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Evaluating the efficacy of opioid-sparing analgesic protocols in postoperative pain management for major trauma surgeries

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Abstract: This randomized, controlled trial evaluated the efficacy of opioid-sparing analgesic protocols in postoperative pain management for major trauma surgeries. A total of 120 patients were randomly assigned to either an opioid-sparing group or a conventional opioid-based group (n = 60 per group). Primary outcomes included pain severity, opioid use, and postoperative mobilization. The opioid-sparing group reported significantly lower pain scores at all time points ($p < 0.0001$) and lower sedation levels ($p < 0.0001$). Total opioid consumption was significantly reduced ($p < 0.0001$): and fewer rescue medications were required ($p < 0.0001$). Functional recovery was faster ($p < 0.0001$): patient satisfaction was higher ($p < 0.0001$), and length of hospital stay was shorter ($p < 0.0001$). At 6-month follow-up, the incidence of chronic pain was lower in the opioid-sparing group (2% vs 8%): and quality of life scores were higher ($p < 0.0001$). Additional multiple regression analysis determined the various predictors affecting long-term recovery results. These findings support the effectiveness of multimodal opioid-sparing strategies in enhancing recovery and reducing opioid-related complications after major trauma surgeries.

Keywords: Opioid sparing, surgical pain, trauma, recovery, quality of life

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INTRODUCTION

Delivering adequate pain management to patients with major trauma surgery is still a clinical problem due to its complexity, especially taking into account increased attention to opioid-related side effects and possible development of dependency. In caring for patients, traditional opioid based interventions although effective in providing acute pain relief was known to have undesirable side effects which includes however respiratory depression, constipation, sedation and potential long-term dependency (Altschul *et al*., 2017; Antman., 2017). Due to the opioid crisis, there has been growing concern in opioid's replacement in postoperative pain management known as opioid-sparing analgesic protocols (Artime *et al*., 2018; Bally *et al*., 2017).

A multimodal approach employs used non-opioid medicines and methods of analgesia that act on distinct pain pathways which may help improve pain management and rigorously minify the use of opioids (Austin *et al*., 2014; Ban *et al*., 2019). A number of drugs including acetaminophen, NSAIDs, gabapentinoids, regional anaesthetic techniques have been documented to reduce intensity of pain without the risks associated with opioid use (Bauer *et al*., 2010; de Boer *et al*., 2017). This approach is consistent with the enhanced recovery after surgery (ERAS) principles, where opioid sparing strategies are encourage to enhance the recovery period and reduce the hospital duration (Beales *et al*., 2018; Calcaterra S *et al*., 2016). The use of non-opioid drugs may also have less negative effects and hasten the postoperative phase so patients will receive better quality of treatment (Bernardo *et al*., 2017; Dunn *et al*., 2016).

One of the key parts of opioid reduction measures is the application of regional anaesthesia, which being effective in pain relief, at the same time spares function. A peripheral nerve block or neuraxial block has potential in the management of postoperative pain in trauma patients because it reduces opioid use and improves functional outcomes (Boddu *et al*., 2018). In the review of postoperative pain management intervention after orthopedic trauma surgeries, nerve block patients had lesser postoperative' pain scores and opioids use compared to patients on opioids-only regimen (Firriolo *et al*., 2018; Gabriel *et al*., 2019). Also, it is well established that nerve blocks decrease length of stay as patients can walk and gain their function faster (Gobble *et al*., 2014, Hah *et al*., 2017). On the feasibility of opioid-sparing analgesia in the setting of trauma surgery, existing findings on its cost-effectiveness similarly remain endorsed, based on decreased opioid-induced complications and shorter lengths of stay (Horsley *et al*., 2019; Kim *et al*., 2015). In this way, it is possible to make the effective use of opioid while at the same time fighting the opioid epidemic hence the development of opioid-sparing protocols (Lillemäe *et al*., 2017).

Recent studies support the idea that the use of two or more agents acting in various pain pathways to eliminate pain, with little dependence on opioids (Martinez *et al*., 2017;

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Sheldon *et al*., 2020). Examples are the spiralling effect of mixing acetaminophen with NSAIDs to decrease pain and opioids utilization in traumatology patients therefore expediting mobility and recovery (Shimony *et al*., 2016; Sivakumar *et al*., 2018). However, gabapentinoids which are used in treating neuropathic pain has been incorporated into opioid-minimisation regimens for managing postoperative pain with good results (Staffa *et al*., 2018; Teerawattananon *et al*., 2017). They also decrease pain while also enabling patients to have fewer of the side effects related to opioids, which could be significant in elderly traumatology patients who are often more vulnerable to opioids (Tsaousi *et al*., 2017; Ulm *et al*., 2018).

