Effectiveness of additional thoracic paravertebral block in improving anesthetic effects of regional anesthesia for proximal humeral fracture surgery in elderly patients: study protocol for a randomized controlled trial

Xiaofeng Wang
shanghai jiaotong university affiliated sixth people's hospital https://orcid.org/0000-0002-4184-0749
Hui Zhang
Shanghai Jiao Tong University School of Medicine
Zhenwei Xie
Shanghai Jiao Tong University School of Medicine
Qingfu Zhang
Shanghai Jiao Tong University School of Medicine
Wei Jiang
Shanghai Jiao Tong University School of Medicine
Junfeng Zhang (zhangjunfeng@sjtu.edu.cn)

Study protocol

Keywords: Elderly, Proximal humeral fracture, Thoracic paravertebral block, Brachial plexus block, Cervical plexus block, Intercostobrachial nerve, Regional anesthesia

Posted Date: August 8th, 2019

DOI: https://doi.org/10.21203/rs.2.12510/v1

Version of Record: A version of this preprint was published on February 19th, 2020. See the published version at https://doi.org/10.1186/s13063-020-4078-9.

Abstract

Background The innervation of shoulder-upper arm area is complicated and unclear. Ultrasound-guided brachial plexus combined with cervical plexus block is probably inadequate for the anesthesia of proximal humeral surgery. Missing blockade of T1-T2 nerves may be the reason. The primary aim of this trial is to investigate the effectiveness of additional T2 thoracic paravertebral block (TPVB) in improving the anesthetic effects of regional anesthesia for elderly patients in proximal humeral fracture surgery. Methods We have designed a two-armed, parallel, randomized controlled trial (RCT) to compare the anesthetic effects of ultrasound-guided brachial and cervical plexus block with or without additional T2 TPVB in terms of the following outcomes: success rate, sensory block and safety. The elderly patients over 65 years old, referred for anterior approach proximal humeral fracture surgery, will be enrolled. Each participant will be randomly assigned 1:1 to receive IC block (combined interscalene brachial plexus with superficial cervical plexus block) or ICTP block (combined thoracic paravertebral block with IC block). The primary outcome is the success rate of surgical anesthesia. The secondary outcomes are as follows: sensory block at surgical area, proportion of participants who need supplementary anesthesia (remifentanil or conversion to general anesthesia), cumulative doses of intraoperative vasoactive medications and adverse events. The necessary sample size is estimated to be 80 patients according to the data of our pilot study. Discussion This RCT aims to demonstrate that whether combined T2 TPVB with brachial and cervical plexus block can provide better anesthetic effects of regional anesthesia in elderly patients undergoing proximal humeral fracture surgery.

Background

Proximal humeral fractures account for 4% to 10% of all fractures occurring in the elderly population over 60 years, with the greatest incidence in women ages 80 to 89 years [1, 2]. The fractures have the potential to affect the quality of life and associate with high rates of mortality [3]. The aged patients are commonly afflicted with severe cardiac or pulmonary co-morbidity, which may increase their perioperative risks. For the high-risk elderly patients who require surgical treatments, the choice of anesthesia is a challenge. Compared with general anesthesia (GA), regional anesthesia can provide more stable hemodynamics and effective opioid-free analgesia [4]. It is also associated with relatively lower incidence of perioperative complications, shorter postoperative stays and greater patient satisfaction [5–8].

The understanding of anatomy and innervation in surgical area is the prerequisite for a well-performed nerve block. The shoulder joint is predominantly innervated by the suprascapular nerve, axillary nerve (C5–6) and lateral pectoral nerves (C7) and part of anterior surface of the shoulder is innervated by the supraclavicular nerve (C3–4). Therefore, blockade of the superior and middle trunk of brachial plexus and cervical plexus (IC block) is basically required [9]. But the innervation of shoulder-proximal upper extremity area is not exactly the same as that of shoulder joint. This is an area where cervical, brachial and thoracic nerves meet together and the nerve distribution required extensive local anesthetic coverage [10, 11]. IC block might not cover the comprehensive dermatome distribution to provide adequate anesthesia for every patient undergoing proximal humeral fracture surgery. Our pilot study found that

40% of patients complained of pain under IC block and they needed intravenous narcotics or local infiltration, even conversion to general anesthesia (unpublished data). We know that interscalene block cannot anesthetize the medial part of upper extremity, which is innervated by T1-T2 segments. T1-T2 segments commonly contribute to brachial plexus, but there is no identical innervation pattern at the shoulders of all the patients due to the anatomical variation [12]. Therefore, they may co-innervate the surgical area with brachial and cervical plexus in portion of population. Missing blockade of T1-T2 probably lead to the inadequate anesthesia in some patients after simply combined brachial with cervical plexus block.

