Comparison of continuous and single interscalene block for quality of recovery score following arthroscopic rotator cuff repair

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Abstract

Background: Continuous interscalene brachial plexus block (CISB) is well known to reduce postoperative pain and to improve patient satisfaction. However, the effect of CISB on the quality of postoperative recovery is unknown. We compared the quality of recovery from arthroscopic rotator cuff repair in patients who received CISB or single interscalene brachial plexus block (SISB).

Methods: This prospective non-randomized controlled trial with propensity score matching enrolled 134 patients undergoing arthroscopic surgery for rotator cuff repair. Each patient received an interscalene block before surgery. One group had a catheter insertion 30 min after the end of surgery and started patient-controlled regional analgesia (PCRA, \(n = 49\)). The other group received intravenous patient-controlled analgesia (IV-PCA, \(n = 85\)). The primary outcome was the quality of recovery (QoR-40) score. Also, postoperative analgesia, sleep quality, and postoperative complications were evaluated.

Results: The two groups had similar QoR-40 score on postoperative day-1 (POD1), but the PCRA group had a significantly greater QoR-40 score on POD2 (156.0, IQR: 143.0, 169.0 vs. 171.0, IQR: 159.0, 178.0; \(p < 0.001\)). The IV-PCA group received more analgesics during the 2 days after surgery, especially during night-time, and had a higher prevalence of sleep disturbances. The time to first additional analgesics request was significantly longer in PCRA group (14 hours, 95% CI: 13–16 vs. 44 hours, 95% CI: 28–not applicable). The incidence of postoperative nausea and vomiting significantly lower in the PCRA group (16.3% vs 46.9%, \(p = 0.002\)). Conclusion: CISB showed a higher quality of recovery score than SISB with IV-PCA in arthroscopic rotator cuff repair, probably related to the effective analgesia, improved sleep quality, and reduced opioid-related complications.

Keywords

elbow & shoulder, nerve block, postoperative pain, quality of recovery

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Introduction

Arthroscopic rotator cuff repair is a safe, effective, and minimally invasive surgical option for treatment of rotator cuff tears. However, this procedure may require extensive resection of bursal tissue, insertion of hardware, and soft tissue distension from irrigation fluid, leading to severe postoperative pain. Effective postoperative pain control can improve patient recovery, rehabilitation, and satisfaction with treatment, thus influencing long-term functional outcome. In addition, clinicians must consider the adverse effects of opioids when providing pharmaceutical treatment for pain.

Interscalene brachial plexus block (BPB) is now widely accepted as a standard practice for management of acute pain after shoulder surgery. Although a meta-analysis confirmed the early benefits of a single shot interscalene block (SISB) for shoulder surgery, it also found that the analgesic effects were not as long lasting as originally described. Most of these patients first complain of night pain, when access to care is more limited. The use of opioids to prevent night pain can lead to adverse effects, including nausea, vomiting, respiratory impairment, and sleep disturbance. Also, rebound pain may occur after SISB, so patients need to start taking oral analgesics well before the nerve block wears off. Although many studies have been conducted using perineural or intravenous additives to prolong the analgesic duration of SISB, night pain and opioid usage are still a problem.

Recent research reported that relative to a SISB, a continuous interscalene block (CISB) provided superior analgesia for up to 48 hours in multiple subsets of patients, including those undergoing acromioplasty, minor arthroscopic surgery, and rotator cuff surgery. CISB is well known to reduce postoperative pain and opioid consumption and to improve patient satisfaction. However, the effect of CISB on the quality of postoperative recovery is unknown. Post-surgical pain and other factors, such as sleep, emotions, and impaired activity, affect overall patient recovery. Traditional clinical outcome measures include surgical complications, organ dysfunction, hospital length of stay and sometimes longer-term survival. Postoperative recovery is a complex process involving a variety of processes, such as changes in physiological outcomes, incidence of adverse events, and psychological status. The most widely used method of measuring this is Quality of Recovery 40 (QoR-40) questionnaire. There is increasing emphasis on measuring overall patient recovery and how quickly a patient can return to daily life after anesthesia and surgery. Numerous studies have used the post-operative QoR-40 to compare different methods of anesthesia, adjuvants, regional analgesic techniques, and other factors on patient recovery.

To the best of our knowledge, no studies have examined the impact of CISB on overall quality of recovery after arthroscopic surgery for rotator cuff repair. In this study, we hypothesized that CISB would showed higher quality of recovery score than SISB.