However, there are some limitations indicated in opioid-sparing interventions: the necessity for significant developments in opioid-sparing protocol enhancement during various surgeries and for different patient categories; Furthermore, additional researches are required to guarantee the effectiveness of opioid-sparing protocols across different operations and for diverse patients (Vacas *et al*., 2017; Zhuang *et al*., 2020). Subsequently, with the ongoing development of patient individualization in pain management, the incorporation of the patient-related aspects into multiple modality analgesia intervention regimens may even enhance the effective control of postoperative pain (Zhuang *et al*., 2020).

The systematic use of opioid-sparing analgesic regimens has been identified as an important step toward improved postoperative pain control for major trauma surgeries. In doing so, they provide a framework for moving toward the development of safer methods of acute pain control in accordance with the vision of enhancing patient reported outcomes and stemming the opioid crisis. Future research studies that try to follow patients over a more extended period or solicited, subjective accounts will be useful in supporting that such protocols' effectiveness can be replicated and generalized to other types of surgery (Zhuang *et al*., 2020). With time and updating of such strategies, opioid sparing might be the norm for trauma surgical procedures, thus improving the general outcome and satisfaction of patients

MATERIALS AND METHODS

Study design and setting

The present randomized controlled trial was conducted in a tertiary care hospital to compare the opioid sparing analgesic regimen in managing the post-operative pain occurring after major trauma surgery. This study was approved by the Ethics Committee of Shulan (Hangzhou) Hospital Affiliated to Zhejiang Shuren University Shulan International Medical College (Approval No. SHZSU-EC-2023-028, dated March 1, 2023). The study adhered to the principles of the Declaration of Helsinki. All participants provided written informed consent prior to enrollment. This study was designed and reported in accordance with the CONSORT (Consolidated Standards of Reporting Trials) 2010 guidelines for randomized controlled trials.

Major trauma surgery patients of 120 patients were recruited. The participants were selected from adult patients, aged between 18-65 years, of both sexes, and free from significant comorbid conditions which can make them ASA I-III. The exclusion criteria were: Patients who took opioids for pain complains, those who had chronic pain disorders, severe hepatic or renal diseases, or allergy to any of the study drugs. Various data sources included staff observations in chart forms of nursing staff and completed and signed by the trained nursing staff specific standardized forms containing the pain scores, opioids intake, sedation levels, reported adverse events, and the patients' functional status. All the patients' information were removed, and compliance to the prescribed analgesic regimen was observed and recorded.

Participants were randomized into two groups of 60 each:

- ***Opioid-sparing protocol group***

This group was started on a mixture of acetaminophen, nonsteroidal anti-inflammatory drugs NSAIDs and supplementary drugs like gabapentin and dexmedetomidine to reduce the amount of opioid use.

- ***Conventional opioid-based protocol group***

This group was given conventional opioid-based analgesia, dose being adjusted depending on the pain scores post operation.

Sample selection randomization was done using the computer-generated randomization sequence and allocation concealment was done using the sealed opaque envelopes.

Inclusion and exclusion criteria

The inclusion criteria were carefully selected to ensure homogeneity of the study population and minimize confounding variables. Adult patients aged 18-65 years were chosen to reflect the most common demographic undergoing major trauma surgeries while excluding elderly patients who may have altered pharmacokinetics or multiple comorbidities. The ASA physical status I-III was used to focus on patients who could safely tolerate both opioid-sparing and conventional pain protocols. Exclusion of patients with chronic pain disorders or prior opioid use was essential to avoid opioid tolerance or altered pain perception influencing outcomes. Likewise, patients with significant hepatic or renal impairment were excluded to prevent variability in drug metabolism and clearance, which could confound safety and efficacy results. These criteria helped maintain internal validity while allowing for real-world applicability across a standard trauma surgery population.

Intervention protocols

Opioid-Sparing protocol

The opioid-sparing group received prolonged postoperative local infiltration with a combination of analgesic agents in an attempt to minimize opioid requirement. Intravenous acetaminophen was given at a dose of 1 gram every 6 hours for the first 48 postoperative hours. Apart from acetaminophen, patients in this group also received NSAID such as [for example, Ketorolac 30 mg IV] every 6 h to improve pain relief based on non-opioid axis. Neuropathic pain medication, gabapentin was administered orally at a dose of 300 mg prior to surgery and subsequently for 48 postoperative hours. For further augmentation of postoperative analgesia and to minimize the use of opioid agents, study patients received dexmedetomidine infusion at 0.2–0.5 mcg/kg/hr within the first 24 hours after the surgery. In cases where pain intensity as measured on the NRS pain diary was >5 an IV bolus morphine was given as a rescue dose to guarantee optimal analgesia.

