Efficacy and safety of ultrasound-guided serratus anterior plane block with different doses of dexmedetomidine for patients undergoing modified radical mastectomy: A randomized controlled trial

Caiping Duan (nmgduancaiping@126.com)
Ordos Central Hospital
Zaijun Hao
Ordos Central Hospital
Junling Yang
Ordos Central Hospital
Fei Song
Ordos Central Hospital
Xiujuan Fan
Ordos Central Hospital
Ruizhen Li
Ordos Central Hospital

Research Article

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ORIGINAL RESEARCH

Efficacy and safety of ultrasound-guided serratus anterior plane block with different doses of dexmedetomidine for patients undergoing modified radical mastectomy: A randomized controlled trial

Running head: SAPB for patients undergoing MRM

Caiping Duan, M.M.*, Zaijun Hao, M.M., Junling Yang, M.M., Fei Song, M.M., Xiujuan Fan, M.M.

Ruizhen Li, M.M.

Department of Anesthesiology, Ordos Central Hospital, Ordos, Inner Mongolia Autonomous Region, China

Correspondence: Caiping Duan

Email: nmgduancaiping@126.com

Abbreviations: MRM= modified radical mastectomy, ERAS= enhanced recovery after surgery, TEB=Thoracic epidural block, INB=intercostal nerve block, PVB=paravertebral block, USG-SAPB= Ultrasound-guided serratus anterior plane block, Pecs=pectoral nerve, DEX=dexmedetomidine, ASA= American Society of Anesthesiologists, PCIA= patient controlled intravenous analgesia, BMI= body mass index, APS= acute pain service, VAS= visual analog

scale, BIS= Bispectral index, PACU= post-anesthesia care unit, PONV= Postoperative nausea and vomiting, LOS= level of sedation, QoR-40=40-item Quality of Recovery questionnaire, MAP=Mean arterial pressure, HR=heart rate, SD=standard deviation, IQR=inter-quartile range, TTPB=transversus thoracic muscle plane block, PSI=parasternal intercostal block

Abstract

Background: Ultrasound-guided serratus anterior plane block (USG-SAPB) has been used for pain management of patients undergoing modified radical mastectomy (MRM), but evidence supporting the adjuvant analgesic benefits is limited. We explored the efficacy and safety of preemptive use of different concentrations of dexmedetomidine and ropivacaine in USG-SAPB for patients undergoing MRM. **Patients and methods:** Ninety-five female patients were randomly allocated to RD1 and RD2 groups. USG-SAPB was performed before anesthesia induction. Consumption of sufentanil, postoperative pain scores, and level of sedation were recorded 1–72 h postoperatively. Intraoperative hemodynamics, PACU length of stay, incidence of moderate-severe pain, one-time puncture success, block procedure time, time to first rescue analgesia, satisfaction scores of patients and surgeons, hospital length of stay, adverse events, the prevalence of chronic pain, and quality of postoperative functional recovery were recorded. **Results:** Dynamic VAS was significantly lower at 4, 8, and 12 h after surgery and sufentanil need was significantly lower at 4, 8, 12, 24, and 48 h after surgery in the RD2 group ($P<0.05$). The incidence of moderate-severe pain was significantly lower in the RD2 group ($P<0.05$). Time to first rescue analgesia was significantly longer in the RD2 group ($P=0.047$). Consumption of

propofol, remifentanil, dexmedetomidine, use of vasoactive agents, and PACU length of stay (LOS) were significantly reduced in RD2 patients ($P<0.05$). There were no significant differences between the two groups with respect to procedural variables or satisfaction scores of patients and surgeons, and/or postoperative complications. The hospital LOS, global QoR-40, and prevalence of chronic pain were comparable. **Conclusions:** Use of 1 μg/kg dexmedetomidine and ropivacaine in USG-SAPB can provide superior postoperative analgesia for patients undergoing MRM without additional adverse effects, and result in similar quality of postoperative functional recovery and prevalence of chronic pain.

Keywords: dexmedetomidine, modified radical mastectomy, pain management, ropivacaine, serratus anterior plane block, ultrasound

Introduction

Breast cancer is the most common cancer in women worldwide, accounting for nearly one-third of all new cancer cases in the female population.[1] Modified radical mastectomy (MRM) is currently the first-line treatment for early, localized breast cancer despite the increasing use of chemotherapy and endocrine therapy before surgery.[2] A previous study has reported that over 35% of patients experience acute postoperative pain following MRM despite the surgical methods being minimally invasive.[3] Postoperative acute pain has been recognized as a high risk factor in the development of postmastectomy pain syndrome, having an incidence rate as high as 25–60%, with a consequent impaired quality of their life.[4, 5] Furthermore, one of the most important reasons for such a high incidence of postoperative pain may be due to the limited attention to perioperative pain relief compared with the other cancer surgeries.[6]

Multimodal analgesia, an important component of enhanced recovery after surgery (ERAS), can effectively reduce surgical stress and pain-related complications, leading to early mobilization and shortened hospital stays.[7, 8] Regional anesthesia, one of the most used opioid-sparing strategies, has been frequently preferred as part of multimodal analgesia for its improved analgesia and fewer side effects in recent years.[9, 10] Thoracic epidural block (TEB), intercostal nerve block (INB), paravertebral block (PVB), and local infiltration are common methods of postoperative analgesia after MRM. However, each method has its own advantages and disadvantages.[11–14] As a result, less invasive multimodal analgesia strategies are being investigated. Thoracic plane blocks have been recently proposed as a novel and rapidly expanding facet of regional anesthesia, and in particular, ultrasound guidance has been

77 introduced to improve the success rate and safety of regional nerve block.[15, 16]

78 Ultrasound-guided serratus anterior plane block (USG-SAPB), first defined by Blanco in
79 2013, has been used for pain control after breast surgery because of its excellent analgesia,
80 reduced invasiveness, simplicity, easy-to-learn technique, and relative safety.[17] It can block the
81 lateral branches of the intercostal nerves of the T2–T9 spinal nerves by injecting local anesthetic
82 into the plane, either superficial or deep to the serratus anterior muscle. As a result, it can
83 provide analgesia in the chest wall, axillary region, and posterior region of the shoulder.[18]
84 USG-SAPB has been used in chest drain insertion, reconstructive breast surgery, cosmetic
85 breast surgery, and video-assisted thoracoscopic surgery.[19] Compared with other thoracic planar
86 blocks such as pectoral nerve (Pecs) I and II blocks, the local anesthetic is injected to a more
87 dorsal region in SAPB. As a result, SAPB may target the thoracic nerves more selectively and
88 anesthetize a greater number of intercostal nerves.[20] Local anesthetic combined with
89 dexmedetomidine (DEX) has been reported to prolong analgesia in brachial plexus blocks.[21]
90 However, it is presently unclear if DEX combined with ropivacaine will provide superior
91 postoperative analgesia of the SAPB. The aim of this study was to explore the efficacy and
92 safety of preemptive use of different concentrations of DEX and ropivacaine in USG-SAPB for
93 patients undergoing MRM.

