Efficacy of ultrasound-guided rectus sheath block, butorphanol for single-incision laparoscopic cholecystectomy: A prospective, randomized, clinical trial

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Abstract

Background: Whether rectus sheath block (RSB) combined with butorphanol can relieve incisional pain and visceral pain in patients undergoing single-incision laparoscopic cholecystectomy (SILC) remains unknown. The goal of this study was to assess the efficacy of ultrasound-guided bilateral RSB, and butorphanol for postoperative analgesia in patients undergoing SILC.Methods: All patients who met the criteria were randomly divided into four groups: group I, (n=29) patient-controlled intravenous analgesia (PCIA) (sufentanil 1 μg/ml); group II, (n=29) PCIA (butorphanol 0. 08 μg/ml); group III, (n=29) ultrasound-guided RSB (ropivacaine 100 mg) combined with PCIA (sufentanil 1 μg/ml); and group IV, (n=29) ultrasound-guided RSB (ropivacaine 100 mg) combined with PCIA (butorphanol 0.08 μg/ml). General anesthesia in all groups, It's noteworthy that we only use general anesthesia, not ultrasound-guided RSB in group I and II. The primary outcome were numeric rating scale (NRS) scores (0-10) of incisional pain and visceral pain. Secondary outcomes were the dose of butorphanol and sufentanil, the number of PCIA presses, the length of hospital stay and the incidence of postoperative adverse events. Results: Both the rest and cough incisional pain scores were lower during the first 2, 6 and 12 h in group Ⅲ than in group I (P□0.05). Similarly, scores in group IV were significantly lower than those in group II (P□0.05). The NRS scores for visceral pain were lower in group II at 2, 6 and 12 h after surgery than in group I (P□0.05) and lower in group IV than in group Ⅲ (P□0.05). Patients in group I needed more butorphanol as a rescue analgesic for pain relief than did those in group III, and patients in group IV needed less butorphanol as a rescue analgesic for pain relief than did those in group II. From the above pairwise comparisons, it is clear that groups III and IV had lower NRS scores. Overall, ultrasound-guided RSB combined with PCIA (butorphanol 0. 08 μg/ml) performed the best. Conclusions: Ultrasound-guided RSB combined with butorphanol can provide sufficient pain treatment after SILC than can general anaesthesia combined with sufentanil.

Background

Currently, opioids are widely used for postoperative analgesia[1], and postoperative pain management has been suggested to be insufficient. On the one hand, opioids are associated with side effects, such as somnolence, postoperative nausea and vomiting (PONV), constipation, uroschesis,

pruritus and respiratory depression, resulting in delayed discharge[2-4]. On the other hand, even though opioid drugs are a primary choice for the management of patients experiencing severe visceral pain[5], these medications cannot produce adequate pain relief. To improve postoperative pain management, multimodal analgesic regimens that include regional block and non-steroidal anti-inflammatory drugs (NSAIDS) are increasingly used. Schleich first used rectus sheath block (RSB) in 1899 to provide muscle relaxation and analgesia[6]. Formerly, RSB was not extensively used because its non-visualization leads to a high incidence of complications, such as neurologic injury, inadvertent peritoneal injury, visceral trauma, and block failure. Nevertheless, with the introduction of ultrasound into regional anaesthesia practice, tissue planes, the bowel and the spread of local anaesthetics can be seen, which may decrease accidental puncture. RSB is mainly used for postoperative analgesia after abdominal surgery. Studies have shown that 10 ml of 0.5% ropivacaine is usually appropriate[7, 8]. Recently, an increasing number of studies have emphasized the clinical value of RSB for pain relief related to midline abdominal incisions and laparoscopic and umbilical surgery[9]. Visceral pain is a complex disorder, that can be caused by mechanical traction, dilation, spasm, inflammation and chemical stimulation. Some studies have suggested that butorphanol, a κ-agonist, produces profound visceral analgesia[10].

The efficacy of RSB has been reported for postoperative analgesia after SILC[11], but the study did not thoroughly examine postoperative pain by distinguishing between incisional pain and visceral pain. Accordingly, we decided to assess the efficiency of ultrasound-guided RSB with butorphanol for incisional pain and visceral pain in patients undergoing SILC .

