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ORIGINAL RESEARCH

The Intraoperative Adherence to Multimodal Analgesia of Anesthesiologists: A Retrospective Study

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ABSTRACT

Introduction: Multimodal analgesia (MMA) is a critical component of enhanced recovery after surgery (ERAS). However, little research revealed its intraoperative implementation by anesthesiologists, who are on the front line defending against surgical pain. Therefore, the objective of our study is to assess the adherence of anesthesiologists to MMA comprehensively.
Methods: A retrospective study was conducted involving patients undergoing lung resection, knee arthroplasty, and radical mastectomy from pre/post-implementation year of MMA (Jan 1, 2013, to Dec 31, 2013, vs. 2019). Intraoperative analgesia regimens (analgesic mode) and hourly rated morphine milligram equivalents (MME) were compared. In addition, patient characteristics associated with continued opioid use after surgery, surgical types, and position level of anesthesiologists (attending-junior; above attending-senior) were also analyzed.
Results: After MMA initiation, the rate of multimodal analgesic regimen (mode ≥ 2) was significantly increased (post- vs. pre-implementation, 31.57 vs. 21.50%, $p < 0.05$). However, MME did not show significant difference (post- vs. pre-implementation, 0.402 vs. 0.456, $p > 0.05$). Patient-level predictors of persistent opioid use after surgery were not related to increased analgesic mode. Lung resection [coefficient, − 0.538; 95% confidence interval (CI), − 0.695 to − 0.383, $p < 0.001$] and knee arthroplasty (coefficient, − 1.143; 95% CI, − 1.366 to − 0.925, $p < 0.001$) discouraged multiple analgesic mode, while senior anesthesiologists (coefficient, 0.674; 95% CI 0.548–0.800, $p < 0.001$) promoted it.
Conclusions: Although anesthesiologists used more analgesics after promoting MMA, the "opioid-sparing" principle was not followed properly. The analgesic mode was not instructed by patients' characteristics appropriately. In addition, surgeries with cumbersome preparation/process impeded the use of multiple

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analgesic modes, while senior anesthesiologists preferred multiple analgesic modes.

Keywords: Multimodal analgesia; Intraoperative adherence; Anesthesiologists' behavior; Related factors

Key Summary Points

Insufficient evidence revealed the application of the multimodal analgesia (MMA) principle by anesthesiologists.

Intraoperative adherence of anesthesiologists to MMA was assessed through analgesic mode, opioid consumption, and related factors.

Post-MMA implementation, more analgesics were used without less opioid consumption and proper consideration of risk factors.

Different behaviors between senior and junior anesthesiologists were observed.

Poor adherence and possible factors were disclosed, encouraging future improvement and facilitation.

INTRODUCTION

As a comprehensive patient care bundle, the enhanced recovery after surgery (ERAS) protocol was developed to treat undesirable perioperative pathophysiological processes associated with patient outcomes [1, 2]. Although the ERAS program includes multiple items, pain management stands in the core place [3, 4], which is also the field anesthesiologists lead in this multidisciplinary teamwork [5, 6].

In the context of the opioid epidemic, multimodal analgesia (MMA) has emerged as the most effective strategy to optimize analgesic efficacy and reduce opioid consumption in perioperative medical care [4, 7]. MMA in an ERAS protocol adopts standardized regimens with concurrent analgesic agents or techniques to achieve an opioid-sparing aim [4]. The regimens include additive non-steroidal anti-inflammatory drugs (NSAIDs), spinal anesthesia, regional anesthesia, and intravenous lidocaine [4, 8].

Prospective randomized clinical trials [9, 10], retrospective cohort study [11, 12], and meta-analysis [13, 14] have reported that application of MMA is associated with improved pain control and less opioid consumption. However, although the benefit of MMA is obvious, adherence to MMA is not reported clearly, which determines the actual outcomes of surgical patients [4, 15]. Also, there are a limited number of studies incorporating the compliance of perioperative MMA in the overall assessment of the adherence to ERAS [3, 15]. Still, there is no further analysis to reveal the anesthesiologists-specific compliance during the intraoperative period and related factors.

In this study, we evaluated the intraoperative adherence to MMA by the anesthesiologists at a tertiary academic hospital. The intraoperative analgesia mode (total number of analgesic agents and techniques in every regimen) and morphine milligram equivalents (MME) were compared. We hypothesized that more multiple analgesia mode and less MME would be used after MMA initiation. After surgery, risk factors associated with persistent opioid use would persuade anesthesiologists to use more analgesic items. The influence of surgery type and anesthesiologists' characteristics on analgesia mode was also assessed. The findings from this study will provide comprehensive feedback and assist future improvement for MMA implementation in anesthesiologists.