94

Methods

Patients

This trial was designed in accordance with the CONSORT 2010 statement. Ethical approval was obtained from the Institutional Review Boards of Ordos Central Hospital and registered at Chinese Clinical Trial Registry (09/06/2020, ChiCTR2000033685). Written informed consent was obtained from patients before trial participation.

Patients who underwent breast cancer surgery in our hospital between June and September 2020 were recruited. Inclusion criteria were the following: patients with American Society of Anesthesiologists (ASA) I–II, age 45 to 60 years, scheduled for unilateral MRM with axillary lymph node dissection, received patient controlled intravenous analgesia (PCIA) at least for 72 h after surgery. Exclusion criteria: patients with contraindications to SAPB (ie, anticoagulant treatment or coagulative abnormality, infection at injection site, severe chest wall deformities), known allergies to the drugs used in the study, radiation before surgery, secondary surgery, smoking, or drug abuse, history of motion sickness, peripheral neuropathy (eg, diabetic neuropathy), severe cardiopulmonary disease, renal and liver dysfunction, history of chronic pain, unable to cooperate or communicate, body mass index (BMI) >30 kg/m^2, refusal to participate in the block procedure.

Randomization and blinding

Patients were randomly allocated by a computer-generated random number list. The results were concealed in sequentially numbered envelopes that were opened after enrolment of

patients. All participants were unaware of the group assignment. Nurses in the acute pain service (APS) team educated patients how to use the visual analog scale (VAS) and PCIA pump, prepared the study drugs, and performed postoperative assessments.

SAPB Procedure

No premedication was given before SAPB. Patients received standard ASA monitoring (ie, noninvasive blood pressure, pulse oximetry, electrocardiography, and temperature) after arriving at the anesthesia preparation room and venous access was established at the contralateral upper limb. Bispectral index (BIS) monitoring electrodes were placed on each side of the patient's forehead according to the manufacturer's instructions. Patients were sedated and received analgesia with a 0.02 mg/kg midazolam and 1 μg/kg fentanyl was administered after applying nasal cannula oxygen at 2 L/min. The same anesthesiologist with sufficient training in ultrasound performed the real-time SAPB under USG as described in a previous study.[22] Briefly, patients were placed in the lateral decubitus position with the operation side up, a high-frequency linear probe was placed over the middle clavicular region in a sagittal plane after routine disinfection. Then, a 22-gauge needle was introduced from caudad to cephalad using plane technology after the subcutaneous tissue, latissimus dorsi, serratus anterior, intercostal muscle, and pleura were identified at the fourth rib in the midaxillary line. After confirming the location of the needle with 2 mL of saline solution without blood or air in aspiration, 20 mL 0.5% ropivacaine with 5 mg dexamethasone and 0.5 μg/kg or 1 μg/kg DEX was injected in the deep layer of serratus anterior plane (between the serratus anterior muscle and external intercostal muscles) for about 10 seconds. We defined a successful block as the loss of cold sensation in more than

two dermatomes 30 min after the block and then were transferred to operating room. Otherwise, the procedure was considered as a failure of block.

Anesthesia

Anesthesia was induced by lidocaine 1.5 mg/kg, dexamethasone 0.1 mg/kg, fentanyl 2–3 μg/kg, propofol 1–2 mg/kg, and cisatracurium 0.1 mg/kg. A laryngeal mask was positioned to control the airway during surgery. DEX 0.2–0.7 μg/kg/h, propofol 3-6 μg/mL, remifentanil 0.05–0.2 μg/kg/min were titrated to maintain BIS at 50–60 and hemodynamics within 20% of baseline. Cisatracurium 0.05 mg/kg was given at the discretion of anesthetists. Tropisetron 5 mg and ketorolac 30 mg were intravenously administered about 30 min before the end of the surgery. Neuromuscular block was reversed by neostigmine 0.02 mg/kg and atropine 0.01 mg/kg if necessary. A volume of 10 mL 2% lidocaine was administered by subcutaneous infiltration in the parasternal and subclavicular areas at the end of the operation for postoperative analgesia by the surgeon according to previous study.[23] The laryngeal mask was removed after patients responded promptly to the verbal command and patients were shifted to the post-anesthesia care unit (PACU). MRM was performed using the same technique by the same surgical team according to previous study.[24]

Postoperative Pain Management

Patients received the same postoperative analgesia protocol in both groups. At the end of surgery, PCIA was started with 0.8 μg/mL sufentanil. The bolus volume was 2 mL, background dose was 1 mL/h, locked time was 5 min, and the 1-h limit was 12 mL. Intravenous flurbiprofen

156 axetil injection 50 mg was administered if VAS>3 . Postoperative nausea and vomiting (PONV)
157 was treated with 5 mg tropisetron.