Methods

Patients and study design

Patients undergoing elective SILC were enrolled in this study from February 2019 to April 2019 at the Affiliated Hospital of Nantong University. The inclusion criteria were as follows: male and female patients between 18 and 59 years of age with an American Society of Anesthesiology (ASA) score of I or II and a body mass index(BMI) of 18-30 kg/□. Patients with preexisting neuropathy, coagulopathy, local skin infection, hepatic, renal or cardiorespiratory failure, local anaesthetic allergy, pregnancy,

complications of gallstones with gallbladder perforation, diffuse peritonitis or acute pyogenic cholangitis were excluded. All patients were randomly allocated to four groups: group I, (n=29) patient-controlled intravenous analgesia (PCIA) (sufentanil 1 μg/ml); group II, (n=29) PCIA (butorphanol 0. 08 μg/ml); group III, (n=29) ultrasound-guided RSB (ropivacaine 100 mg) combined with PCIA (sufentanil 1 μg/ml); and group IV, (n=29) ultrasound-guided RSB (ropivacaine 100 mg) combined with PCIA (butorphanol 0.08 μg/ml).

The study was registered prospectively with the Chinese Clinical Trial Registry□reg no.ChiCTR1900020738) and approved by the ethics committee of Affiliated Hospital of Nantong University (approval number: 2018-K067), and written informed consent was obtained.

The primary outcome was NRS scores (0-10) of incisional pain at rest and during cough and visceral pain. Secondary outcomes were the dose of butorphanol and sufentanil, the number of PCIA presses, the length of hospital stay and the incidence of postoperative adverse events.

Randomization and blinding

All patients scheduled for elective, SILC were randomly divided into four groups using a computer-generated random sequence concealed in consecutively numbered, opaque, sealed envelopes, which were opened on the morning of surgery.

Anaesthesia

In all patients, anaesthesia was induced with intravenous midazolam 0.1 mg/kg, propofol 2 mg/kg, sufentanil 0.5 μg/kg and cisatracurium 0.15 mg/kg. Anaesthesia was maintained with an infusion of 10 mg/ml propofol at 4 mg/kg/h and 50 μg/ml remifentanil at 0.2 μg/kg/min. To ensure an adequate depth of anaesthesia, response entropy indexes were kept between 40 and 60 during the entire anaesthesia period by adjusting the rate of infusion of sufentanil and propofol.

After systemic anaesthesia was induced, in groups III and IV, the probe was transversely placed at the lateral level of the umbilicus. Using the in-plane technique, the needle was advanced until the posterior aspect of the rectus muscle was penetrated. No blood and no gas were drawn back; furthermore, a small volume of saline (□2 ml) was initially injected to ensure that the needle tip was correctly positioned. When the needle was located between the posterior rectus muscle and posterior

sheath, 20 ml of 0.5% ropivacaine was injected bilaterally (Figure 1).

Patients in groups II and IV received an intravenous infusion of 1 mg of butorphanol 30 min before the end of surgery. Those in groups I and III received an intravenous infusion of 10 μg of sufentanil 30 min before the end of surgery.

Vital signs, such as blood pressure, heart rate, oxygen saturation, and electrocardiogram pattern, were recorded during the operation. The operative duration, haemorrhage volume and consumption of remifentanil and propofol were also recorded.

PCIA with a bolus dose of 2 μg of sufentanil, a lock-out interval of 15 min and a maximum dose of 2 μg/h was used for routine analgesia in groups I and III. In groups II and IV, all patients received butorphanol PCIA at a background rate of 170 μg/h and a demand dose of 170 μg every 15 min as rescue analgesia for postoperative pain management. During a preoperative visit, patients were adequately informed about the concept of the NRS and trained how to use PCIA.

All patients were treated by the same experienced anaesthesiologist, who specialized in ultrasound-guided regional anaesthesia and did not participate in the postoperative data collection.

Assessment of postoperative pain and measurements

Postoperative pain after SILC is considered to arise from 2 main sources: incision site (incisional pain), visceral structures (visceral pain). The incisional pain was defined as superficial pain on the abdominal wall, the visceral pain was defined as pain inside the abdomen, which may be deep, dull, and more difficult to localize.