METHODS

Study Design and Subjects

The study was presented as a retrospective cohort, single-center, comparative effectiveness study [16, 17]. It was approved by the Research Ethics Board (REB) of Peking Union Medical College Hospital (PUMCH), Beijing, China (Num. SK1350, Evaluation of Intraoperative

Application on Multimodal Analgesia by Anesthesiologists). Patient consent requirements were waived because the study involves minimal patient risks during data collection.

Three surgery types with high chronic postsurgical pain prevalence (lung resection, radical mastectomy, and knee arthroplasty) from 1 year before and 5 years after MMA initiation were selected [18]. An MMA program was launched in our hospital in 2014. To achieve the most establishment of MMA, consecutive patients undergoing lung resection (pulmonary wedge resection, sleeve resection, lobectomy, segmentectomy, total lung resection), knee arthroplasty, and radical mastectomy (modified or not) were included as the study population (post-implementation group), from Jan 1 to Dec 31, 2019, and patients undergoing the same surgeries above 1 year before implementation (from Jan 1 to Dec 31, 2013) were chosen for comparison (pre-implementation group). Data were collected through anesthesia recording in the hospital information system (HIS) of PUMCH. Patients with unclear anesthesia records (loss of opioid dose, infusion concentration, etc.) and receiving combined surgeries that do not meet the inclusion criteria were excluded.

Procedures

All eligible patients were identified through HIS. From anesthesia records, surgical procedure, the total opioid consumption, non-opioid analgesia, route of opioid administration, surgery duration, position level of anesthesiologists (attending and above attending) were obtained. Total opioid consumption was transferred to morphine milligram equivalents [19, 20] and divided by surgery duration to be comparable. Non-opioid analgesia available in our hospital included intravenous NSAIDs, lidocaine, tramadol, regional anesthesia techniques (neuraxial and peripheral anesthesia) without opioids [4, 21]. Intravenous lidocaine was supposed to be at a dose of 1–2 mg/kg/h or 1–2 mg/kg bolus [22–24]. Ventricular arrhythmia-related lidocaine use was identified through records and excluded. Non-systemic opioid (neuraxial opioid) was considered additional analgesia [4]. The total analgesia, including intravenous opioids, was concluded as analgesic mode (mode = 1, mode = 2, etc.). Dexmedetomidine infusion was not considered an analgesic component of the MMA regimen in the ERAS protocol of our hospital (Table 1).

Meanwhile, patient characteristics associated with persistent opioid use after surgery (greater age, female, tobacco use, alcohol drinking, diabetes mellitus, angiotensin-converting enzyme inhibitor, chronic pulmonary disease, mental disorder including depression, anxiety, and schizophrenia, psychotic drugs including antidepressant use, benzodiazepine, and selective serotonin reuptake inhibitor) were collected from medical history [25–27].

Outcome Measures

The primary outcome was the number of surgical cases intraoperatively using multiple analgesic modes (mode ≥ 2) by anesthesiologists. The secondary outcome was hourly rated MME. We also performed subgroup analysis for patient-level predictors of persistent opioid use after surgery and the positional level of anesthesiologists.

Statistical Analysis

We analyzed the outcome depending on the difference of analgesic mode and hourly rated MME between patients who belonged to pre-/post-implementation. Patient characteristics, including those associated with persistent opioid use after surgery, were summarized. The age cut-off for ongoing opioid use after surgery was 50 years old [26, 28]. Means (standard deviation) and numbers (percentage) were used for continuous and categorical variables.

For our primary outcome, we compared the number of multiple analgesic modes (mode ≥ 2) from pre-/post-implementation using the Pearson Chi-square test first to study MMA adherence. Subsequently, we subdivided the sample into different surgery types and repeated the analysis to check whether groups from different surgery types show consistent change.

Table 1 PUMCH ERAS Protocol (Clinical Practice Guidelines for ERAS in China)