In the peripheral branches of T1-T2 segments, the intercostobrachial nerve (ICBN) most possibly involves the innervation of this surgical area. It is responsible for the sense of upper half of the anteromedial area of upper extremity. The ICBN is mainly originated from T2 with occasional contribution from T1 and T3. Some peripheral techniques to block ICBN such as ultrasound-guided selective block [13, 14], pectoral nerve block (PECS II) [15–17] and subcutaneous ring infiltration [18] have been described in the literatures, however, the efficacy of them are not certain owing to the variations of ICBN at axilla [19, 20]. Except for ICBN, whether other branches of T1-T2 involve the innervation is also unclearly. T1-T2 segments require to be blocked additionally for that the usual approaches to brachial plexus anesthesia cannot block them. Thoracic paravertebral block (TPVB) is a regional anesthesia technique that can be used for analgesia in thoracic, cardiac, breast surgeries and its effectiveness has been demonstrated in many studies [21–25]. However, whether combined T2 TVPB with IC block could provide more definite anesthetic effects at the shoulder-upper extremity area has not been sufficiently investigated. Therefore, this study is designed to assess the effectiveness of additional T2 TPVB in improving the anesthetic effects of regional anesthesia in elderly patients undergoing anterior approach proximal humeral surgery.

Methods/design

Trial design and setting

This prospective, two-armed, parallel RCT will be performed at Shanghai Jiao Tong University Affiliated Sixth People's Hospital, China. The study is developed based on the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 Statements, Fig.1 (the SPIRIT checklist is available as Additional file 1) [26]. The Consolidated Standards of Reporting Trials (CONSORT) flow diagram will be followed in reporting the final results of this trial. A flowchart of the trial design is shown in Fig.2.

Informed consent

Written informed consent shall be obtained from each participant before enrollment. They will be informed that they are free to withdraw their consent from the study at any time. The procedure, benefits,

risks, and data management of this study will be clarified in detail for the participants during the preoperative conversation.

Participants and recruitment

Elderly patients scheduled open reduction and internal fixation (ORIF) for unilateral with proximal humeral fracture will be recruited and screened for eligibility. An independent researcher (QZ) will finish the recruitment when performing the preoperative interview one day before the surgery.

Inclusion Criteria:

- Participant age≥ 65 years
- Body mass index (BMI) < 30kg/m2
- American Society of Anesthesiologists (ASA) classification I-II
- Anterior operative incision approach

Exclusion Criteria:

- Request for general anesthesia
- Nerve block is unable to be performed due to various reasons
- Coagulation dysfunction or anticoagulation therapy
- History of upper limb nerve injury or phrenic nerve injury
- Multiple trauma
- Uncontrolled respiratory disease (severe chronic obstructive pulmonary disease, asthma, pulmonary infection, pneumothorax, etc.)
- Uncontrolled hypertension (systolic pressure over 180mmHg or diastolic pressure over 110mmHg)
- Uncontrolled heart disease (coronary heart disease, valvular disease or arrhythmia, etc.)
- Stroke or cognitive dysfunction (unable to communicate or cooperate)
- Hypersensitivity or allergy to anesthetics (ropivacaine or remifentanil)

Randomization and blinding

Random allocation will be performed by a researcher (HZ) before the trial using a randomization sequence (generated on http://www.randomization.com). The allocation concealment strategy is achieved with sequentially numbered, opaque, sealed envelopes to conceal the sequence until the intervention is assigned. The envelopes will be opened sequentially before the nerve block is performed. Participants will be randomly assigned in a 1:1 ratio to receive IC block (combined interscalene brachial plexus with superficial cervical plexus block) or ICTP block (combined thoracic paravertebral block with IC

block). As the nerve block intervention cannot be blinded from participants and staff implementing the intervention, only the outcome assessor and data statistician (ZX) will be kept blinded to the randomized allocation and intervention. The envelope will be resealed after confirming the allocation. Emergency un-blinding rules apply if a serious adverse event (total spinal block or pneumothorax) occurs during the course of the study.

Interventions

All the participants will undergo preoperative fasting for 8 hours and water deprivation for 2 hours. After placement of standard ASA monitors, intravenous access for fluid infusion will be established in the forearm. No sedatives or analgesic medication will be given prior to the block. The participant will receive ultrasound-guided IC block or ICTP block according to the allocation. It will be performed following standard skin disinfection with a SonoSite S-Nerve^{TM} ultrasound machine (Bothell, WA, USA). The entire nerve block procedure of all the participants will be performed by the same anesthesiologist, who is skilled in performing ultrasound-guided regional anesthesia (XW).