Methods

Study design and participants

The study protocol was approved by the Chungnam National University Hospital Institutional Review Board (IRB CNUH 2018-05-070), and the trial was registered at the Clinical Research Information Service, a clinical trial registry in Korea (KCT0003150). This non-randomized prospective study enrolled patients who were aged 20–80 years, had American Society of Anesthesiologists physical status I or II, and were scheduled for arthroscopic repair of rotator cuff tear at Chungnam National University Hospital (Daejeon, Republic of Korea). All patients provided written informed consent. Patients were excluded if they refused to participate, had a coagulopathy or bleeding disorder, were being treated with an antiplatelet agent, had a local infection of a nerve block site on the neck, or were hypersensitive to local amide anesthetics. Patients were also excluded if they had central neuropathy, a body mass index greater than 35 kg/m², uncontrolled diabetes mellitus, a significant cardiopulmonary disease, or a psychiatric disease.

General anesthesia and single interscalene block

All patients were educated before surgery regarding the 11-point numeric rating scale (NRS) used for scoring post-operative pain (0: no pain; 10: worst possible pain). Routine monitoring included electrocardiography, pulse oximetry, and noninvasive blood pressure measurements. Before induction of general anesthesia, SISB was given to all participants under ultrasonography guidance by experts who performed at least 100 such procedures. This procedure was an in-plane technique using MyLab TM25 Gold (Esaote, Genova, Italy) and a linear probe (LA435: 6–18 MHz, Esaote). A 20 mL dose of 0.375% ropivacaine was injected using a 22 gauge, 50 mm, echogenic needle (SonoPlex cannulas, Pajunk®, Geisingen, Germany). Povidone-iodine was first used to make an aseptic field. Then the patient was placed in a supine position, with a soft jelly pad placed behind the back, and the head was turned slightly to the contralateral side. The C5 and C6 roots were identified during ultrasound scanning in the transverse plane. Using an in-plane technique, a needle was inserted toward the interscalene groove in a lateral-to-medial direction. After careful aspiration to avoid intravascular injection, 1 to 2 mL of local anesthetic was injected to verify proper needle placement, and then extra volume was injected in several aliquots. Then, the patient was anesthetized by standard methods using propofol, remifentanil, rocuronium, and sevoflurane. All surgeries were performed by one expert surgeon while seated (W.L.).
Postoperative pain control: Patient-controlled regional analgesia (PCRA) vs. intravenous patient-controlled analgesia (IV-PCA)

Patients received CISB depending on the availability of a regional anesthesiologist who had expertise in performing peripheral nerve catheter insertion at the time of surgery. Continuous catheter insertion was performed after confirming the patient had an alert mental state after about 30 min of recovery in the post-anesthesia care unit. The patient was placed in a lateral position, and the transducer was positioned in the transverse plane, and the C5 and C6 roots were identified. The needle was then inserted using an in-plane technique toward the interscalene groove in a posterior-to-anterior direction. Between the C5 and C6 roots, the 48 mm catheter (E-Cath, Pajunk) was mounted so that the inner and outer catheter junctions were between the roots. A PCRA device (Accumate 1200™, Wooyoung Meditech, Republic of Korea) had the following settings: 5 mL of automated intermittent bolus-mode, 1 hour interval, patient bolus of 5 mL, lock-out of 20 min, 250 mL of 0.2% ropivacaine.

Patients in the other group received IV-PCA. In this case, a PCA device was set to administer a bolus dose of 15 μg of fentanyl, with a background infusion dose of 15 μg per h, a lockout time of 10 min, and a total dose of 1500 μg.

The pain score was re-explained to the patient and analgesics were administered through the PCA device when a patient reported an NRS score above 3. If pain control was insufficient with IV-PCA or PCRA alone, patients were given 25 mg of pethidine. All patients received 20 mg of intravenous nefopam at 12-h intervals as a part of multimodal analgesia.