Primary outcome: In both groups, a blinded investigator who was not involved in patient recruitment or the anaesthesia procedure recorded the incisional pain at rest and during cough and the visceral pain using a NRS score (NRS; 0 =no pain; 10 =worst pain) at 2,6,12 and 24 h after the operation.

Secondary outcomes: PONV, somnolence, constipation, uroschesis, pruritus, and respiratory depression were separately assessed by a blinded observer. Butorphanol 1 mg was administered intravenously as rescue analgesia in patients with a NRS score□3 in all groups. The blinded observer recorded the doses of butorphanol and sufentanil and the number of PCIA presses.

Statistical analyses

Statistical analysis was performed using IBM SPSS 21. *Normality testing was performed using the Levene method. Continuous data (age, BMI, NRS scores, butorphanol consumption, sufentanil consumption in PCIA, duration of the operation, bleeding amount, length of stay, the numbers of PCIA presses,* frequency of analgesic request) *were presented as the mean ± standard deviation (SD) if they are normally distributed, otherwise, they will be presented as the mean and interquartile range; Categorical data (sex, ASA, adverse events) were expressed as frequency and analyzed by the chi-squared (χ2) test or Fisher exact test. The patient characteristics, duration of the operation, bleeding amount, length of stay, the numbers of PCIA presses,* frequency of analgesic request *were compared among the four groups by* one-way ANOVA□after the equal check of variance, two-two comparisons among the means were done by LSD method. *NRS scores of incisional or visceral pain* use the means of LSD or Tamhane's T2 test for unequal variances. *P□0.05 was considered statistically significant. Power Analysis and Sample Size (PASS) software (NCSS, LLC, Kaysville, UT, USA) was used for the* power *calculation. An α=0.05, n□29, and* absolute NRS reduction of 1 *were used to calculate the sample size,* after many operations, we find that the power value is above 97%. *Thus, 116 patients (29 in each group) met our experimental needs.*

Results

Patients

The study flow diagram is presented in Figure 2. A total of 128 participants (64 males, 52 females) were recruited into the study; eleven of them were excluded from the study, including six patients due to complications involving gallstones with gallbladder perforation during surgery, three patients due to BMI□30 kg/□, and two patients because of age□59. Other patients met the inclusion criteria. Individual characteristics of patients are expressed in Table 1. There were no significant differences.

Table 1**.** Patient Characteristics

	GroupⅠ(n=29)	GroupⅡ(n=29)	Group Ⅲ (n=29)	Group Ⅳ (n=29)	P-value
Age, mean±SD, y	37.2±10.9	39.3±10.5	38.8±11.4	41.5±11.4	0.521
Sex, no. male/no. female	17/12	15/14	16/13	16/13	0.964
BMI, mean±SD, kg/□	23.9±3.31	24.0±3.52	24.8±3.18	23.6±3.13	0.521
ASA Ⅰ / Ⅱ, n	19/10	16/13	15/14	14/15	0.582

The four groups showed no statistically significant differences in patients' characteristics.

BMI, body mass index; ASA, American Society of Anesthesiologists.