Pre-operative	Intra-operative	Post-operative
Preoperative education and counseling: explain anesthesia, surgery, and perioperative pre/rehabilitation to patients and their family to relieve anxiety; obtain the overall physiological condition of patients through physical examination and lab tests	Antimicrobial prophylaxis: systemic antibiotics prophylaxis for abdominal surgery; infusion 30–60 min before incision; single type targeting potential infective bacteria; second dose only for long-term surgery (> 3 h or 2 half-lives of antibiotics) and blood loss > 1500 ml	Postoperative pain management: combined patient-controlled epidural analgesia and NSAIDs; combined patient-controlled intravenous analgesia with low-dose opioids and peripheral nerve block;
Smoking and alcohol cessation: 4 weeks or more smoking and alcohol cessation	Anesthesia, anesthetics, and anti-stress management: general anesthesia combined with epidural anesthesia, paravertebral block or wound infiltration is recommended; short-acting sedatives and opioids are recommended (remifentanil 0.2–0.4 μg/(kg.min) or TCI 6–8 μg/l; propofol TCI mode maintaining BIS 40–60); continuous infusion of dexmedetomidine is recommended for major abdominal surgery with risk of ischemia–reperfusion injury; sugammadex should be used as muscle relaxant antagonist for lower pulmonary complication	Post nausea and vomiting (PONV) prevention: identify risk factors; multimodal PONV prophylaxis and treatment for patients with risk factors
Preoperative patient optimization: identify and correct anemia; pre-emptive analgesia (NASIDs and COX-2 selective inhibitors are recommended for patients without contraindication); assess frailty using clinical frailty scale; preoperative exercise; evaluate cognitive condition using mini-mental state examination (MMSE) and Montreal cognitive assessment scale (MoCA); anti-inflammatory therapy; identify and intervene mental disorder using hospital anxiety and depression scale (HADS)	Multimodal analgesia: opioid-sparing strategy includes NSAIDs 30 min before incision; epidural anesthesia or paravertebral before anesthesia; wound infiltration before surgery; κ-receptor agonist is used for visceral pain	Postoperative diet: early return to normal diet is recommended; when oral intake is less than 60%, supplemental nutrition should be given

Table 1 continued

Pre-operative	Intra-operative	Post-operative
Preoperative nutritional support: use nutritional risk screening 2002 (NRS 2002) to identify patients with malnutrition risk	Anti-inflammatory management: general anesthesia combined with regional anesthesia, and ketamine, lidocaine and dexmedetominide for anti-stress; precise and minimally invasive techniques; glucocorticoid and protease inhibitor for prophylaxis	Postoperative anemia: screening 1–3 h after surgery for patients receiving major surgery or with preoperative moderate-to-severe anemia; intravenous iron supplement can be used according to blood iron level; EPO is recommended for patients with cancer or inflammatory condition; blood infusion when measures above are insufficient; maintain Hb 70-80 g/l
Antithrombotic prophylaxis treatment: patients with malignant tumor and receiving major surgery should receive heparin or low-molecular heparin for 7–10 days perioperatively; mobilization and gradient intermittent compression can be combined with anti-thrombotic medication to enhance the effect; patients with high risk of venous thromboembolism should receive 4 weeks treatment after surgery	Lung protective ventilation: methyl-prednisolone 20–40 mg or hydrocortisone 100 mg before intubation; tidal volume 6-8 ml/kg; PEEP 5-8 cmH_2O; I: E: 1.0:(2.0–2.5); I: E: 1.0:(3.0–4.0) for COPD patients; $FiO_2 < 60\%$; $PaCO_2$ 35–45 mmHg; at least once lung expansion before extubation	Early mobilization: patients should be mobilized as early as they are able to
Preoperative fasting: intake of clear fluids until 2 h before surgery; 6-h fast for solid food; carbohydrate fluid is recommended (12.5% carbohydrate fluid 800 ml 10 h before surgery, $\leq$ 400 ml 2 h before surgery)	Brain protection: BIS 40–60; BIS 50–60 and B.P. fluctuation between $\pm$ 10% baseline for elderly patients; PaCO2 35–45 mmHg; Hb > 80 g/l; non-invasive monitor of brain oxygen if available	Criteria-based discharge: return to oral intake of semi-fluid or nutrition supplement; no need for intravenous infusion; satisfactory pain control by oral analgesic; surgical wounds heal smoothly without infection; free mobilization; organs function well; patients agree to discharge
Pre-anesthetic medication: the routine administration of sedatives to reduce anxiety preoperatively is not recommended especially for elderly patients	Fluid and circulation management: goal-directed fluid therapy (GDFT)	Continuous follow-up and evaluation: routine follow-up 24–48 h after surgery by phone call; schedule out-patient visit 7–10 days after surgery; continue follow-up up to 30 days after surgery

Table 1 continued

Pre-operative	Intra-operative	Post-operative
	Maintain normothermia: active warming for intravenous infusion line, mattress etc. to maintain core body temperature $\geq$ 36 °C	
	Surgical technique and quality: precise, minimally invasive, shorten surgical time, decrease blood loss	
	Perioperative blood glucose management: preoperative HbA1c < 7.0%; intraoperative blood glucose $\leq$ 8.33 mmol/L	
	Drainage: routine drainage is not recommended	
	Gastric feeding tube: only used for temporarily emptying gastric gas before intubation	
	Urinary catheter: when used they should be removed as soon as the patient is able to void, ideally within 24 h after completion of surgery	

COX cyclooxygenase; *TCI* target-controlled infusion; *BIS* bispectral index; *PEEP* positive end-expiratory pressure; *I:E* inspiratory rate: expiratory rate; *COPD* chronic obstructive pulmonary disease; *B.P.* blood pressure; *Hb* hemoglobin; *HbA1c* hemoglobinA1c

We compared hourly rated MME from pre-/-post-implementation for our secondary outcomes using the Wilcoxon rank-sum test to study opioid-sparing behavior. Next, we repeated the analysis between single and multiple analgesic modes in different surgery types to examine the consistency in other circumstances.