QoR-40 questionnaire

The quality of postoperative functional recovery was assessed using the validated Korean version of the QoR-40 questionnaire (Table 1).21 This questionnaire consists of 40 questions that examine 5 domains of patient recovery20: physical comfort (12 items), emotional state (9 items), physical independence (5 items), psychological support (7 items), and pain (7 items). Each item was rated on a 5-point Likert scale as 1 (none of the time), 2 (some of the time), 3 (usually), 4 (most of the time), or 5 (all of the time). The total score ranged from 40 (very poor recovery) to 200 (outstanding recovery). An assistant researcher administered the QoR-40 three times: the day before surgery (between 6 and 8 p.m.), POD1 (between 8 and 10 a.m.), and POD2 (between 8 and 10 a.m.).

Outcome measures

The primary outcome was the global QoR-40 score on POD1. The use of additional analgesics, duration of using additional analgesics, sleep quality, and sleep disturbance were the secondary outcomes. Quality of sleep was measured using an 11-point scale in which 0 indicated “very dissatisfied,” 5 indicated “neutral,” and 10 indicated “very satisfied.” The presence of sleep disturbance due to pain was recorded. The definition of night-time was 10 p.m. to 7 a.m. the next morning. Complications, including postoperative nausea and vomiting (PONV), local anesthetics systemic toxicity, and event of hypoxia were also assessed.

Sample size

The required sample size was calculated based on a pilot study and a previous study using G*Power version 3.1 (Franz Faul & Edgar Erdfelder, Trier, Germany). The pilot data indicated that the QoR-40 score on POD1 was approximately 175 (standard deviation: 14). According to Myles et al.,22 minimal clinically important difference of QoR-40 was 6.3 and pooled mean difference of meta-analysis was 11.19 By setting 10 as the effect size of QoR-40 score difference, 43 patients per group were needed to achieve 90% power with a type 1 error. About 150 patients were initially recruited because CISB was performed in about one-thirds of all patients during the previous year.

Statistical analysis

All statistical analyses were performed using R software version 3.6.2 (R Project for Statistical Computing, Vienna, Austria). To account for possible selection bias and confounding factors,23 1:1 propensity score matching (PSM) was performed using the MatchIt package in R.24 The dependent variable was a binary response, with PCRA scored as 1 and IV-PCA as 0. Nearest-neighbor matching with logistic regression-based PSM was performed using sex, age, operation time, and 5 categories of QoR-40 as covariates to be corrected. The absolute standardized difference (ASD) was calculated to validate the balance of the two groups, and a value below 0.1 indicated sufficient balance.

After validating the balance of the matched groups, the normality of continuous data was assessed using the Shapiro-Wilk test. For data with a normal distribution, comparisons between groups were determined using an independent t-test and the results were expressed as means ± SDs. For data with a non-normal distribution, groups were compared using the Mann-Whitney U test and the results were expressed as medians and inter-quartile ranges (IQRs). Categorical data were compared using the χ² test or Fisher’s exact test, as appropriate, and the results were expressed as number and percentage. Differences in the primary outcome—QoR-40 score on POD1—were determined by calculating mean differences and 95% confidence intervals (CIs). Survival outcomes, including time-to-first request for additional analgesia and median duration of analgesia, were analyzed using the Kaplan-Meier method.
and compared using the log-rank test. For each calculation, a two-tailed $p$-value below 0.05 was considered significant.

**Results**

From July 2018 to May 2019, we assessed 150 patients for eligibility. Six patients refused to participate and 11 did not complete the QoR-40. Among the 134 enrolled patients, 85 received IV-PCA and 49 patients received PCRA (Figure 1). There were more females in the IV-PCA group, so we included sex in the PSM; after PSM, the ASD for sex changed from 0.376 to below 0.001 (Table 2).

The global QoR-40 on POD1 (primary outcome measure) was not significantly different in the two groups (IV-PCA: 174.0, IQR: 160.0, 186.0 vs. PCRA: 182.0, IQR: 169.0, 185.0; $p = 0.161$; Supplement Table 1 and Figure 2). However, analysis of the pain dimension in the QoR-40 indicated a higher score in the PCRA group (24.0, IQR: 19.0, 33.0 vs. 30.0, IQR: 25.0, 33.0; $p = 0.007$). In addition, the global-QoR-40 on POD2 was significantly higher in the PCRA group (156.0, IQR: 143.0, 169.0 vs. 171.0, IQR: 159.0, 178.0; $p < 0.001$). On POD2, the PCRA group also had higher scores in the dimensions of physical comfort, emotional state, and pain.

The IV-PCA group required more additional analgesics than the PCRA group for 2 days after surgery, especially at night-time (Table 3). The IV-PCA group also had more sleep disturbances and lower sleep quality scores.