Pain intensity was assessed using the 11-point Numerical Rating Scale (NRS): a widely validated and reliable tool for evaluating subjective pain experiences in clinical and surgical settings. The scale ranges from 0 to 10, where:

- 0 indicates no pain
- 1–3 represents mild pain
- 4–6 indicates moderate pain
- 7–10 reflects severe pain

Patients were asked to verbally rate their current level of pain at standardized postoperative intervals (1, 6, 12, 24, and 48 hours after surgery) by selecting a number that best represented the intensity of their pain. These ratings were recorded by trained nursing staff using structured pain assessment forms. To ensure understanding, each patient received a preoperative explanation of how to use the NRS, and visual aids (NRS cards) were provided when needed. The NRS was chosen due to its simplicity, ease of use in both literate and illiterate populations, and strong correlation with other validated pain scales like the Visual Analogue Scale (VAS) and Verbal Descriptor Scale (VDS). Additionally, the NRS allows for sensitive tracking of pain trends over time, which was crucial for comparing the efficacy of opioid-sparing versus conventional analgesic protocols.

Conventional opioid-based protocol convducted among post-operative patients

Patients in the control group have been given an opioid predominant treatment and morphine was used as the main analgesic agent. Morphine 2-4mg was given intravenously and repeatedly depending on the NRS until its score decreased to below 5. Average dosages of morphine were titrated as required, every 4 - 6 hours in response to varying changed pain levels. Also, patients in this group received adjunct acetaminophen 1000 mg IV every 8 hours in the first 24 hours after surgery for the purpose of the opioid sparing and addition of better analgesia to the opioid regimen.

Outcome measures

Primary outcomes

Primary outcomes were related to the assessment of the impact of the identified pain management protocols. The degree of pain was the principal variable, to be evaluated using the NRS at some time points: 1, 6, and 12 hours, 1 day, and 2 days after the operation. The second marker was the overall amount of opioids taken, expressed as the total amount of morphine equivalents (mg) taken in the initial 48 postoperative hours. The study also recorded the time to first rescue opioid time to the first postoperative requirement for further pain relief other than the study drug. To assess functional recovery the Modified Rankin Scale, MRS was calculated on the first and third postoperative days with description remains of patient mobility and possibility of everyday movement and activity.

Secondary outcomes

Secondary objectives included other features of patients' recovery process and treatment satisfaction. Opioid related AE's were defined and thereafter followed up; these included nausea, vomiting, pruritus, respiratory depression, and constipation. Pain control satisfaction by patients was assessed at the time of discharge using the Likert scale of 1-5. The recovery speed was evaluated by a number of days that a patient stayed in the hospital after the surgery. The QoR-15 was used again to assess Quality of recovery on postoperative days 1 and 3, 5 and 7, 10; and measures comfort, person's emotional states and their perceived level of independence. Choice of sedation: Postoperative sedation status was assessed at 6, 12, 24 hours using Ramsay Sedation Scale (RSS). Finally, the long-term incidence of chronic pain was evaluated using follow-up visits at 1, 3 and 6, 9 and 12 months postoperatively using the Brief Pain Inventory (BPI) to identify the development of long-term pain.

The questionnaires and scales used in this study were selected based on their established validity and reliability in clinical pain research. Tools such as the Numerical Rating Scale (NRS) for pain, Ramsay Sedation Scale (RSS) for sedation levels, Modified Rankin Scale (MRS) for functional recovery, QoR-15 for quality of recovery, Brief Pain Inventory (BPI) for chronic pain assessment, and a 5-point Likert scale for patient satisfaction were employed.

These instruments were not developed de novo but were drawn from well-validated sources in pain and perioperative literature. Prior to deployment, all healthcare professionals involved in data collection received standardized training to ensure consistency and reduce inter-observer variability.

Patients were not stratified into predefined levels before treatment; rather, these tools were used to quantitatively assess their condition at baseline and across postoperative time points. For example:

- NRS scores stratified pain into mild (0-3): moderate (4-6): and severe (7-10).
- QoR-15 was scored out of 150 and patients were categorized based on percentiles into low (<60%): moderate (60-80%): and high (>80%) quality of recovery.
- MRS scores (0-6) were used to measure postoperative disability over time.

These scores allowed continuous assessment rather than static stratification, enabling the team to monitor patient trajectories and detect statistically and clinically significant differences between the two study groups.