158 *Data collection*

159 The primary outcome was consumption of sufentanil 72 hours after operation. Secondary
160 outcomes included postoperative pain scores: VAS 0 cm=no pain, 10 cm=worst imaginable pain)
161 and level of sedation (LOS, 6-point scale: 0=alert; 1=mildly drowsy; 2=moderately drowsy, easily
162 arousable; 3=very drowsy, arousable; 4=difficult to arouse; and 5=unarousable), which were
163 recorded at 1, 2, 4, 8, 12, 24, 48 and 72 h postoperatively, intraoperative hemodynamics, PACU
164 length of stay, PONV (5-point scale: 0=no nausea, 1=mild nausea, 2=severe nausea, 3=one
165 episode of vomiting, 4=vomiting more than once), incidence of moderate-severe pain (dynamic
166 VAS >3), one-time puncture success, block procedure time, time to first rescue analgesia,
167 satisfaction scores of patients and surgeons (5-point scale: 1=extremely unsatisfied;
168 5=extremely satisfied), hospital length of stay, adverse events and the prevalence of chronic pain.
169 The quality of postoperative functional recovery (40-item Quality of Recovery questionnaire
170 (QoR-40): 40 to 200) was assessed the day before surgery, the first day, on discharge, and three
171 months after surgery.

172 Mean arterial pressure (MAP) and heart rate (HR) were recorded at the following time points:
173 arrival at the operating room (T0), before SAPB procedure (T1), after SAPB Procedure (T2),
174 before anesthesia induction (T3), after anesthesia induction (T4), before incision (T5),
175 immediately after skin incision (T6), and extubation (T7). Hypotension was defined as MAP
176 decreased by >20% compared with baseline and treated with 40 μg phenylephrine or 6 mg

177 ephedrine. Bradycardia was defined as HR<60 beats/min or decrease >20% compared with
178 baseline and treated with 0.2 mg atropine.

179 *Statistical Analysis*

180 The sample size was calculated on the basis of a 15% reduction in the cumulative amount of
181 sufentanil 72 h after the surgery in our preliminary trial (85.92 ± 24.08 μg in the RD1 group). For
182 a study power of 80% (α=0.05, β=0.2), 42 participants were required each group according to
183 PASS 11.0 (NCSS Statistical Software, Kaysville, UT, USA). Assuming a dropout rate of 15%, the
184 final sample size was determined to be 49 patients in each group.

185 The Kolmogorov-Smirnov test was used to assess distribution of variables. Homogeneity of
186 variance was determined using Levene's tests. Quantitative data were expressed as the
187 mean±standard deviation (SD) or median and inter-quartile range (IQR). Differences between
188 groups were compared using repeated-measures analysis of variance with the Bonferroni
189 correction for normally distributed data. For nonnormally distributed data, groups were compared
190 with the Mann-Whitney U test. Categorical data were expressed as number, frequency, or
191 percentage, and analyzed using chi-squared tests or Fisher's exact tests. Time between surgery
192 completion and first request of rescue analgesics was plotted as Kaplan-Meier survival curves
193 and compared using the Log rank test. P<0.05 was considered statistically significant. Statistical
194 analysis was performed with SPSS for Windows Version 22.0 (SPSS Inc. Chicago, IL, USA).

195

Results

Baseline Characteristics

A total of 201 patients who underwent MRM in our hospital between June and September 2020 were recruited using the CONSORT diagram (Fig 1). Overall, 103 patients were excluded for the following reasons: ASA of 15 patients >II, age of 27 patients <45 or >60 years, 7 patients with contraindications to SAPB, 3 patients radiation before surgery, 2 patients with the secondary surgery, 4 patients with history of smoking, 6 patients with history of motion sickness, 1 patient with peripheral neuropathy, 8 patients with history of chronic pain, 5 patients unable to cooperate or communicate, 11 patients with BMI >30 kg/m^2, and 14 patients who refused to participate in the block procedure. Finally, 98 patients were included and divided into two equal groups: Group RD1 (20 mL 0.5% ropivacaine with 5 mg dexamethasone and 0.5 μg/kg DEX in SAPB) and Group RD2 (20 mL 0.5% ropivacaine with 5 mg dexamethasone and 1 μg/kg DEX in SAPB). In addition, 3 patients were excluded because of the failure of the SAPB procedure (2 patients from the RD1 group and 1 patient from the RD2 group). There were no significant differences between the two groups with respect to demographic data (Table 1).

Intraoperative variables

Both MAP and HR were not significantly different between the two groups from T0 to T7 (P>0.05, Fig 2). Compared with the RD1 group, consumption of propofol, remifentanil, and DEX were significantly reduced in the RD2 group (P<0.05, Table 2). There were no significant differences between the two groups with respect to surgery and anesthesia duration,

consumption of cisatracurium, one-time puncture success, or block procedure time (P>0.05, Table 2). The number of patients using vasoactive agents was significantly reduced in the RD2 group during surgery (P<0.05, Table 2). Additionally, PACU length of stay was significantly shorter in the RD2 group (P<0.01, Table 2). Although the total dermatomal spread was comparable between the two groups (4 [range, 3–5] vs. 4 [range, 3–5] segments, P=0.487), more patients in the RD2 group achieved T1and T2 dermatomal spread compared with the RD1 group (P<0.01, Table 3).

Postoperative variables

Compared with the RD1 group, only dynamic VAS was significantly lower in the RD2 group at 4, 8, and 12 h after surgery (P<0.05, Fig 3). Consumption of sufentanil was significantly lower in the RD2 group at 4, 8, 12, 24, and 48 h after surgery than in the RD1 group (P<0.05, Fig 4). The incidence of moderate-severe pain was significantly lower in the RD2 group (P<0.05, Fig 5).

Time to first rescue analgesia was significantly longer in the RD2 group (P=0.047, Fig 6). There was no difference between the two groups with respect to the level of sedation, or in satisfaction scores of patients and surgeons (P>0.05, Table 4).

The most common postoperative complication was PONV, which was more frequent in the RD1 group. However, the difference was not significant (21.28% vs. 16.67%, P=0.253, Table 5). There were no cardiovascular, respiratory, or block-related complications in either group. The hospital length of stay, global QoR-40, and prevalence of chronic pain 3 months after surgery were comparable between the two groups (P>0.05, Table 5).

Discussion

The findings of this study indicate that USG-SAPB with 1 μg/kg dexmedetomidine could provide superior postoperative analgesia for patients undergoing MRM. Moreover, there were no significant differences between the two groups with respect to one-time puncture success, block procedure time, the total dermatomal spread, satisfaction scores of patients and surgeons, postoperative complications, the hospital length of stay, global QoR-40, or the prevalence of chronic pain 3 months after surgery.