In the IC group, the procedure will be performed as followed.

The participant will be placed in the lateral decubitus position with the operative side upwards. A linear array transducer (6–13 MHz) with a sterile cover and a 22G (gauge) block needle will be used. An in-plane approach, advancing the needle along the longitudinal axis of the transducer and visualizing the entire shaft, will be employed. Twenty ml of 0.375% ropivacaine will be injected between superior and middle trunk of brachial plexus at C7 level to reduce phrenic nerve palsy. The transducer will be then moved cephalad until the superficial cervical plexus emerges from the C4 intervertebral foramen. Ten ml of 0.25% ropivacaine will be injected to block the nerve [27–29].

In the ICTP group, the procedure will be performed as followed.

On the basis of IC block, T2 TPVB will then be performed. The T2-T3 intervertebral space should be determined by ultrasound image scanning and palpation counting from C7 spinous process. A curve array transducer (2–5 MHz) will be placed at the T2-T3 intercostal level with a slightly oblique scan to visualize the transverse process, costotransverse ligament, internal intercostal membrane and parietal pleura. A 10cm, 22G needle will be introduced into the thoracic paravertebral space beyond the internal intercostal membrane with its tip positioned outside the transverse process. Following negative aspiration of air, blood or cerebrospinal fluid in the needle, 10 ml of 0.25% ropivacaine will be injected into the paravertebral space[30, 31].

Then the participant will be placed in the supine position. Twenty minutes later, after the sensory block assessed, the participant will be transferred to the operating room and placed in a beach-chair position. One mg midazolam will be given intravenously. Oxygen will be routinely given via a nasal catheter at the flow rate of 3L/min until the end of operation. In case of inadequate analgesia, remifentanil (50μg/ml),

propofol (10mg/ml) and laryngeal mask airway (LMA) insertion will be prepared. The anesthetic effects will be assessed since the operation begin: 1) if it is successful, the operation will be continued; 2) if it is failed, the operation will be paused and remifentanil will be given intravenous at the rate of 0.25μg/kg/min. Two minutes later, the operation will be continued if the participant is satisfied with the anesthetic effect. The rate of intravenous remifentanil can be appropriately regulated (no more than 0.25μg/kg/min) in the following operation according to the $P_{ET}CO_2$ and respiratory rate of the participant. On the contrary, the intolerable participant will be induced with propofol (1.5–2 mg/kg) for converting to GA with LMA. The participant who received GA will be transferred to post-anesthesia care unit (PACU) after the operation.

Intraoperative monitoring and management

Blood pressure, heart rate, SpO_2 and $P_{ET}CO_2$ (via an intranasal catheter connected to the monitor) will be recorded at 10-minute intervals throughout the operation. Intraoperative mean arterial pressure (MAP) higher (or lower) than 30% from the baseline value will be defined as hypertension (or hypotension). Hypotension will be treated promptly with intravenous (IV) ephedrine 5–10mg or deoxyepinephrine 50–100μg, while hypertension will be treated with urapidil 5–10mg. Bradycardia (defined as heart rate <60 beats/min) will be treated with IV atropine 0.25–0.5mg. Other adverse events including dyspnea, pneumothorax will also be recorded. Dyspnea caused by interscalene brachial plexus block or remifentanil infusion will be managed with mask ventilation or reducing dose of remifentanil. Absolute risk of pneumothorax under ultrasound-guided TPVB is low as it never happened before in our center. However, it should be one of the most serious potential complication caused by TPVB and the participants must be screened with clinical monitoring. Chest fluoroscopy will be used to eliminate pneumothorax if aggravated hypoxemia happens. Closed thoracic drainage then may be administered according to the severity of pneumothorax.

Outcome definitions

Primary outcome evaluation

The primary outcome is the success rate. The anesthetic effects will be recorded by “successful” and “failed”. “Successful” is equivalent to surgical anesthesia, defined as the ability to proceed with surgery without the need for intravenous narcotics, general anesthesia, rescue blocks or local infiltration by the surgeon. The participants who complain painful during the operation will be defined as “failed”.