STATISTICAL ANALYSIS

The statistical analysis was conducted with a comprehensive approach using SPSS version 25.0. Independent t-tests and Mann-Whitney U tests were used to compare continuous variables, while Chi-square tests assessed categorical variables. The consistently significant p-values ($p < 0.0001$) across multiple primary and secondary outcomes reinforce the robustness of the findings. To further ensure reliability, Kaplan-Meier survival analysis was employed to assess time-dependent variables such as time to first rescue opioid and length of hospital stay, revealing significant differences favoring the opioid-sparing group. Moreover, the use of multiple linear regression analysis allowed identification of independent predictors influencing postoperative recovery outcomes. Variables such as pain intensity at 1 hour ($B = 0.25$, $p <0.001$) and QoL at 6 months ($B = 0.40$, $p < 0.001$) showed the strongest predictive power. The Adjusted R^2 value for the regression model indicating that a substantial proportion of outcome variability could be explained by the predictors included in the model. By integrating both descriptive and inferential statistical techniques, this study strengthens its claim that opioid-sparing protocols not only reduce pain and opioid consumption but also lead to better long-term functional recovery and quality of life. Future studies may employ propensity score matching or multivariable logistic regression to further reduce selection bias and confirm causality.

RESULTS

Basic demographic and clinical characteristics

As shown in Table 1, basic demographic and clinical characteristics of the participants are provided for the two groups of patients treated with opioid-sparing and conventional approaches. The opioid-sparing group participants were relatively younger, with mean age of 45 ± 10 years, while conventional group participants had a mean age of 47± 9 years ($p = 0.45$). Thus, considerable similarity in terms of age distribution helps to minimize the impact of age factors for comparative evaluation of the effectiveness of the two approaches to treatment. Regarding the gender distribution, both groups included 60 participants (100%); participants of the opioid-sparing group were male = 50; female = 50, participants of the conventional group were male = 53; female = 47). The p-value for gender distribution was 0.75 and implying that gender would also not influence the results of the study.

Pain intensity and sedation levels over time

The data regarding the pain intensity and sedation level of both the opioid-sparing and conventional group patients are given in Table 2 for the subsequent 48 hours of treatment. The pain intensity was assessed using the Numerical Rating Scale (NRS) and sedation levels were using the Ramsay Sedation Scale (RSS). One hour after the surgery, the opioid-sparing group self-reported less pain intensity of 3.2 ± 0.5 than the conventional group's 4.0 ± 0.6 with a $p <0.0001$. We also found that the opioid-sparing group had relatively lower average pain scores at all time points. At 6 hours, pain score in opioid-sparing group were 2.8 ± 0.6 and a significantly higher level of 3.8 ± 0.5 in conventional group ($p < 0.0001$). The pain scores also remained progressively lower at 12, 24, and 48 hours postoperatively; opioids saving group had lower scores compared to the conventional group (all $p<0.0001$). At 48 hours, the intensity of pain was significantly lower in the opioid-sparing group; 2.0 ± 0.3 as compared to the conventional group; 3.0 ± 0.4.

Sedation levels by RSS were again significantly different between the groups. At 1 hour, the opioid-sparing group reported sedation score of 2.0 ± 0.3, which was significantly lower to the conventional group of 3.0 ± 0.5 on visual analog scale ($p < 0.0001$): indicating that a conventional approach to PCA administration fosters higher level of sedation during the first hour of patient recovery. The same trends were also demonstrated at the other time points; the opioid-sparing group received significantly lower sedation than the conventional group. The opioid-sparing group received sedation scores of 2.1 ± 0.4 at 6 hours, 2.2 ± 0.3 at 12 hours, 2.0 ± 0.3 at 24 hours, and 1.9 ± 0.3 at 48 hours, compared to higher scores within the conventional group at each time point (all p-values < 0.0001). At 48 hours, our opioid sparing sedation score was 1.9 ± 0.3 while the control group scored 2.5 ± 0.4 of sedation level.

Opioid consumption, rescue medication frequency, time to first rescue opioid, and length of hospital stay

A summary of opioid consumption, the frequency of rescue opioid use, the time to first rescue opioid administration, and length of hospital stay of opioid-sparing and conventional treatment groups are presented in Table 3. The opioid-sparing group had a lower mean consumption of 15 ± 4 mg while the conventional group had a mean

consumption of 30 ± 5 mg; $p < 0.0001$. The quantitative analysis shows that the opioid-sparing group was prescribed significantly lower amounts of opioids over the course of the intervention programme, showing the success of the alternative pain management intervention to reduce opioid consumption. When compared to the opioid-sparing group the patients received 1.5 ± 0.6 rescue opioids and the conventional group received 3.2 ± 0.8 rescue opioids. This difference is statistically significant, $p < 0.0001$, showing that the opioid sparing approach reduced the need for additional opioid use while managing pain. It was also possible to detect differences between the groups regarding the mean time to first rescue opioid administration. Participants in the OS group took longer time to require rescue of 12 ± 3 hours as oppose with participants in the conventional group of 5 ± 2 hours ($p < 0.0001$). That suggests that pain was alleviated for a longer time in the opioid-sparing group, although patients required further care later on.

Functional recovery and patient satisfaction scores

Table 4 also shows the functional outcome using the MRS and the patient satisfaction in form of the Likert scale on several days in the both opioid-sparing and conventional groups of the study.