Postoperative pain

There were no significant differences in the time needed for the block procedure or the quality of ultrasound images. By comparisons between groups III and I, we found that the NRS score of incisional pain was lower during the first 2, 6 and 12 h in group III than in group I at rest and during cough (2.41±1.05 vs 3.83±1.28, P□0.05; 1.93±1.00 vs 2.79±1.11, P□0.05; 1.72±0.70 vs 2.38±1.05, P □0.05; 4.03±0.87 vs 4.97±1.38, P□0.05; 3.55±0.69 vs 4.28±1.07, P□0.05; 3.38±0.68 vs 4.14±1.25, P □0.05), in the meantime, the score was significantly lower in group IV than in group II (2.03±0.98 vs 3.90±1.29, P□0.05; 1.83±0.89 vs 2.76±0.99, P□0.05; 1.41±0.50 vs 2.10±1.14, P□0.05; 3.83±1.00 vs 5.07±1.33, P□0.05; 3.41±0.91 vs 4.17±1.10, P□0.05; 3.07±0.70 vs 3.83±1.07, P□0.05). From the above pairwise comparisons, it is clear that groups III and IV had lower NRS scores. The NRS scores of visceral pain were lower in group II at 2,6 and 12 h after surgery than in group I (3.90±1.14 vs 5.21±1.21, P□0.05; 3.69±0.93 vs 5.28±1.07, P□0.05; 3.38±0.82 vs 4.55±1.33, P□0.05) and lower in group IV than in group III (3.97±1.12 vs 4.97±1.38, P□0.05; 3.90±1.14 vs 5.03±1.18, P□0.05; 3.41±0.91 vs 4.00±0.96, P□0.05). From the above pairwise comparisons, it is clear that groups II and IV had lower NRS scores. Patients in group I needed more butorphanol as a rescue analgesic for pain relief than did those in group III (5.57±0.81 vs 2.45±0.99, P□0.05). Similarly, the required dose in group IV was less than that in group II (4.90±2.02 vs 5.17±1.07, P□0.05). The patients who were treated with less sufentanil in groups II and IV experienced less PONV. Overall, ultrasound-guided RSB combined with PCIA (butorphanol 0.08 μg/ml) performed the best.

Table 2.1 NRS scores of incisional pain at several time points

	Time point	GroupⅠ(n=29)	Group Ⅲ (n=29)	P-value (group Ⅰvs Ⅲ)	GroupⅡ(n=29)	Group Ⅳ(n=29)	P-value(group Ⅱvs Ⅳ)
At rest	2h	3.83±1.28	2.41±1.05	0.000*	3.90±1.29	2.03±0.98	0.000*
	6h	2.79±1.11	1.93±1.00	0.001*	2.76±0.99	1.83±0.89	0.001*
	12h	2.38±1.05	1.72±0.70	0.044**	2.10±1.14	1.41±0.50	0.030**
	24h	2.03±0.82	1.83±0.85	0.345*	1.86±0.88	1.62±0.78	0.271*
During cough	2h	4.97±1.38	4.03±0.87	0.003*	5.07±1.33	3.83±1.00	0.000*
	6h	4.28±1.07	3.55±0.69	0.005*	4.17±1.10	3.41±0.91	0.003*
	12h	4.14±1.25	3.38±0.68	0.036**	3.83±1.07	3.07±0.70	0.015**
	24h	3.66±0.97	3.38±0.78	0.258*	3.55±1.09	3.48±0.83	0.777*

All data are expressed as the mean±SD.

*P-value were calculated by LSD.

**P-value were calculated by Tamhane’s T2 test.

Table 2.2 NRS scores of visceral pain at several time points

	Time point	GroupⅠ(n=29)	GroupⅡ(n=29)	#P-value(group Ⅰvs Ⅱ)	Group Ⅲ (n=29)	Group Ⅳ(n=29)	#P-value(group Ⅲvs Ⅳ)
Visceral pain	2h	5.21±1.21	3.90±1.14	0.000	4.97±1.38	3.97±1.12	0.002
	6h	5.28±1.07	3.69±0.93	0.000	5.03±1.18	3.90±1.14	0.000
	12h	4.55±1.33	3.38±0.82	0.000	4.00±0.96	3.41±0.91	0.031
	24h	2.72±0.88	2.55±0.74	0.425	2.66±0.86	2.28±0.80	0.081

All data are expressed as the mean±SD.

#P-value were calculated by LSD.

Table 3 Cumulative butorphanol and sufentanil consumption

	group I (n=29)	group II (n=29)	group Ⅲ (n=29)	group Ⅳ (n=29)	P-value
Butorphanol consumption (mg)	5.57±0.81*	5.17±1.07#	2.45±0.99	4.90±2.02	0.000
Sufentanil consumption in PCIA (ug)	84.8±11.0	/	70.6±17.0	/	0.000

* P□0.000 compared to group Ⅲ, # P□0.000 compared to group Ⅳ.