Secondary outcomes evaluation

- Assessment of sensory block at surgical area [It will be evaluated on a 3-point rating scale (0 = normal sensation, 1 = decreased sensation and 2 = no perception) 20mins after nerve block by a pinprick and an alcohol swab, respectively. The testing area will be divided into 4 portions: distal clavicle area, deltoid area, upper medial and upper lateral area of upper extremity]
- Proportion of participants completed the surgery with remifentanil
- Proportion of participants conversed to GA with LMA
- Cumulative doses of intraoperative vasoactive medications (urapidil, atropine, ephedrine and deoxyepinephrine, etc.)
- Complications related with anesthesia (local anesthetic systemic toxicity, pneumothorax, epidural block, total spinal block, hematoma, etc.)
- Intraoperative adverse reactions (hypertension, hypotension, bradycardia, tachycardia, dyspnea, etc.)

Participant timeline

For a given participant, enrolment will be performed 1 day prior to surgery and confirmed again on the day of surgery. Then random allocation will be performed by HZ before anesthesia. And then intervention will be performed. The participant will be followed up for postoperative complications on 1 day after surgery. The accrual period of this trial is expected to be about 1 year. The timeline is shown in Fig.1.

Sample size calculation

Calculation of the sample size is based on the primary outcome. A study included 27 patients underwent shoulder or upper extremity surgery using brachial plexus block showed that the success rate was 85.2% [32]. In our study, only patients undergo anterior approach ORIF for proximal humeral fracture will be included. So we assume the actual success rate of IC group will be lower than that in the previous study. On the other hand, we conducted a pilot study with 10 patients in each group. The success rate was achieved in 60% of patients in IC group and in 90% of the ICTP group (unpublished data). Therefore, using the formula of Two Independent Sample Rates (Testing Two Proportions using the Z-Test with Pooled Variance), group sample size of 32 for each group will achieve 80% power to detect this difference rate of success rate with a two-tailed 5% significance level. Then the sample size for each group will be 40 including the possible missing (20%).

Statistical analysis

Primary analyses will be undertaken on an intention-to-treat basis, including all participants as randomized, except whose who withdraw consent for the use of their data [33]. Data will be expressed as mean ± standard deviation (SD), median (interquartile range), or percentage. Continuous variables will be analyzed with a two-sample t test with equal/unequal variance or with a Mann and Whitney U test, if

appropriate. A chi-square test or Fisher's exact test will be used for categorical variables (primary outcome). The statistical analysis will be performed using SPSS V.24.0 (IBM Corporation, Armonk, New York, USA) with a significance level of 0.05.

Data collection, monitoring and management

Preoperative, intraoperative and one-day postoperative follow-up data will be collected from electronic medical record, monitor machines and relevant manual records by the research staff ZX. All electronic and handwriting data will be stored on a password-protected computer. Data and safety monitoring will be the responsibility of the principle investigator (XW) and study director (JZ).

Harms

All the severe adverse events related to the study intervention will be recorded in the study database and reported as required to Shanghai Jiao Tong University Affiliated Sixth People's Hospital Institutional Review Board.

Auditing

No formal auditing process is proposed for this trial.

Participant retention and withdrawal

All reasonable efforts will be made to ensure optimum participant engagement and to reduce study attrition. However, the study involves an intention-to-treat analysis. Therefore, all participants will have the right to withdraw from the study at any stage. If the participant is willing to provide them, any data already collected from that participant will be analyzed.

Data retention

To enable evaluations and audits from regulatory authorities, data obtained from participants will retained confidential and stored securely at the department of anesthesiology of Shanghai Jiao Tong University Affiliated Sixth People's Hospital for a minimum of 5 years. The investigators shall keep records including the identity of all participants, all original signed informed consents, serious adverse event recordings and case report forms. The data will be kept safely and not revealed to other people without appropriate permission.

Protocol amendments

Any change in the study protocol will require an amendment. Any proposed protocol amendments will be initiated by the principal investigators. All amended versions of the protocol will be signed by the staff in the study and the amendment forms will be submitted to the ethics committee for approval.

Trial dissemination

The outcomes of the study shall be disseminated in a peer-reviewed journal or at scientific conferences.