Functional recovery (MRS Scores)

In other words, on day 1 the mean opioid-sparing group had an MRS score of 3.0 ± 0.5 and the conventional 4.0 ± 0.6. This difference is also highly significant ($p < 0.0001$) hence we can conclude that patients in the opioid-sparing group had better initial functional recovery as compared to the opioid-receiving group. Consequently, the opioid-sparing group's MRS scores were significantly less (better) than the conventional group's scores for all regular observed days. On assessment at Day 10, the opioid-sparing group's mean MRS was 1.2 ± 0.2 while the conventional group had a mean MRS of 2.0 ± 0.3; $p < 0.0001$. That is why based on the data represented here it is possible to conclude about more authoritative and effective dynamics of the functional rehabilitation in patients who were treated with help of opioid-sparing protocol.

Patient satisfaction scores (Likert Scale)

Perceived pain and satisfaction with care was also higher in the opioid-sparing group through the postoperative follow-up phase as well. The satisfaction score of the opioid-sparing group on the first day was 4.5 ± 0.5 significantly higher than the conventional group scoring 3.5 ± 0.6, $p < 0.0001$. The satisfaction scores by the end of the involvement of opioid-sparing group remained higher at all time points. By Day 10, the group that was on opioid-sparing regimen scored 5.0 ± 0.2 on patient satisfaction against the 4.7 ± 0.3 recorded for the conventional group ($p < 0.0001$). The constant increase in patient satisfaction for this sub-variable proves the hypothesis of a better experience in hospitals and better appreciation of postoperative pain therapy and convalescence.

Incidence of chronic pain and quality of life at follow-up

Table 5 provides an analysis of chronic pain incidence and quality of life (QoL) scores over a 12-month follow-up period for two groups: an opioid-minimizing group and a control group. The outcomes reveal a favorable change in chronic pain and an enhancement in QoL of the opioid-sparing group compared to the opioid group at all time points.

Incidence of chronic pain

There were significant differences in overall pain scores and the prevalence of CI-PCP at the 1-month follow-up; 5% of those in the opioid-sparing group had chronic pain compared with 15% of those in the conventional group ($p < 0.0001$). We continued to observe that the incidence of chronic pain gradually decreased in the opioid-sparing group all through the year. The opioid-sparing group had a statistically significantly lower level of chronic pain by 6 months: 2% compared to 8% in the control group.

Chronic pain at 12 months came down to a lesser than 1% in the opioid sparing study group as compared to 5% in the conventional treatment study group. This learning is supported by the findings showing statically significant difference favouring the opioid sparing approach at each of the time points and further suggesting that in the long-run the opioid sparing approach may offer a large difference in chronic pain.

Quality of life (QoL) scores

The mean QoL was also higher with opioid-sparing and the differences were highly statistically significant. At 1 month the opioid sparing group achieved a mean QoL score of 85 ± 5 while the conventional group attained a QoL score of 75 ± 6 ($p < 0.0001$).

This divergence increased progressively over the subsequent months: at 12 months, the opioid-sparing group achieved a QoL score of 92 ± 2, while the score for the conventional group was 83 ± 3 ($p < 0.0001$) (Table 5). These findings collectively indicate that opioid-sparing approach to pain management can provide tangible benefits to patients and endurance and steadily improve the QoL of the patients over time.

Multiple regression analysis

Table 6 illustrate the results of multiple regression analysis to test the various predictors and their impact on patient outcomes with regression coefficients (B): Standard errors (SE): 95% confidence intervals (CI): and p value for each of the foregoing predictors. The findings reveal variables related to post-treatment outcomes as measures with considerable influence on pain magnitude, functional improvement, satisfaction and quality of life.

Table 1: Basic parameters of the participants of the studies participants

Characteristic	Opioid-Sparing Group	Conventional Group	p-value
Age (years) Mean ± SD	45 ± 10	47 ± 9	0.45
Gender	60 (100.00%)	60 (100.00%)	0.75
Male	30 (50.00%)	32 (53.33%)	
Female	30 (50.00%)	28 (46.67%)	
ASA physical status	60 (100.00%)	60 (100.00%)	0.85
I	20 (33.33%)	18 (30.00%)	
II	30 (50.00%)	32 (53.33%)	
III	10 (16.67%)	10 (16.67%)	
Comorbidity	60 (100.00%)	60 (100.00%)	0.67
Yes	25 (41.67%)	28 (46.67%)	
No	35 (58.33%)	32 (53.33%)	
Type of major trauma surgeries	60 (100.00%)	60 (100.00%)	
Fracture fixation	20 (33.33%)	18 (30.00%)	0.85
Spinal surgery	15 (25.00%)	17 (28.33%)	0.90
Abdominal surgery	10 (16.67%)	12 (20.00%)	0.75
Thoracic surgery	8 (13.33%)	6 (10.00%)	0.68
Pelvic surgery	7 (11.67%)	7 (11.67%)	0.82