MRM can be performed under general anesthesia, regional anesthesia, or regional anesthesia combined with general anesthesia. The sources of pain after MRM include incision of surgery, surgical drain, and neuromuscular injury.[25] It has been reported that this acute pain may transform into chronic pain at a rate of 25–60%.[5] As a result, it is very important to control postoperative acute pain effectively. A previous study has demonstrated that the high consumption of opioids may lead to greater pain sensitization through activation of N-methyl-D-aspartate pronociceptive systems, increase post-operative opioid use, and the risk of developing sensory disturbances following surgery.[26] As a result, regional anesthesia has gained popularity for its opioid-sparing strategies. TEB and PVB are recommended as standard approaches for analgesia as they can reduce respiratory complications, the incidence of postoperative chronic pain, stress-induced immunosuppression, and the systemic anti-inflammatory response.[11, 13] Though ultrasound technology has been applied in the TEB and PVB, there are still performed with technically difficulty, are time consuming, have high failure

257 rates, and complications because of the deep injection site. Furthermore, these methods
258 demands normal coagulation patterns, advanced surgical skills, and a longer learning curve.[27]

259 Thoracic plane blocks have been proposed as they can offer excellent analgesia and reduce
260 pulmonary complications, stress responses, inflammation, and neurohumoral modulation.[28] A
261 previous study has reported that Pecs I block anesthetizes the medial and lateral pectoral nerves
262 (C8–1) and the anterior cutaneous branches if the local anesthetic penetrates the external
263 intercostals muscles.[29] Pecs II block is performed to obtain blockade of the upper intercostals
264 nerves; however, it has been avoided due to concerns regarding the disruption of the surgical
265 tissue within the axilla.[30] Though Pecs blocks could reduce rest and dynamic pain scores and
266 morphine equivalent consumption at 2, 12, and 24 postoperative hours, and required more than
267 one injection.[31] A previous study reported that Pecs II block may be more effective for short-term
268 postoperative analgesia than SABP during breast cancer surgery. However, this study was a
269 retrospective study and MRM only account for less than 10% of the surgical procedures.[32]

270 USG-SAPB is a new approach proposed to provide analgesia to the hemithorax. A previous
271 study has reported that the analgesic effect derived from SAPB is influenced by many factors
272 such as the position of the patient, volume, concentration, the physicochemical characters of the
273 local anesthetic, local tissue conditions, the site and rapidity of injection and whether an adjuvant
274 was used or not, among which the volume maybe the critical factor impacting on the extent of
275 injectate spread.[33] Compared with other long-acting local anesthetics, such as bupivacaine and
276 levobupivacaine, and ropivacaine has been widely used in regional anesthesia for its larger
277 maximum dosage and lower systemic toxicity and neurotoxicity.[34] Although Kunigo et al reported

that SAPB with 40 mL of 0.375% ropivacaine diffuses to a greater extent than 20 mL, there was no significant difference between the two groups with respect to the time to first need of analgesic rescue and impact on posterior spread. Furthermore, the clinical analgesic effect cannot necessarily be reflected by cadaveric results evaluating the direct staining of individual nerve branches. As a result, 20 mL ropivacaine could be safer and would avoid local anesthetic systemic toxicity.[20, 35] A previous study has also reported the comparison of 0.5% and 0.75% ropivacaine and showed there was no significant difference in postoperative analgesia, but both were superior to 0.375% ropivacaine. This indicated that an increased concentration of ropivacaine may be a better approach to improve the analgesic efficacy of SAPB and prolong the duration of pain relief.[36] Wong et al reported that high concentrations of ropivacaine may lead to respiratory complications.[37] As a result, we adopted SAPB using 0.5% ropivacaine for preemptive analgesia in this study. Several reports have shown that low concentrations of ropivacaine can be detected in the blood, which might result in sedation by suppressing the function of the sodium channel in the central nervous system.[38, 39] As a result, we recorded the level of sedation at 72 h after surgery, although the results were similar between the two groups.

The deep block did not disrupt the surgical tissue planes and spared the block of the long thoracic nerve, which would occur in a superficial block, and thus preserved scapula function.[40] Moreover, the deep block could avoid the need for the injection of local anesthetic into the plane during lymph node dissection or axillary clearance and may promote greater caudad local anesthetic spread.[41] Thus, we adopted the technique of deep block of SAPB given the higher risk of pneumothorax.[42] We defined a successful block as the loss of cold sensation in more than two

299 dermatomes before surgery instead of after surgery in this study to reduce the recall bias. We
300 used SAPB as the preemptive analgesia before surgery, which might be more effective in
301 reducing hyperalgesia, allodynia, central sensitization, and provides a better risk-benefit ratio.[43]
302 In addition, DEX probably produces peripheral analgesic effects by inhibiting the transmission of
303 nerve signals through the Aδ and C-fibers and stimulates the release of enkephalin-like
304 substances in the peripheral regions, although the specific analgesic pathway involved is still
305 unclear.[44] A previous study also reported that corticosteroids, as an adjuvant therapy, can
306 significantly prolong analgesia, decrease postoperative pain while the level of glycemia was only
307 slightly increased on the first postoperative day.[45] As a result, the postoperative analgesia time of
308 SAPB in our study was longer than that of previous studies. Consistent with the results of a
309 previous study, we also recorded rebound pain 24 h after surgery. The reason may be due to the
310 higher number of younger female patients recruited in this study who experienced more intense
311 pain after the analgesic effects of SAPB disappeared and an acute state of opioid-induced
312 tolerance and hyperalgesia.[46]

313 In our study, the time to first rescue analgesia was significantly longer and the rescue
314 analgesia requirement was significantly higher in the RD2 group, which had achieved superior
315 postoperative analgesia. However, there was no difference between the two groups with respect
316 to satisfaction scores of patients and surgeons. Though 10 mL of 2% lidocaine was administered
317 by subcutaneous infiltration into the parasternal and subclavicular areas at the end of the
318 operation, most postoperative rescue analgesia requirements were attributed to an incomplete
319 analgesia in the internal mammary area. USG-transversus thoracic muscle plane block (TTPB)

320 or parasternal intercostal block (PSI) was recently introduced to provide analgesia in the internal
321 mammary area, which cannot be completely blocked by SAPB.[47, 48]