Discussion

Ultrasound-guided brachial plexus combined with cervical plexus block is probably inadequate for the anesthesia of proximal humeral fracture surgery. T2 TPVB is performed near the ventral root of the second thoracic nerve and the anesthetic solution can spread to T1 and T3 along the limited thoracic paravertebral space. We intend to block the branches of T1-T2 segments including ICBN by T2 TPVB to improve the intraoperative analgesia. In this trial, our primary purpose is to evaluate the anesthetic effects of additional T2 TPVB in the elderly patients undergoing proximal humeral surgery. The effectiveness will be mainly assessed by the success rate of surgical anesthesia, which is the most convincing evidence. Meanwhile, the sensory block will also be assessed in four areas around the surgical incision. The upper medial area of upper extremity will be tested in order to confirm the anesthetic effect of T2 TPVB technique. The purpose of sensory assessment in other three areas is to eliminate the influence on primary outcome evaluation from failed blockade of brachial or cervical plexus. These areas are innervated by suprascapular nerve, axillary nerve and supraclavicular nerve. Combined sensory assessment of dermatome with actual anesthetic effectiveness could be helpful for us to better understand the contribution of T1-T2 nerves for proximal humeral surgery.

Except for the benefits, the potential risks of TPVB performed in elderly patients should also be taken into consideration. As the paravertebral space is in close relation to the pleural space, an important issue concerning of TPVB is obviously a reasonable degree of safety regarding pleural puncture and pneumothorax [34]. Also medially, it is communicated with the epidural space via the intervertebral foramen [35]. The incidence of epidural block and total spinal block must be recorded as well. In our study, the in-plane technique of TPVB will be performed by an experienced anesthesiologist who is skilled in ultrasound-guided regional anesthesia to minimize the aforementioned risks. In addition to the skill and monitoring, low concentration ropivacaine will be used in this trial to reduce the toxicity. Nevertheless, the safety and necessity of additional TPVB in the elderly patients undergoing proximal humeral surgery must be carefully assessed by analyzing the risks and benefits. The proportion of patients who can complete the surgery with remifentanil or LMA insertion is a useful reference to evaluate the necessity of TPVB. We will observe whether the patients with insufficient intraoperative analgesia can be rescued by

low dose of opioids. The results can help us determining the indispensability of this potentially risky technique.

In conclusion, this trial enables us to better assess the effectiveness of regional anesthesia in elderly population undergoing proximal humeral fracture, with a potential possibility to avoid opioids or general anesthesia. It might provide us an ideal combination mode of nerve blocks for the surgery at the boundary of shoulder-upper extremity area. It will also advance the understanding of innervation in this surgical area.

Trial status

At the time of manuscript submission, the study had been launched and a few patients had participated in the trial. The current version of protocol was 1.1 on March 21, 2019. The recruitment was began on May 5, 2019 and it will be estimately completed in April, 2020.

Abbreviations

IC: combined interscalene brachial plexus with superficial cervical plexus block; ICTP: IC combined with thoracic paravertebral block; BMI: body mass index; SpO_2: pulse oxygen saturation; ASA: American Society of Anesthesiologists; ORIF: open reduction and internal fixation; ISPB: interscalene brachial plexus; SCPB: superficial cervical plexus block; TPVB: thoracic paravertebral block; SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials; CONSORT: Consolidated Standards of Reporting Trials; G: gauge; LMA: laryngeal mask airway; PACU: post-anesthesia care unit; GA: general anesthesia; MAP: mean arterial pressure; IV: intravenous.

Declarations

Acknowledgements

Not applicable.

Availability of data and materials

All investigators will have access to the final de-identified study dataset for the purpose of scientific publications. The datasets without participant identification will be available from the corresponding author on reasonable request after the study.

Funding

This trial was conducted with no external funding and was instead funded from college funding of Shanghai Jiao Tong University Affiliated Sixth People's Hospital (owned by Principle Investigator XW, NO.1729).

Author's contributions

JZ and WJ conceived and led the study design. XW draft this manuscript. HZ will administer the randomization and group allocation. QZ will recruit the participants. XW will perform the nerve block. ZX will assess the outcomes and analyze the data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

This manuscript report study protocol involving human participants and human data. This study has been approved by the Ethics Committee of Shanghai Sixth People's Hospital (No.2019–030, protocol version 1.1). The trial has been registered on ClinicalTrials.gov (NCT03919422, 19 April 2019). Written informed consent will be obtained from all the participants. Results will be disseminated via an international peer-reviewed publication.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests

References

1. Bell J-E, Leung BC, Spratt KF, Koval KJ, Weinstein JD, Goodman DC, Tosteson ANA. Trends and variation in incidence, surgical treatment, and repeat surgery of proximal humeral fractures in the elderly. J Bone Joint Surg Am. 2011;93:121–31. doi:10.2106/JBJS.I.01505.

2. Bahrs C, Bauer M, Blumenstock G, Eingartner C, Bahrs SD, Tepass A, et al. The complexity of proximal humeral fractures is age and gender specific. J Orthop Sci. 2013;18:465–70. doi:10.1007/s00776-013-0361-x.