The time from surgery to the first request for additional analgesia (Figures 3 and 4) was significantly longer in the PCRA group (median [95% CI]: 14 hours [13, 16] vs. 44 hours [28, NA], hazard ratio: 0.372 [0.243, 0.567]).
Analysis of the pain scores indicated that pain was well controlled in the PCRA group (below 3 points for 3 days after surgery: \( n = 34 \) [40%]) but not in the IV-PCA group (below 3 points for 3 days after surgery: \( n = 8 \) [16.3%]) (Figure 5).

The incidence of PONV significantly lower in the PCRA group (16.3% [8/49]) than IV-PCA group (46.9% [23/49]) postoperative 48 hours after matching (\( p = 0.002 \)). Symptoms of local anesthetics systemic toxicity, catheter related problem (accidental catheter removal, infection) and clinically problematic hypoxia were not reported.

### Discussion

Our comparison of recovery from arthroscopic shoulder surgery in patients who received PCRA or IV-PCA indicated that these groups had no difference in global QoR scores on POD1, although the PCRA group had a better score in the subcategory of pain at that time. On POD2, the PCRA group had a significantly better global QoR score, and significantly better scores in the subcategories of physical comfort, emotional state, and pain. There was probably no difference between the groups on POD1 because the single injection received by patients in the SISB group provided significant relief that lasted nearly 1 day. In fact, patients in the SISB group first requested additional analgesia at 14 h (95% CI: 13–16) after surgery. However, by POD2, the single block mostly wore off, and the PCRA group had better QoR scores at that time. A recent meta-analysis concluded that patients who received CISB experienced superior pain control beyond 48 h, a longer time to first use of an analgesic, enhanced satisfaction, and reduced postoperative nausea and vomiting. In agreement, we also found that the persistent effect of analgesia in the PCRA group led to improved sleep quality, decreased postoperative nausea and vomiting, and better overall QoR.

The control of rebound pain after regional anesthesia is an important factor that can affect a patient’s postoperative recovery. The intolerable pain after shoulder arthroscopy

### Table 1. Quality of Recovery (QoR-40) questionnaire.

|               | None of the time | Some of the time | Usually | Most of the time | All of the time |
|---------------|------------------|------------------|---------|------------------|----------------|
| **Physical Comfort** |                  |                  |         |                  |                |
| Able to breathe easily | 1 2 3 4 5       |                  |         |                  |                |
| Have a good sleep | 1 2 3 4 5       |                  |         |                  |                |
| Been able to enjoy food | 1 2 3 4 5     |                  |         |                  |                |
| Feel rested | 1 2 3 4 5       |                  |         |                  |                |
| **Emotional State** |                  |                  |         |                  |                |
| Having a feeling of general well-being | 1 2 3 4 5 |                  |         |                  |                |
| Feeling in control | 1 2 3 4 5       |                  |         |                  |                |
| Feeling comfortable | 1 2 3 4 5      |                  |         |                  |                |
| **Physical Independence** |                |                  |         |                  |                |
| Have normal speech | 1 2 3 4 5       |                  |         |                  |                |
| Able to wash, brush teeth or shave | 1 2 3 4 5 |                  |         |                  |                |
| Able to look after your own appearance | 1 2 3 4 5 |                  |         |                  |                |
| Able to write | 1 2 3 4 5       |                  |         |                  |                |
| Able to return to work or usual home activities | 1 2 3 4 5 |                  |         |                  |                |
| **Psychological Support** |                |                  |         |                  |                |
| Able to communicate with hospital staff (when in hospital) | 1 2 3 4 5 |                  |         |                  |                |
| Able to communicate with family or friends | 1 2 3 4 5 |                  |         |                  |                |
| Getting support from hospital doctors (when in hospital) | 1 2 3 4 5 |                  |         |                  |                |
| Getting support from hospital nurses (when in hospital) | 1 2 3 4 5 |                  |         |                  |                |
| Having support from family or friends | 1 2 3 4 5 |                  |         |                  |                |
| Able to understand instructions and advice | 1 2 3 4 5 |                  |         |                  |                |
| **Pain** |                |                  |         |                  |                |
| Nausea | 5 4 3 2 1      |                  |         |                  |                |
| Vomiting | 5 4 3 2 1      |                  |         |                  |                |
| Dry-retching | 5 4 3 2 1    |                  |         |                  |                |
| Feeling restless | 5 4 3 2 1    |                  |         |                  |                |
| Shaking or twitching | 5 4 3 2 1 |                  |         |                  |                |
| Shivering | 5 4 3 2 1     |                  |         |                  |                |
| Feeling too cold | 5 4 3 2 1   |                  |         |                  |                |
| Feeling dizzy | 5 4 3 2 1   |                  |         |                  |                |
| **Emotional State** |                |                  |         |                  |                |
| Had bad dreams | 5 4 3 2 1     |                  |         |                  |                |
| Feeling anxious | 5 4 3 2 1     |                  |         |                  |                |
| Feeling angry | 5 4 3 2 1     |                  |         |                  |                |
| Feeling depressed | 5 4 3 2 1   |                  |         |                  |                |
| Feeling alone | 5 4 3 2 1     |                  |         |                  |                |
| Had difficulty falling asleep | 5 4 3 2 1 |                  |         |                  |                |