322 Consistent with the results of a previous study, we did not record any complications
323 associated with SABP. The explanation may be that the targeted point of SAPB is superficial and
324 we also adopted real-time USG-SAPB to prevent misplacement of the needle tip in this trial.[40]
325 Fewer patients in our study experienced PONV than in a previous study, and the reason may be
326 due to treatment with a prophylactic antiemetic before the completion of surgery and the lower
327 consumption of opioids. [36] In addition, another previous study reported that DEX also reduced
328 the incidence of PONV by reducing the movement of the stomach and intestines, by inhibiting
329 glandular secretion, and by reducing opioid dosage.[29] Inconsistent with the results of a previous
330 study, we did not record any differences between the two groups with respect to chronic pain,
331 although the consumption of opioids was lower in the RD2 group. This finding can be explained
332 by our recruitment being limited to patients with axillary lymph node dissection, which is an
333 independent risk factor of chronic pain.[49]

334 Our study had several limitations. First, we did not design a sham group of local anesthetic
335 block with placebo injectate for ethical reasons. Second, we only recruited patients with ASA I–II,
336 although the recruitment of patients with obstructive sleep apnea maybe has been more
337 meaningful. Finally, a larger multicenter prospective randomized double blind study is needed to
338 verify the conclusions of this study.

Conclusion

Administration of 1 μg/kg dexmedetomidine and ropivacaine in USG-SAPB may provide superior postoperative analgesia for patients undergoing MRM without causing additional adverse effects.

Ethics approval, guidelines and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments, or with comparable ethical standards. Ethical approval was obtained from the Institutional Review Boards of Ordos Central Hospital and registered at Chinese Clinical Trial Registry (09/06/2020, ChiCTR2000033685). Written informed consent was obtained from patients before trial participation.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request

Competing interests

Not applicable

Funding

Not applicable

Authors' contributions

Caiping Duan, Zaijun Hao, Junling Yang, and Fei Song conceived and designed the trial; Xiujuan Fan analyzed the data; Caiping Duan, Junling Yang, Fei Song, and Ruizhen Li collected the data; and Caiping Duan, Zaijun Hao and Junling Yang wrote this paper

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508

509 ## Figure legends

510 Figure 1 Patient enrollment flow diagram.

511 Figure 2 Intraoperative hemodynamics.

512 Figure 3 Postoperative pain intensity between the two groups. *P<0.05 vs. group RD1.

513 Figure 4 Postoperative sufentanil consumption in both groups. *P<0.05 vs. group RD1.

514 Figure 5 The incidence of moderate-severe pain between the two groups.

515 Figure 6 Time to first rescue analgesia.

516

517

Figures

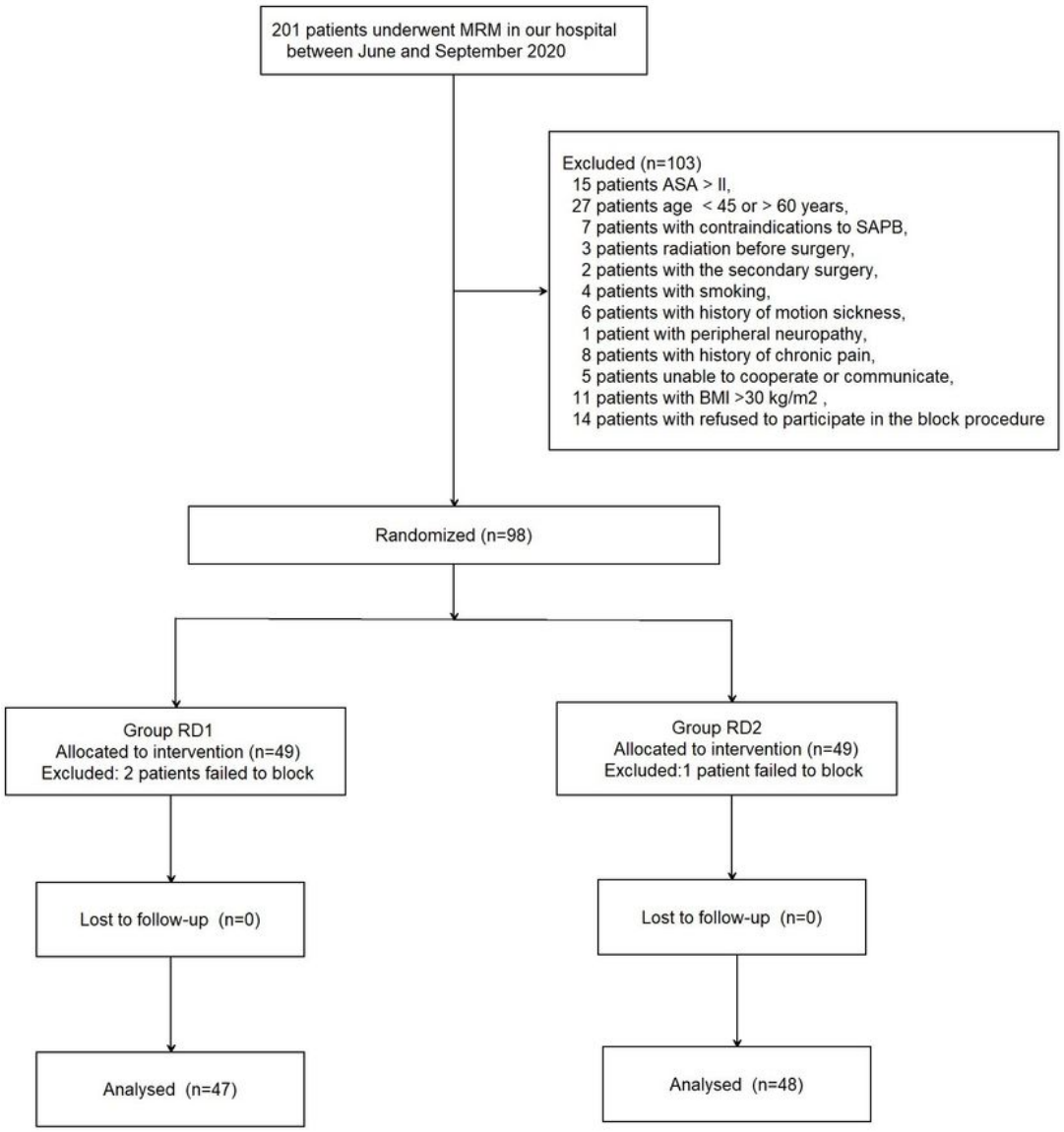
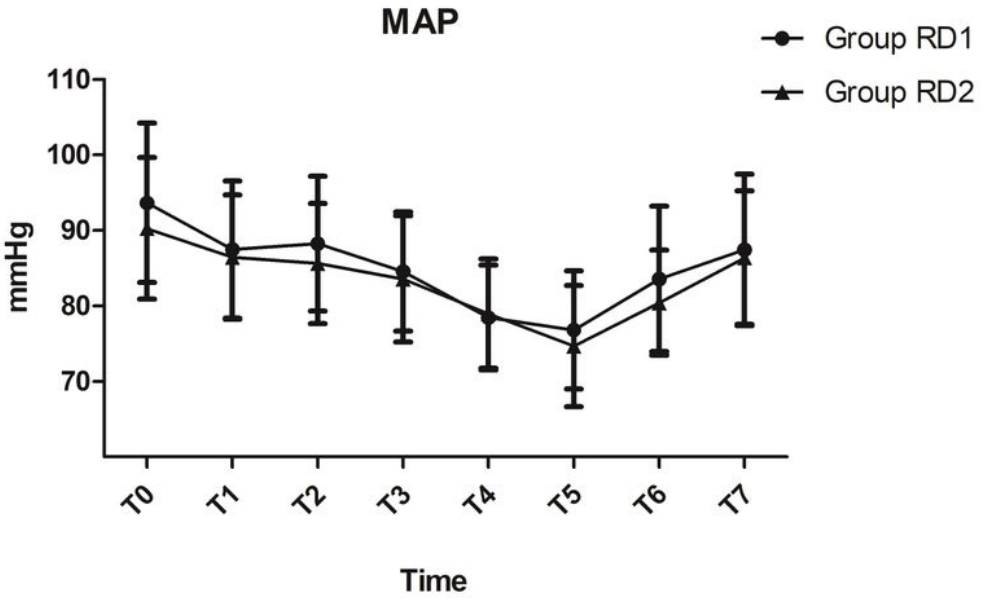