3. Slobogean GP, Johal H, Lefaivre KA, MacIntyre NJ, Sprague S, Scott T, et al. A scoping review of the proximal humerus fracture literature. BMC Musculoskelet Disord. 2015;16:112. doi:10.1186/s12891-015-

0564-8.

4. Mirza F, Brown AR. Ultrasound-guided regional anesthesia for procedures of the upper extremity. Anesthesiol Res Pract. 2011;2011:579824. doi:10.1155/2011/579824.

5. Hausman MS, Jewell ES, Engoren M. Regional versus general anesthesia in surgical patients with chronic obstructive pulmonary disease: does avoiding general anesthesia reduce the risk of postoperative complications? Anesth Analg. 2015;120:1405–12. doi:10.1213/ANE.0000000000000574.

6. Brox WT, Chan PH, Cafri G, Inacio MCS. Similar mortality with general or regional anesthesia in elderly hip fracture patients. Acta Orthop. 2016;87:152–7. doi:10.3109/17453674.2015.1128781.

7. Xu R, Lian Y, Li WX. Airway Complications during and after General Anesthesia: A Comparison, Systematic Review and Meta-Analysis of Using Flexible Laryngeal Mask Airways and Endotracheal Tubes. PLoS ONE. 2016;11:e0158137. doi:10.1371/journal.pone.0158137.

8. Herrick MD, Liu H, Davis M, Bell J-E, Sites BD. Regional anesthesia decreases complications and resource utilization in shoulder arthroplasty patients. Acta Anaesthesiol Scand. 2018;62:540–7. doi:10.1111/aas.13063.

9. Conroy PH, Awad IT. Ultrasound-guided blocks for shoulder surgery. Curr Opin Anaesthesiol. 2011;24:638–43. doi:10.1097/ACO.0b013e32834c155f.

10. Christian R Falyar. Ultrasound-Guided Interscalene-Supraclavicular Block for an Intramedullary Nailing of a Pathologic Humeral Fracture: Practical Application of Ultrasound-Guided Regional Anesthesia. Anesthesiol Res Pract 2014. doi:10.1155/2011/579824.

11. Fredrickson MJ, Krishnan S, Chen CY. Postoperative analgesia for shoulder surgery: a critical appraisal and review of current techniques. Anaesthesia. 2010;65:608–24. doi:10.1111/j.1365-2044.2009.06231.x.

12. Loukas M, El-Zammar D, Tubbs RS, Apaydin N, Louis RG, Wartman C, Shoja MM. A review of the T2 segment of the brachial plexus. Singapore Med J. 2010;51:464–7.

13. Chang K-V, Mezian K, Naňka O, Wu W-T, Lou Y-M, Wang J-C, et al. Ultrasound Imaging for the Cutaneous Nerves of the Extremities and Relevant Entrapment Syndromes: From Anatomy to Clinical Implications. J Clin Med 2018. doi:10.3390/jcm7110457.

14. Magazzeni P, Jochum D, Iohom G, Mekler G, Albuisson E, Bouaziz H. Ultrasound-Guided Selective Versus Conventional Block of the Medial Brachial Cutaneous and the Intercostobrachial Nerves: A Randomized Clinical Trial. Reg Anesth Pain Med. 2018;43:832–7. doi:10.1097/AAP.0000000000000823.

15. Schuitemaker R. JB, Sala-Blanch X, Rodriguez-Pérez CL, Mayoral R. JT, López-Pantaleon LA, Sánchez-Cohen AP. The PECS II block as a major analgesic component for clavicle operations: A description of 7

case reports. Revista Española de Anestesiología y Reanimación (English Edition). 2018;65:53–8. doi:10.1016/j.redare.2017.11.003.

16. Blanco R, Fajardo M, Parras Maldonado T. Ultrasound description of Pecs II (modified Pecs I): a novel approach to breast surgery. Rev Esp Anestesiol Reanim. 2012;59:470–5. doi:10.1016/j.redar.2012.07.003.

17. Quek KH, Low EY, Tan YR, Ong ASC, Tang TY, Kam JW, Kiew ASC. Adding a PECS II block for proximal arm arteriovenous access - a randomised study. Acta Anaesthesiol Scand. 2018;62:677–86. doi:10.1111/aas.13073.

18. Roussel J, Thirkannad S. Comparison of 3 ultrasound-guided brachial plexus block approaches for cubital tunnel release surgery in 120 ambulatory patients. AANA J. 2014;82:121–6.