Table 4 Comparison of postoperative outcomes

	GroupⅠ(n=29)	GroupⅡ(n=29)	Group Ⅲ (n=29)	Group Ⅳ (n=29)	P-value
Duration of the operation (min)	59.4±11.3	61.4±10.8	62.2±9.86	61.7±11.0	0.785
Bleeding amount (ml)	16.8±5.42	14.2±5.54	13.9±4.66	15.1±5.15	0.138
Length of stay (days)	4.62±1.29	3.97±0.94	3.28±0.84	2.24±0.69	0.000
The numbers of PCIA presses(n)	3.55±1.09	2.79±0.90	1.59±1.21	0.52±0.74	0.000
Frequency of analgesic request (n)	2.45±0.99	1.45±0.91	1.17±0.80	0.38±0.56	0.000

The data are expressed as the mean±SD.

Table 5 Adverse events during the first 24 h after surgery.

	GroupⅠ(n=29)	GroupⅡ(n=29)	Group Ⅲ (n=29)	Group Ⅳ(n=29)	p-value
PONV	21 (72.4□	6 (20.7)	13 (44.8)	3 (10.3)	0.000
Constipation,	3 (10.3□	1 (3.4□	0 (0.0□	0 (0.0□	0.632
Uroschesis	5 (17.2□	0 (0.0)	1 (3.45)	2 (6.90)	0.057
Somnolence	11 (37.9)	8 (27.6)	5 (17.2)	3 (10.3)	0.069
Pruritus	1 (3.45)	0 (0.0)	1 (3.45)	0 (0.0)	0.565
Respiratory depression	1 (3.45)	0 (0.0)	0 (0.0)	0 (0.0)	0.388

Values are the number of patients (%). PONV: postoperative nausea and vomiting

Discussion

Cholecystolithiasis is a common and frequently occurring disease. Laparoscopic cholecystectomy is the “gold standard” for treating cholecystolithiasis. Nevertheless, Progression to minimally invasive surgery has occurred from open surgery to laparoscopic surgery, single-incision surgery and robotic surgery, and surgeons have embraced the concepts of less invasiveness, less pain, earlier recovery, and shorter operations. Compared with laparoscopic cholecystectomy, single-incision laparoscopic cholecystectomy (SILC) has an outstanding cosmetic effect[12]. SILC is becoming increasingly popular[13].SILC involves only a 2-cm incision into the umbilicus between the T7 and T11 intercostal nerves[14]. RSB mainly blocks the sheath nerve plexus between the rectus abdominis and posterior sheath of the rectus muscles, which is dominated by the ventral rami of the 6th to 11th intercostal nerves, providing analgesia for the peritoneum, muscle and skin involved in anterior abdominal wall incisions[6]. In the post-anaesthesia care unit (PACU), we found that the range of sensory blockade was measured as a circular area with a radius of 5 cm centred on the umbilicus. RSB covers all the nerves that innervate the umbilicus, provides pre-emptive analgesia and avoids central sensitization

caused by nociceptive stimuli before surgery[15, 16]. According to our data, RSB in these patients resulted in low incisional pain scores at rest and during movement at 2, 6 and 12 h after surgery, which shows that RSB can effectively relieve incisional pain in patients. There were no marked differences about incisional pain at 24 h after SILC among the four groups, perhaps because the efficacy of ropivacaine wears off after 12 h. The sufentanil consumption and number of PCIA presses in group III were lower than those in group I. Theoretically, RSB block should provide excellent analgesia for the abdominal wall, but unfortunately, visceral pain was still evident in groups I and III. By limiting postoperative opioid use in groups II and IV, patients have fewer adverse biological reactions, but have a poor effect on visceral pain.