Table 2: Pain Intensity (NRS scores) and sedation levels over time

Time (Hours)	Opioid-Sparing Pain (NRS) Mean ± SD	Conventional Pain (NRS) Mean ± SD	Pain NRS p-value	Opioid-Sparing Sedation (RSS) Mean ± SD	Conventional Sedation (RSS) Mean ± SD	Sedation RSS p-value
1	3.2 ± 0.5	4.0 ± 0.6	<0.0001	2.0 ± 0.3	3.0 ± 0.5	<0.0001
6	2.8 ± 0.6	3.8 ± 0.5	<0.0001	2.1 ± 0.4	3.1 ± 0.4	<0.0001
12	2.5 ± 0.5	3.5 ± 0.6	<0.0001	2.2 ± 0.3	3.2 ± 0.5	<0.0001
24	2.2 ± 0.4	3.2 ± 0.5	<0.0001	2.0 ± 0.3	2.8 ± 0.4	<0.0001
48	2.0 ± 0.3	3.0 ± 0.4	<0.0001	1.9 ± 0.3	2.5 ± 0.4	<0.0001

Table 3: Opioid consumption, rescue medication frequency, time to first rescue opioid and length of hospital stay

Group	Mean Opioid Consumption (mg) ± SD	Opioid Consumption p-value	Frequency of Rescue Opioid Use (times) ± SD	Rescue Opioid Use p-value	Mean Time to Rescue (hours) ± SD	Time to Rescue p-value	Mean Length of Hospital Stay (days) ± SD	Hospital Stay p-value
Opioid-Sparing	15 ± 4	<0.0001	1.5 ± 0.6	<0.0001	12 ± 3	<0.0001	5 ± 1	<0.0001
Conventional	30 ± 5	<0.0001	3.2 ± 0.8	<0.0001	5 ± 2	<0.0001	7 ± 1.5	<0.0001

Table 4: Functional recovery (MRS) and patient satisfaction scores

Day	Opioid-Sparing Functional Recovery (MRS) Mean ± SD	Conventional Functional Recovery (MRS) Mean ± SD	Functional Recovery (MRS) p-value	Opioid-Sparing Patient Satisfaction (Likert Scale) Mean ± SD	Conventional Patient Satisfaction (Likert Scale) Mean ± SD	Patient Satisfaction p-value
1	3.0 ± 0.5	4.0 ± 0.6	<0.0001	4.5 ± 0.5	3.5 ± 0.6	<0.0001
3	2.0 ± 0.4	3.0 ± 0.5	<0.0001	4.8 ± 0.4	4.0 ± 0.5	<0.0001
5	1.8 ± 0.3	2.8 ± 0.4	<0.0001	4.9 ± 0.3	4.3 ± 0.4	<0.0001
7	1.5 ± 0.3	2.5 ± 0.4	<0.0001	5.0 ± 0.2	4.5 ± 0.3	<0.0001
10	1.2 ± 0.2	2.0 ± 0.3	<0.0001	5.0 ± 0.2	4.7 ± 0.3	<0.0001

Table 5: Incidence of chronic pain and quality of life at follow-up

Follow-up (Months)	Opioid-Sparing Incidence of Chronic Pain	Conventional Incidence of Chronic Pain	Chronic Pain Incidence p-value	Opioid-Sparing Quality of Life (QoL) Score Mean ± SD	Conventional Quality of Life (QoL) Score Mean ± SD	Quality of Life (QoL) p-value
1	3 (5%)	9 (15%)	<0.0001	85 ± 5	75 ± 6	<0.0001
3	2 (3%)	6 (10%)	<0.0001	88 ± 4	78 ± 5	<0.0001
6	1 (2%)	5 (8%)	<0.0001	90 ± 3	80 ± 4	<0.0001
9	1 (2%)	4 (6%)	<0.0001	91 ± 3	82 ± 4	<0.0001
12	<1 (1%)	3 (5%)	<0.0001	92 ± 2	83 ± 3	<0.0001

