REPORTS

9.1 Subject Consent and Information

Written/signed consent will be collected from participants in the holding area before surgery.

9.2 Subject Data Protection

- HSS tries to minimize those risks by (i) removing some direct identifiers from information stored [(i.e., names, social security numbers, medical record numbers)]; (ii) securing, in a separate location, and limiting access to information linking codes (i.e., linkage codes) assigned to the registry information with direct participant identifiers; and (iii) limiting access to information stored to HSS investigators.
- Access to the REDCap program is password-protected, and access to a specific study's information within the program is limited to the research assistant and other IRB-approved study personnel who have been given permission to view and/or enter study data. REDCap program access is authorized by the CTSC; particular study access is granted by the research assistant. For data exports, fields marked as protected health information (PHI) in REDCap will be de-identified, if feasible.
- All transmission of data will occur via encrypted networks in password-protected files. Any paper-based data sheets utilized for the study will have personal identifiers removed whenever possible and will be stored in the department's locked office. Each subject will be assigned a unique study number for identification, and that number will not be derived from or related to information about the individual. Presentations and publications that result from this study will not contain any individual identifiers (at most the unique study numbers may be

referred to). Thus our research presents a minimal risk of harm to subjects' privacy.