19. Soares EWS. Anatomical variations of the axilla. Springerplus. 2014;3:306. doi:10.1186/2193-1801-3-306.

20. Deshmukh VR, Bhardwaj H, Khan F, Jacob TG. Aberrant Cutaneous Nerve Loops in the Axilla. Acta Medica (Hradec Kralove). 2017;60:51–4. doi:10.14712/18059694.2017.50.

21. D'Ercole F, Arora H, Kumar PA. Paravertebral Block for Thoracic Surgery. J Cardiothorac Vasc Anesth. 2018;32:915–27. doi:10.1053/j.jvca.2017.10.003.

22. Abdallah FW, Morgan PJ, Cil T, McNaught A, Escallon JM, Semple JL, et al. Ultrasound-guided multilevel paravertebral blocks and total intravenous anesthesia improve the quality of recovery after ambulatory breast tumor resection. Anesthesiology. 2014;120:703–13. doi:10.1097/ALN.0000436117.52143.bc.

23. Head LK, Lui A, Boyd KU. Efficacy and safety of bilateral thoracic paravertebral blocks in outpatient breast surgery. Breast J. 2018;24:561–6. doi:10.1111/tbj.13008.

24. Krediet AC, Moayeri N, van Geffen G-J, Bruhn J, Renes S, Bigeleisen PE, Groen GJ. Different Approaches to Ultrasound-guided Thoracic Paravertebral Block: An Illustrated Review. Anesthesiology. 2015;123:459–74. doi:10.1097/ALN.0000000000000747.

25. Koyyalamudi VB, Elliott C, Gibbs CP, Boezaart AP. Perioperative analgesia for forequarter amputation in a child: a dual paravertebral approach. Anesth Analg. 2010;110:761–3. doi:10.1213/ANE.0b013e3181c920b6.

26. Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ. 2013;346:e7586. doi:10.1136/bmj.e7586.

27. Soeding P, Eizenberg N. Review article: anatomical considerations for ultrasound guidance for regional anesthesia of the neck and upper limb. Can J Anaesth. 2009;56:518–33. doi:10.1007/s12630-009-9109-7.

28. El-Boghdadly K, Chin KJ, Chan VWS. Phrenic Nerve Palsy and Regional Anesthesia for Shoulder Surgery: Anatomical, Physiologic, and Clinical Considerations. Anesthesiology. 2017;127:173–91. doi:10.1097/ALN.0000000000001668.

29. Senapathi TGA, Widnyana IMG, Aribawa IGNM, Wiryana M, Sinardja IK, Nada IKW, et al. Ultrasound-guided bilateral superficial cervical plexus block is more effective than landmark technique for reducing pain from thyroidectomy. J Pain Res. 2017;10:1619–22. doi:10.2147/JPR.S138222.

30. Boezaart AP, Lucas SD, Elliott CE. Paravertebral block: cervical, thoracic, lumbar, and sacral. Curr Opin Anaesthesiol. 2009;22:637–43. doi:10.1097/ACO.0b013e32832f3277.

31. Taketa Y, Irisawa Y, Fujitani T. Comparison of analgesic efficacy between two approaches of paravertebral block for thoracotomy: A randomised trial. Acta Anaesthesiol Scand. 2018;62:1274–9. doi:10.1111/aas.13216.

32. Nguyen HC, Fath E, Wirtz S, Bey T. Transscalene brachial plexus block: a new posterolateral approach for brachial plexus block. Anesth Analg. 2007;105:872–5. doi:10.1213/01.ane.0000271916.26357.8d.

33. Fergusson D, Aaron SD, Guyatt G, Hébert P. Post-randomisation exclusions: the intention to treat principle and excluding patients from analysis. BMJ. 2002;325:652–4.

34. Naja MZ, Gustafsson AC, Ziade MF, El Rajab M, Al-Tannir M, Daher M, Lönnqvist PA. Distance between the skin and the thoracic paravertebral space. Anaesthesia. 2005;60:680–4. doi:10.1111/j.1365-2044.2005.04232.x.

35. Luyet C, Eichenberger U, Greif R, Vogt A, Szücs Farkas Z, Moriggl B. Ultrasound-guided paravertebral puncture and placement of catheters in human cadavers: an imaging study. Br J Anaesth. 2009;102:534–9. doi:10.1093/bja/aep015.