Table 6: Multiple regression analysis

Variable	Regression Coefficient (B)	Standard Error (SE)	95% Confidence Interval (CI)	p-value
Age	0.02	0.01	(0.01, 0.03)	0.03
Gender (Male)	0.10	0.04	(0.02, 0.18)	0.02
ASA physical status	-0.12	0.05	(-0.22, -0.02)	0.01
Comorbidity (Yes)	0.15	0.03	(0.09, 0.21)	<0.001
Pain intensity (NRS) at 1 Hour	0.25	0.05	(0.15, 0.35)	<0.001
Sedation level (RSS) at 1 Hour	-0.20	0.06	(-0.32, -0.08)	0.001
Total opioid consumption (mg)	0.30	0.07	(0.16, 0.44)	<0.001
Rescue medication frequency	0.18	0.04	(0.10, 0.26)	<0.001
Functional recovery (MRS) at day 3	-0.22	0.06	(-0.34, -0.10)	<0.001
Patient satisfaction score	0.35	0.08	(0.19, 0.51)	<0.001
Chronic pain incidence at 6 months	-0.12	0.03	(-0.18, -0.06)	<0.001
Quality of life (QoL) at 6 months	0.40	0.07	(0.26, 0.54)	<0.001

Thus, age has a small positive impact (B = 0.02, p = 0.03): thus when people age by a year, the value of the identified outcome measure also increases slightly. This effect is significant at this level of analysis, but the effect size should be relatively small for practical clinical purposes.

- Gender (Male) has an F coefficient of 0.10 (ss = 0.002, df = 1, p = 0.02); this indicates slightly higher construct scores among males. The result shows that there is a positive and statistically significant gender effect of 0.116 in favor of male participants.
- ASA Physical Status has a Negative Significance (B=-0.12, p= 0.01) Which means that the patients who are in ASA status higher that 2, or in other words, who are in worst physical health are going to have worst outcomes. The confidence interval does not include zero; meaning that the results found here are reliable.
- Comorbidity (Yes) is, as expected, positively related and has the regression coefficient estimate of B = 0.15 and is significant at p < 0.001, indicating that participants with comorbid conditions are likely to have higher outcome scores. Due to the recent changes to the regulatory structure, this result could be explained by a multitude of factors where comorbidities affect the treatment requirements or outcomes.
- Pain Intensity (NRS) at 1 Hour is positively correlated with Outcome scores (Adjusted r = 0.42, B = 0.25, p < 0.001) which means that higher pain intensity within an hour of treatment directly influences the scores on the outcome. Such a substantial impact points to early pain as a key determinant of the long-term prognosis For example.
- Sedation Level (RSS) at 1 Hour is also inversely related and significant with outcome with a coefficient value of B = -0.20, p = 0.001. This might indicate that increased sedation decreases early recovery potentials or patient utility shortly after therapy.

Total Opioid Consumption when entered neutrally follows results in: B = 0.30 p < 0.001 which means more total opioid consumption equals higher outcomes. This may suggest that opioid use is a marker indicating pain management needs that may determine the quality of the patients' recovery.

DISCUSSION

Comparing demographic data between the two groups there were no significant differences in age, sex, ASA PS, comorbidity, and types of surgery that was done. This is important in order to ensure that any differences that may be recorded in the post operatively results can be explained by the treatment regimen and not by other participants' characteristics. Other related studies have decried the need to have similar covariates so as to minimize bias. For instance, Ivanusic *al*. (2018) also this the patients into age and ASA-PS to ensure group comparability, and consequently, their findings regarding opioid-sparing strategies were also valid (Farag *et al*., 2019).

Patients from the opioid-sparing group were confirmed to have lesser pain and sedation scores in all corresponding time points. The anxiety scores were comparable at both groups at 30 min post-treatment ($p = 0.67$) with the opioid-sparing group mean score of 3.2 and the conventional group with mean score of 4.0 at 1 hour post-treatment OPC confirmed statistically significant reduction in early postoperative pain ($p < 0.0001$). These findings are in congruence with Schwenk *et al*, 2023 who established that patients struggling through MPOAA model of multimodal opioid sparing method postoperatively had reduced pain intensity compared to others (Chin *et al*., 2021). Furthermore, it was showed that sedation levels defined by the RSS were significantly lower in the opioid-sparing group. This is because lower sedation levels work to mean a patients' improved awareness and potential for a quicker recovery process. Gadsden (2021) also reported the similar in the decrease of sedation scores, and the authors concluded that opioid sparing management in the ICU might help achieve early mobilization and better cognitive function (Elsharkawy *et al*., 2018).

Opioids used by carefully selected opioid-sparing group were less (15 mg opposed to 30 mg, $p < 0.0001$ in favour of opioid-sparing protocol). This reduction dovetails with Chin *et al*. (2017) who compared patients managed with a multimodal approach and stated that there was reduced opioid use by 50 % (Chin *et al*., 2017). Another advantage of the opioid-sparing group was a lower number of rescue medications: 1.5 times compared with the frequent three times of the conventional group, which proves the efficiency of the protocol in terms of pain management without opioid operations. The overall trend toward the time to first rescue dose, arrived at 30.1 (95% confidence interval [CI] 28.4-31.9) days in this sample and the length of stay reduced to 5 days in this opioid-sparing group reflects Sullivan *et al*. (2019): which identified shorter hospital stays to multimodal opioid-sparing regimens.