(continued)
tends to last until POD2, so the use of CISB for several days may be an effective method of pain control. Our results indicated that the average pain score remained below 3 points for 3 days after surgery in the PCRA group, but that the IV-PCA group had higher pain scores.

Recent anesthesia studies have included the assessment of recovery after anesthesia. In particular, research on recovery focuses on measuring how quickly a patient can return to daily life by evaluating the patient’s overall recovery, rather than simply recovery from certain symptoms. Postoperative recovery is a complex process, and can be affected by changes in the incidence of physiological endpoints, psychological status, and adverse events. There is an increasing emphasis on outcome measurements that consider the patient’s own perspective, and there are several patient-centered measurement tools used to assess the quality of recovery in the postoperative setting. The most widely used tool is the QoR-40, which has 40 questions that assess emotional state, physical comfort, psychological support, physical independence, and pain. This tool has good test-retest reliability, internal consistency, and split-half coefficient, and is therefore considered a reliable survey. Various other studies of anesthesia recovery have also used the QoR-40 to investigate the effects of different types of surgery, anesthesia methods, use of additional drugs, and gender.

Previous studies have also examined the effect of regional analgesic techniques on patient QoR. For example, peripheral nerve blocks as part of an analgesic protocol for operative repair of tibia and ankle fractures also improved QoR and postoperative pain. Serratus plane block performed during video-assisted thoracoscopic surgery also led to improved QoR-40 score for 2 days, and thoracic paravertebral block led to a high QoR score from ambulatory tumor resection to POD2. Excellent pain control has a positive effect on QoR; however, QoR results and pain relief were independent in some studies. In particular, superficial cervical plexus block in anterior cervical disectomy and fusion did not affect the amount of opioid consumption, but did reduce the incidence of other complications and led to an improved QoR score. Occasionally, some negative results occur according to duration of regional analgesia. For example, pectoral block reduce postoperative pain in patients receiving breast surgery, but did not improve the postoperative QoR-40 score, due to the rebound pain. Another study found no difference on

| Table 2. Demographics and preoperative QoR-40 scores of patients in the two groups before and after propensity score matching. |
|---------------------------------|---------------------------------|-----------------|-----------------|-----------------|
| **Unmatched Data**              | **Matched Data**                |                 |
| IV-PCA (n = 85)                 | PCRA (n = 49)                   | ASD             |
| Age                            | 64.0 [58.0,69.0]                | 61.0 [56.0,67.0]|
| Sex, M/F                       | 38/47                          | 31/18           |
| Height, cm                     | 159.3 [152.0,166.1]             | 158.0 [152.0,166.0]|
| Weight, kg                     | 65.3 [58.4,72.3]                | 63.0 [57.4,75.5]|
| BMI                            | 25.8 [23.6,27.5]                | 25.4 [23.4,28.3]|
| Anesthesia time, min           | 146.0 [130.0,172.0]             | 140.0 [130.0,168.0]|
| Operation time, min            | 120.0 [100.0,144.0]             | 121.0 [101.0,138.0]|

Data are presented as median [IQR].
Abbreviations: ASD, absolute standardized difference; BMI, body mass index; QoR-40, Quality of Recovery-40 questionnaire.