Visceral pain is mainly transmitted by unmyelinated C fibres, is a complex sensory experience caused by trauma and inflammation, and is generally described as dull, diffuse and poorly localized[5]. Visceral pain is difficult to manage effectively, largely because the visceral sensory mechanisms and factors that contribute to the pathogenesis of visceral pain are poorly understood[17]. Visceral hyperalgesia and central sensitization have been suggested to be part of the pathophysiology[18]. At present, some studies have shown that the management of visceral pain can be achieved by activating κ-receptors[19, 20]. Opioids have been reported to have a small effect on visceral pain[5], which agrees with our data: the NRS scores of visceral pain were lower in group II at 2, 6 h after surgery than in group I and lower in group IV than in group III. Butorphanol, a mixed agonist-antagonist opioid, induces analgesia by opioid pathways[10]. Some studies have shown that butorphanol relieves visceral pain by indirectly suppressing cyclooxygenase activity and thus preventing prostaglandin formation in response to injury[5, 15]. In addition, the main metabolite of butorphanol activates K-receptors and has dual effects of excitation and antagonism on μ-receptors. In contrast to μ-receptor agonists; (such as sufentanil), which cause side effects, such as respiratory depression, nausea and vomiting, butorphanol alleviated pruritus, and the incidence of side effects was low [10].

Compared with other methods, RSB and butorphanol are useful for multimodal postoperative pain management in SILC patients. This combination also facilitates earlier mobilization and discharge and

follows the trend of enhanced recovery after surgery (ERAS). Indeed, analgesia management has a far-reaching impact on the perioperative period.

limitations

Like all research, there are a number of limitations to this study. First, this study did not examine whether prolonged postoperative analgesia could be achieved with continuous infusion through rectus sheath catheter placement, Second, we did not study the optimal volume or dose of RSB as a postoperative analgesic method for SILC patients. Third, The sample size used in the experiment is limited, so it may not be able to make a definite answer to these questions, but according to the existing results, we can draw a preliminary conclusion, which needs to be further increased for further study.

Conclusions

Our results suggest that ultrasound-guided RSB combined with butorphanol can significantly relieve postoperative incisional and visceral pain in patients undergoing SILC. Adding adjuvants to prolong the duration of local anaesthesia should be considered for in-depth study.

Abbreviations

RSB: rectus sheath block; SILC: single-incision laparoscopic cholecystectomy; PCIA: patient controlled intravenous analgesia; NRS: numeric rating scale; PONV: postoperative nausea and vomiting; NSAIDS: non-steroidal anti-inflammatory drugs; ASA: American Society of Anesthesiology; BMI: body mass index; ERAS: enhanced recovery after surgery

Declarations

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Authors’ contributions

HMF carried out the studies, and drafted the manuscript. CCZ performed the statistical analysis and helped to collect the data. XGX and YTG helped to revise the manuscript. All authors read and approved the final manuscript.

Availability of data and materials

All necessary data supporting our findings have been presented within the manuscript. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Approval for this study was obtained from the ethics committee of the Affiliated Hospital of Nantong University (approval number: 2018-K067), and each patient provided a written informed consent.

Consent for publication

Not applicable

Competing interests

The authors declare that we have no competing interests.

Statement

The study adheres to CONSORT guidelines.

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Figures

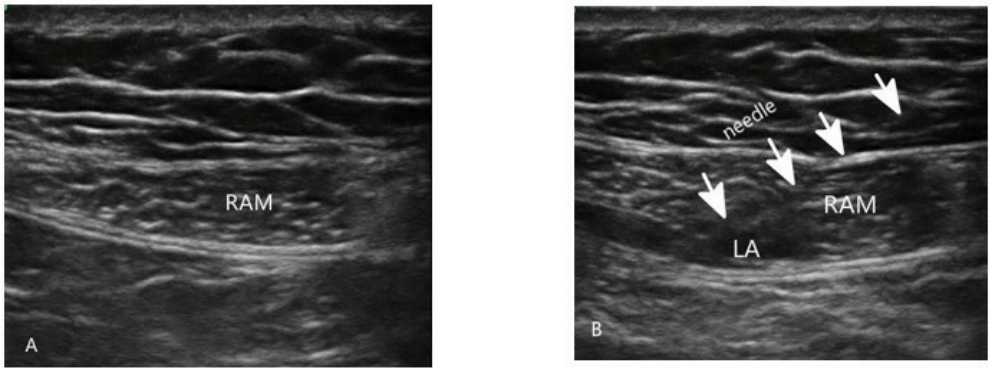

Figure 1

Ultrasound images (a) before and (b) after rectus sheath block RAM, rectus abdominal muscle, LA, local anaesthetic