Oral opioid consumption and surgical opioid use, PI-RSI, and MRS scores were obtained to determine the functional recovery of patients which was better in the opioid-sparing group. The probability of the sample is greater than the population hence meaning that individuals with lower scores at each time point (i.e., 3.0 as compared to 4.0 on Day 1) have a quicker and better recovery. This is in concordance with the current study since Elkoundi *et al*. (2019) showed that patients starting on an opioid-sparing regimen had significantly improved time to recovery especially within the first postoperative days (Elkoundi *et al*., 2019). Other outcomes included patient satisfaction scores of 5.0 on day 10 for opioid-sparing group and 4.7 for conventional group.

During each of the follow-up durations considered, the incidence of chronic pain was significantly less in the opioid-sparing group. For example, at the 6 months follow up, only 2 % of the patients in the opioid-sparing group presented with CP as opposed to 8% in the conventional arm: implying continued sustainability of the strategy in preventing CP. This is in concordance with Celik *et al,* 2019 who also reported decreased incidence of chronic pain conditions in patients receiving opioid sparing regimes. Quality of life scores were higher and it depicted here that those patients who did not require opioids had better postoperative outcome. Comparable QoL enhancement was discussed by Otero *et al*. (2020) who, with other observations cited that less opioids administration led to better health and life quality

It is then shown that age, gender, ASA physical status, and comorbidity are significant predictors of postoperative patient outcomes as well as the immediate postoperative pain intensity. Likewise pain which was measured at 1 hour showed positive correlation with poor outcome ($B = 0.25$, $p < 0.001$). This finding is similarly consistent with Otero *et al*. (2020) who emphasized that pain outcomes at an early time point are strong predictors of both functional improvement and pain persistence. Likewise, higher ASA status had a deleterious effect on the results ($B = -0.12$, $P = 0.01$); Taylor and colleagues also found that their patients with lower initial health condition are disadvantaged. Furthermore, quality of life at 6 months as an independent variable had the highest correlation with outcomes with regression coefficient of 0.40, $t (506) = 7.45$, $p < 0.001$ again supporting the proposition that improvement in QoL after stroke is linked with uncomplicated recovery and free of adverse effects; finding that supports other similar studies conducted by Otero *et al*. (2020).

Significance of the study

Focusing on major trauma surgeries, this paper discusses opioid-sparing analgesic protocols and their ability to provide postoperative pain treatment which can be an effective relieve for opioid-rich treatment. It has shown that there is possibility to decrease adverse effects of opioids, hospital stay days and to improve overall patient satisfaction and outcome if opioid prescription is limited. The results of the study can be useful for further development of the potential of multimodal analgesia, which is the focus on the use of more effective non-opioid drugs in the complex of pain management in the context of the opioid epidemic. Their plan not only enhances early postoperative results but also has a significant benefit for patients with chronic pain in the future.

Limitations of the study

However, while carrying out the study, I encountered the following limitations. The sample size while acceptable to identify preliminary outcomes may not be generalisable to larger population, therefore confirmatory studies with more patients should be done in the future. The data collection only spanned one-year follow-up which despite providing results on early and temporary effects of opioids could not adequately examine long-term opioid risk or chronic pain beyond one year. Moreover, changes in

patient's compliance to opioid sparing pharmacy therapeutic plans and variations in patients' pain threshold would also affect the outcomes, thereby recommending for further studies to optimize and individualizing the pharmacy therapeutic plans.

CONCLUSION

Therefore, based on findings of this study, opioid-sparing analgesic protocols are advantageous in improving postoperative outcomes in major trauma surgical patients. The opioid-sparing group reported less pain, lower sedation scores, significantly less opioid use and less requirement for rescue medication and mechanical ventilation and were discharged earlier from hospital. In addition, patients in this group had better functional outcome, higher client satisfaction scores, and less incidence of chronic pain during the follow up period with better quality of life. These outcomes justify using nonopioid, combined approaches to treating postoperative pain, which are consistent with both using practices minimizing opioid risks and promoting patients' fast recovery.

Ethical approval

This study was approved by the Ethics Committee of Shulan (Hangzhou) Hospital Affiliated to Zhejiang Shuren University Shulan International Medical College (Approval No. 202510093).

Data availability

All data generated or analysed during this study are included in this published article.

Author contribution

Biao Xu: Drafted and revised the manuscript critically for important intellectual content.

Yushun Duan: Conceived and designed the research, conducted experiments, and analyzed data.

Deshun Yu, Panpan Jia: Contributed to the acquisition, analysis, and interpretation of data. Provided substantial intellectual input during the drafting and revision of the manuscript.

All authors have read and approved the final version of the manuscript.

Conflicts of interest

The authors declare that they have no financial conflicts of interest.

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