Figures

	STUDY PERIOD		
	Enrollment	Allocation	Follow-up
TIMEPOINT (Day 0 = Day of surgery)	***Day -1***	***Day 0***	***Day 1***
ENROLLMENT:			
Eligibility screen	X		
Informed consent	X		
Confirmation of diagnosis	X		
Allocation		X	
INTERVENTIONS:			
IC Group		X	
ICTP Group		X	
ASSESSMENTS:			
Height and weight	X		
Blood pressure, SpO_2 and pulse	X	X	
Health history	X	X	
ASA classification	X	X	
Effects of anesthesia		X	
Intraoperative adverse events		X	
Doses of vasoactive medications		X	
Complications		X	X

Figure 1

SPIRIT recommended content for the schedule of enrolment, interventions, and assessments.

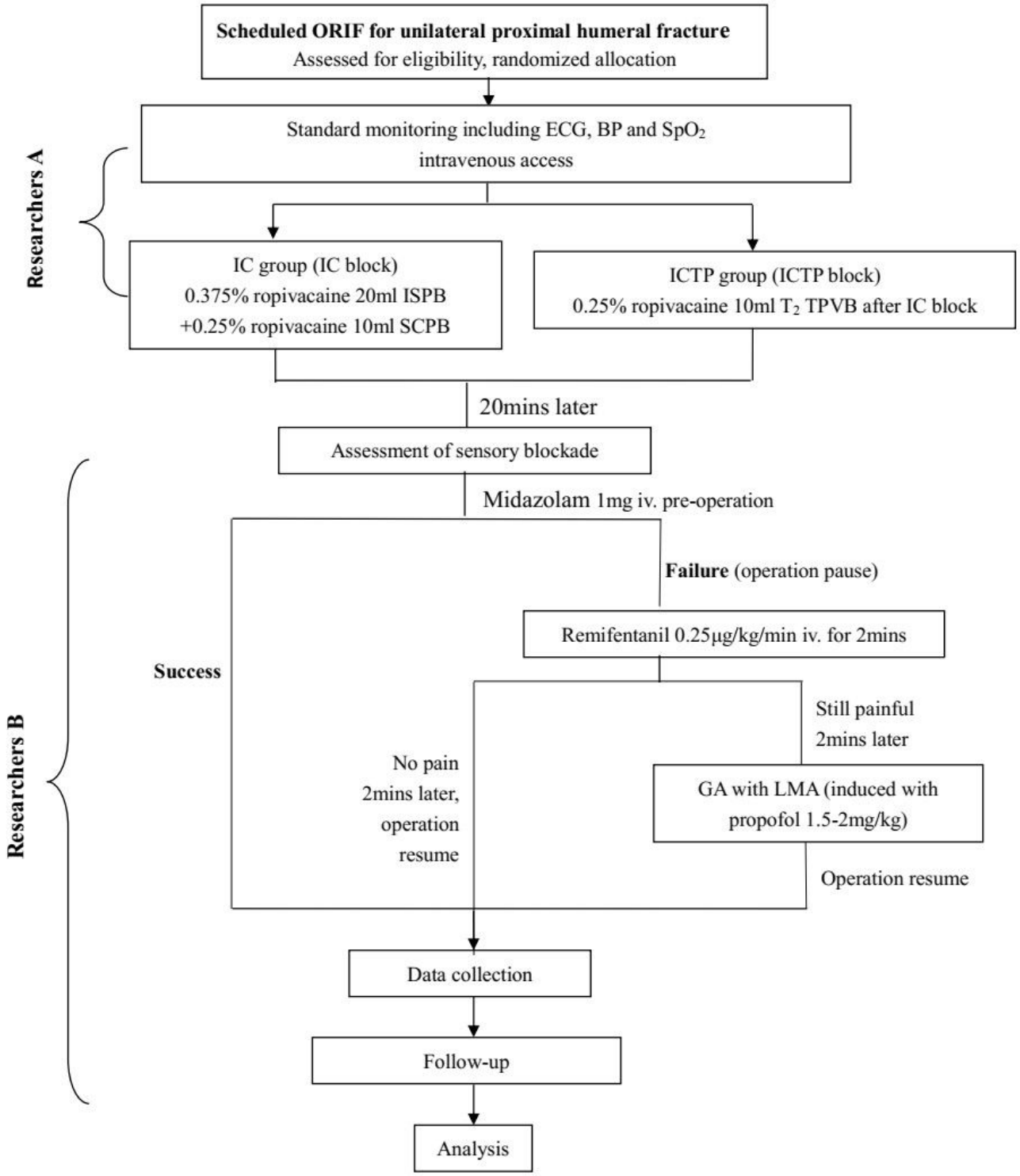

Figure 2

Flowchart of trial procedures.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- supplement1.doc