Figure 1

Patient enrollment flow diagram.



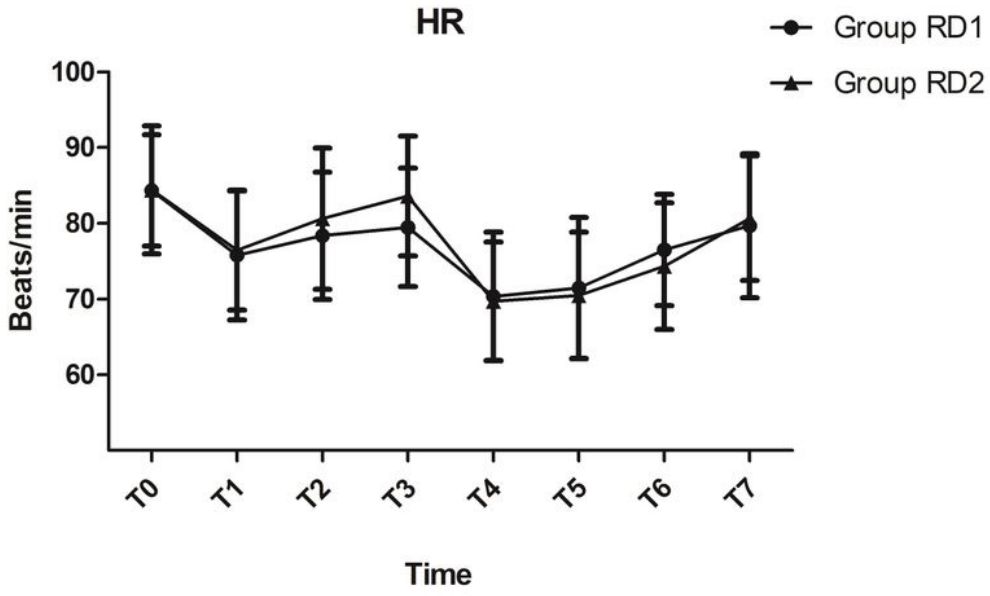


Figure 2

Intraoperative hemodynamics.