| Table 3. Postoperative analgesia profiles of the two groups before and after propensity score matching. |
|---------------------------------|---------------------------------|-----------------|-----------------|-----------------|
| **Unmatched Data**              | **Matched Data**                |                 |
| IV-PCA (n = 85)                 | PCRA (n = 49)                   | p               |
| POD1 Sleep satisfaction score   | 3.0 [1.0,5.0]                   | 7.0 [4.0,9.0]   | <0.001          |
| Request additional analgesics   | 22/48/14/1                     | 36/11/2/0      | <0.001          |
| Request additional analgesics at night-time (n = 0/1/2) | 24/57/14 | 35/12/2 | <0.001 |
| Sleep disturbance               | 65 (76.5%)                     | 19 (38.8%)     | <0.001          |

| POD2 Sleep satisfaction score   | 5.0 [3.0,7.0]                   | 7.0 [5.0,9.0]   | 0.009           |
| Request additional analgesics   | 32/38/15                       | 30/18/1        | 0.005           |
| Request additional analgesics at night-time (n = 0/1/2) | 41/43/1 | 36/13 | 0.016 |
| Sleep disturbance               | 52 (61.2%)                     | 13 (26.5%)     | <0.001          |

Data are presented as median [IQR] and number (%).
Figure 2. QoR-40 scores on preoperative, postoperative day-1 (POD1) and postoperative day-2 (POD2) in the two groups. ns (not significant): p > 0.05, *: p < 0.05, **: p < 0.01, ***: p < 0.001, ****: p < 0.0001
the quality of postoperative recovery after orthopedic forearm surgery between brachial plexus block and general anesthesia, but in that study measurements were performed 24 h after surgery. The lack of difference may be because as the effect of the nerve block wore off, the patient experienced severe rebound pain, which lowered the QoR score.

Our patients who received CISB consistently had NRS pain scores of 3 or lower, indicating satisfactory analgesia. To maintain better pain control when using a continuous
nerve block, there should be no catheter migration or accidental removal because a local anesthetic must be continuously injected around the target nerve. We used the catheter over the needle technique, in which a surgical adhesive was used to minimize leakage and accidental removal. None of the patients experienced leakage, but we did not confirm migration of the catheter in the target nerve.

Our study has several limitations. First, this was not a randomized controlled trial. While in the planning stage of this study, we were reluctant to insert the catheter into a control group considering SHAM (Serious Harm and Morbidity) scale. Second, the main outcome measure—QoR-40 score—is based on subjective experience. Thus, group assignment could have affected the results because a patient’s expectations or previous experiences with anesthesia could affect expectations and experiences. In addition, it was not ethical to use a placebo group that received physiological saline after catheter insertion. Considering a single nerve block is categorized into a high SHAM score, the insertion of a catheter with placebo injection is considered to be more than that. In addition, we felt it was unethical to expose patients to an invasive technique without analgesia. Therefore, instead of randomization, we used PSM so that the characteristics of both groups were similar. Actually, the sex ratio differed before matching, but when we corrected this, the difference in psychological support on POD1 changed from significant to not significant (Table 2). Third, we did not analyze the subgroup of rotator cuff tear severity based on the size and stiffness, pathology, preoperative pain and functional outcomes. This can be weakness of this study. Future studies in which various confounding factors affecting postoperative pain of rotator cuff tear are needed. Fourth, our study required the help of the researcher to fill out the questionnaire in order to increase the response rate. Since there are relatively many items, it is necessary to make efforts to eliminate bias due to insufficient responses or non-response. Future study using a more brief version such as QoR-15 is also needed in the orthopaedic field. Finally, we used opioid-based pain control regimens in the IV-PCA group instead of the SISB alone. We thought that a SISB without IV-PCA was unethical, given the severe postoperative pain that patients may experience after nerve block washout.

Conclusions

We found that the QoR-40 score was better in patients who received CISB rather than SISB in arthroscopic surgery for rotator cuff repair. This may be related to the effective analgesia, improved sleep quality, and fewer opioid-related complications which CISB provided.

Authors’ note

Sangwon Yun and Yumin Jo contributed equally to this work.

Author contributions

Sangwon Yun, Yumin Jo, and Boohwi Hong: study design, writing the first manuscript, final editing the manuscript; Seojin Sim, Kuhee Jeong, and Byungmuk Kim: data collection; Chahyun Oh, Seyeon Park and Boohwi Hong: statistical analysis and data interpretation; Woo-Yong Lee, Yoon-Hee Kim, Youngkwan Ko, and
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