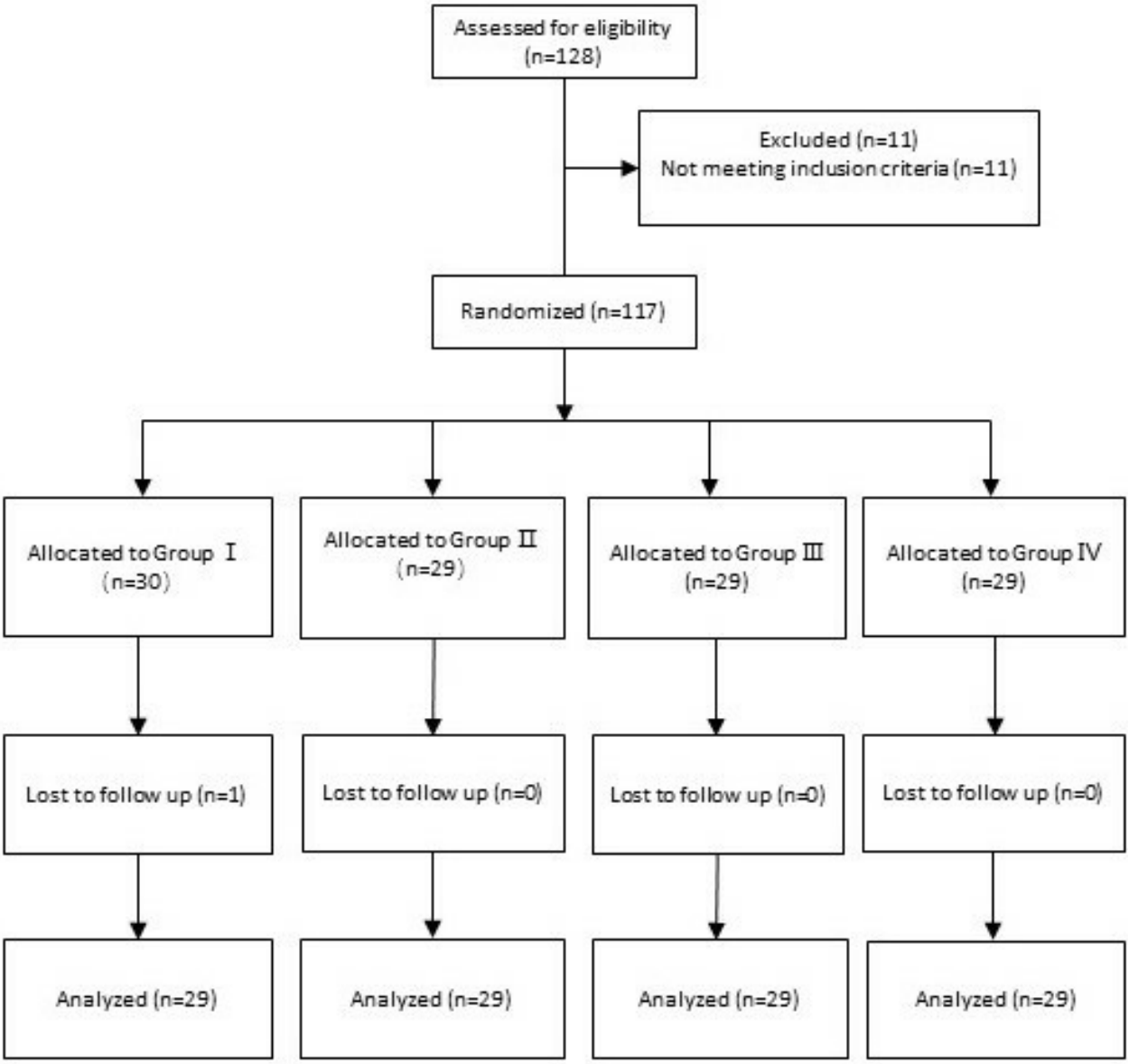

Figure 2

Flow chart of the study

Supplementary Files

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

CONSORT 2010 Checklist.doc
experimental data.xlsx