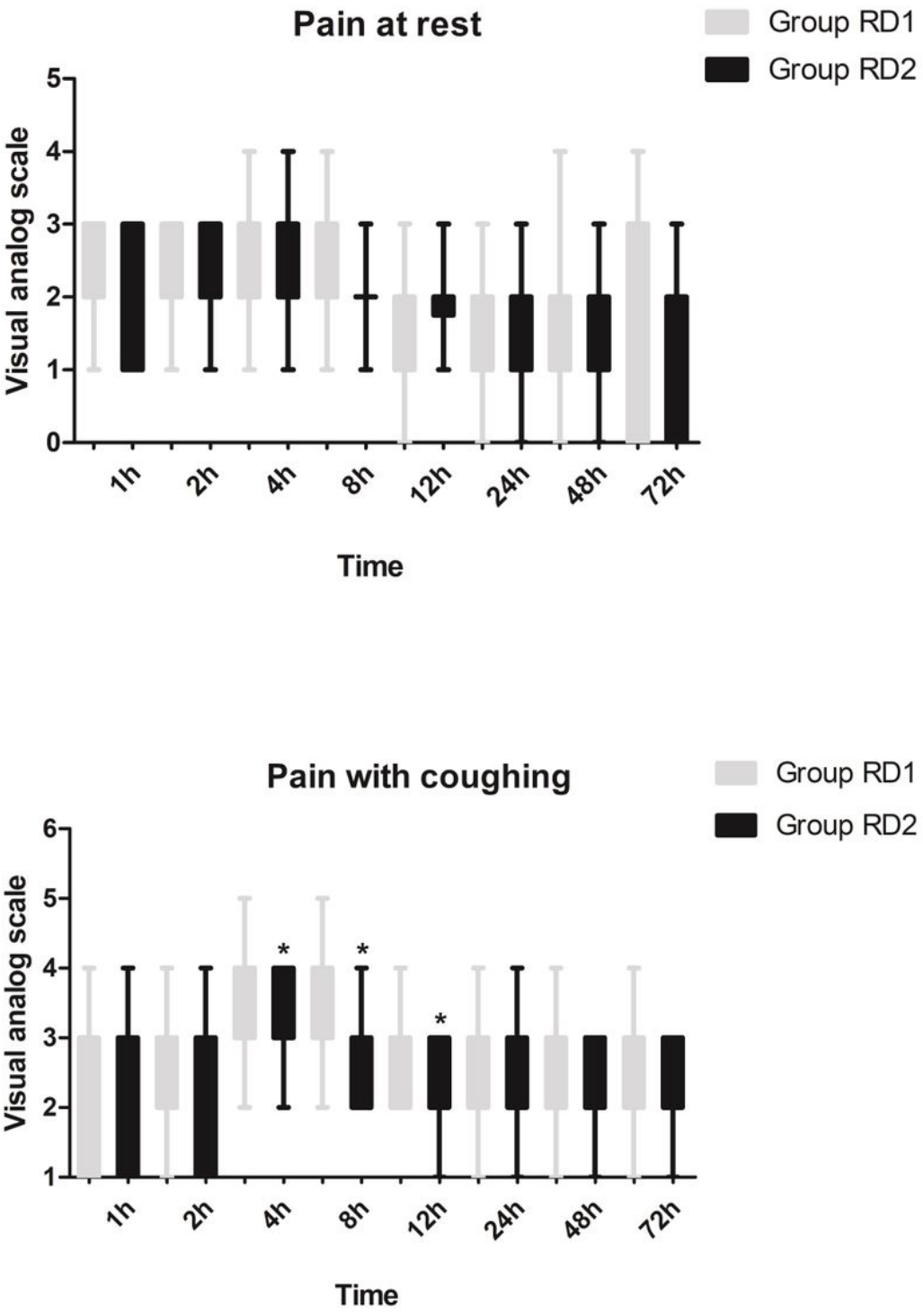


Figure 3

Postoperative pain intensity between the two groups. *P<0.05 vs. group RD1.

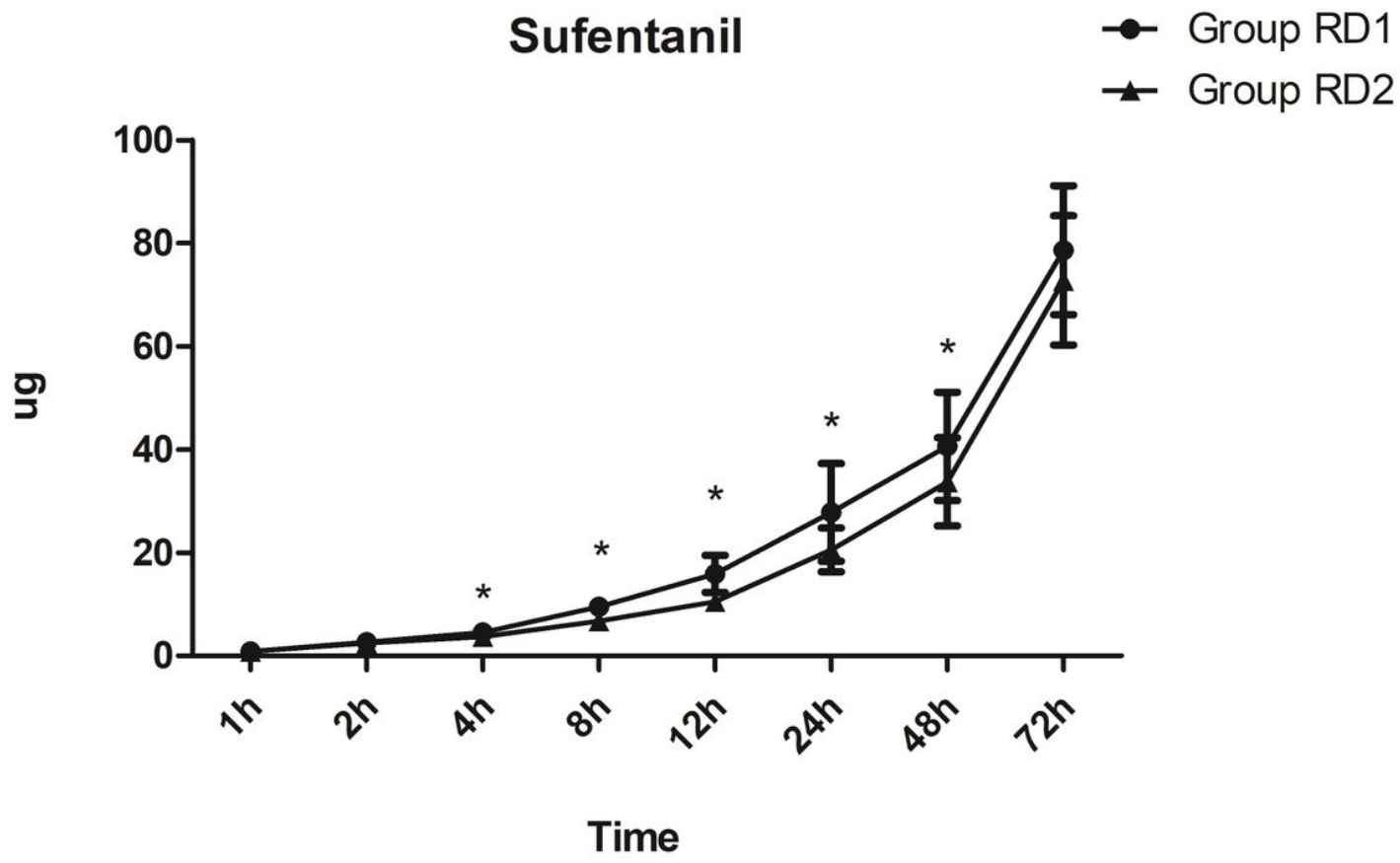


Figure 4

Postoperative sufentanil consumption in both groups. *P<0.05 vs. group RD1.

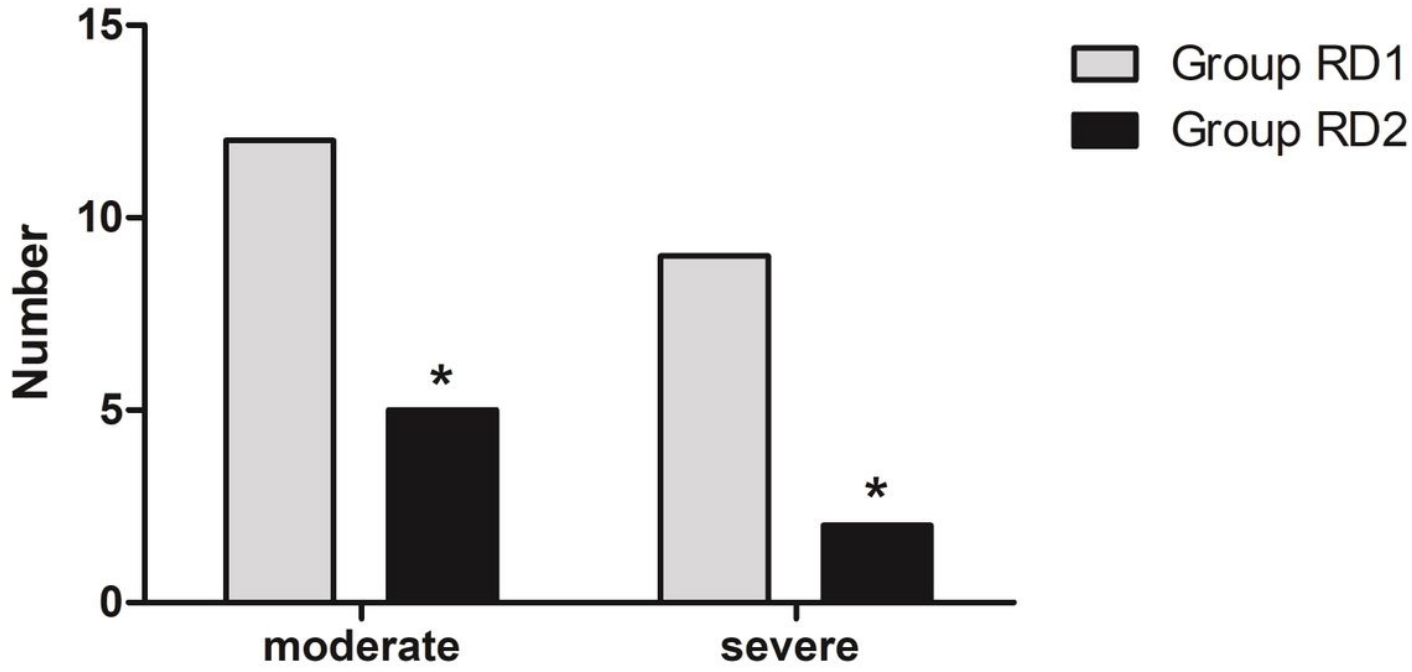


Figure 5

The incidence of moderate-severe pain between the two groups.

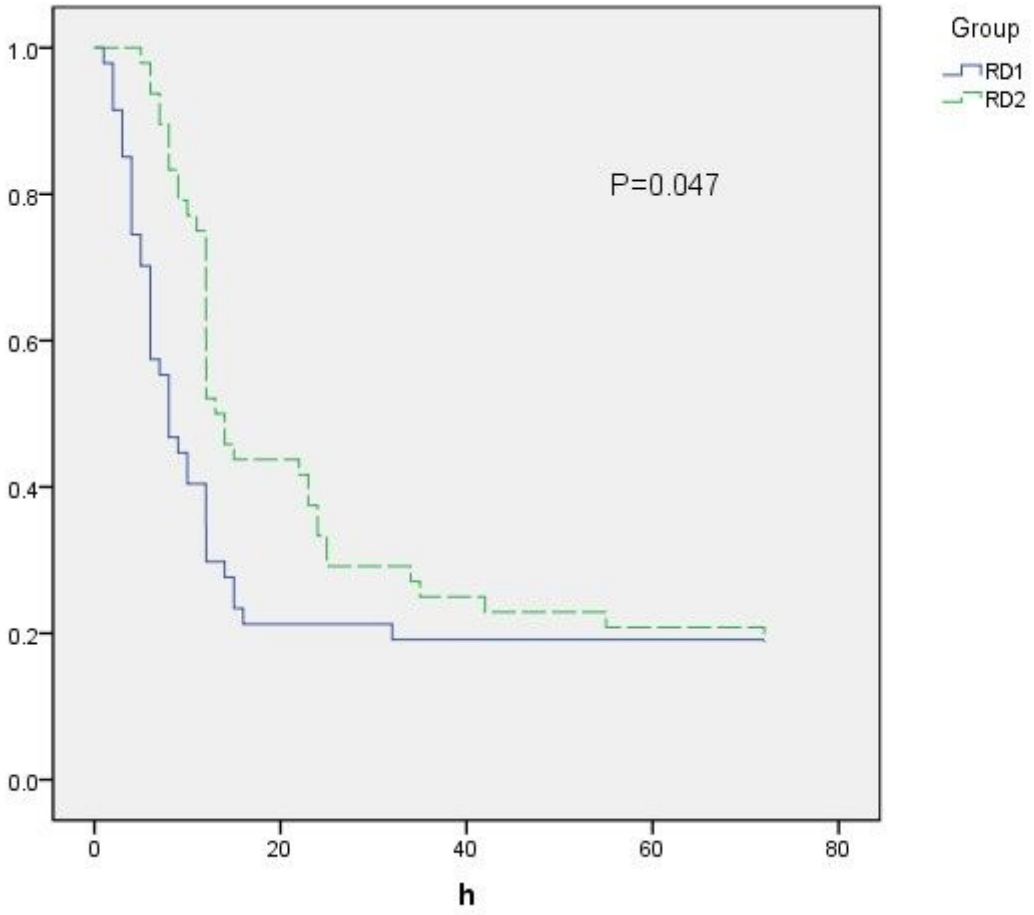


Figure 6

Time to first rescue analgesia.