Finally, a total number of nine patient-level predictors of persistent opioid use after surgery was included, along with the positional level of anesthesiologists, surgery types and pre-/post-implementation. Before modeling, we categorized age: 0, < 50; 1, $\geq$ 50 and surgery types were converted into two dummy variables: lung resection or knee arthroplasty as one and the others as zero. Analgesic mode was categorized as 0 (mode = 1) and 1 (mode $\geq$ 2). All the other data were recorded as categorial data originally. As the analgesic mode was converted to binary variable, logistic regression was used to investigate the association between analgesic mode (dependent variable) and the predictors mentioned above (independent variables). Multicollinearity of all variables was assessed by checking the Variance Inflation Factor (VIF) on a multiple regression model. VIF less than 10 was regarded as no significant interaction between variables. All variables were considered clinically independent. Statistical summaries and figures are presented. R 4.0.3 was used for statistical analysis. We considered p values below 0.05 were statistically significant.

RESULTS

Subjects

A total of 1577 patients were included in the pre-implementation group from Jan 1 to Dec 31, 2013. In the post-implementation period, 3753 patients were included from Jan 1 to Dec 31, 2019. There were 587 patients undergoing lung resection, 306 undergoing knee arthroplasty, and 684 undergoing mastectomy in the pre-implementation group. Of these, 1191 were women, and 386 were men, with mean age of 54.9 (13.2) years old. There were 2167 patients undergoing lung resection, 626 undergoing knee arthroplasty, and 960 undergoing mastectomy in the post-implementation group. Of these, 2797 were women, and 956 were men; the mean age was 56.8 (12.3) years old. Demographic and clinical characteristics of patients from pre-/post-implementation groups were presented in Table 2.

Outcomes

A total of 339 patients (21.50%) from the pre-implementation group received multiple analgesic modes during surgery by anesthesiologists (Table 3). Of these, 12 patients (3.54%) received three-mode analgesia, and 327 patients (96.46%) received two-mode analgesia (Fig. 1A). The most frequently used non-opioid was intravenous NSAIDs (265 cases, 78.17%, including flurbiprofen and parecoxib). The rest included intravenous lidocaine (47 cases, 13.86%), regional anesthesia (38 cases, 11.21%) including femoral block, lumbar plexus block, sciatic nerve block, epidural and spinal anesthesia, and intravenous tramadol (two cases, 0.59%) (Fig. 2A). The most frequently used anesthesia for knee arthroplasty in patients with single analgesia mode is general anesthesia (pre-implementation: 218/234; post-implementation 536/554), the second most frequently used anesthesia is regional anesthesia (combined spinal and epidural anesthesia, CSEA) (pre-implementation: 16/234; post-implementation 18/554). For the other two surgery types, the anesthesia for patients with single analgesia mode is only general anesthesia.

For patients from the post-implementation group, the number of multiple analgesic mode cases was significantly higher (31.57% post-implementation vs. 21.50% pre-implementation, $p < 0.001$) (Table 3). Of these, 53 patients

Table 2 Patients' demographic and clinical characteristics

Characteristics	Total	Pre-implementation (n = 1577)	Post-implementation (n = 3753)
Age, mean (standard deviation), years	56.2 (12.6)	54.9 (13.2)	56.8 (12.3)
Female	3988 (74.82%)	1191 (75.90%)	2797 (74.53%)
Tobacco use	835 (15.67%)	261 (16.55%)	574 (15.29%)
Alcohol drinking	307 (5.76%)	99 (6.28%)	208 (5.54%)
Diabetes mellitus	552 (10.36%)	127 (8.05%)	425 (11.32%)
ACEI	650 (12.20%)	141 (8.94%)	509 (13.56%)
CPD	172 (3.23%)	44 (2.79%)	128 (3.41%)
Mental disorder	59 (1.11%)	16 (1.01%)	43 (1.15%)
Psychotic drugs	56 (1.05%)	14 (0.89%)	42 (1.12%)

ACEI angiotensin-converting enzyme inhibitor; *CPD* chronic pulmonary disease

Table 3 Comparison of the numbers of multiple analgesic mode

Groups	Pre-implementation	Post-implementation	p value[a]
Number of patients with multiple mode analgesia/total number of surgical patients			
Total	339/1577 (21.5%)	1185/3753 (31.57%)	$p < 0.001$
Lung resection	89/587 (15.16%)	675/2167 (31.15%)	$p < 0.001$
Knee arthroplasty	72/306 (23.53%)	72/626 (11.50%)	0.007
Radical mastectomy	178/684 (26.02%)	438/960 (45.63%)	$p < 0.001$

[a] $p < 0.05$ was considered significant

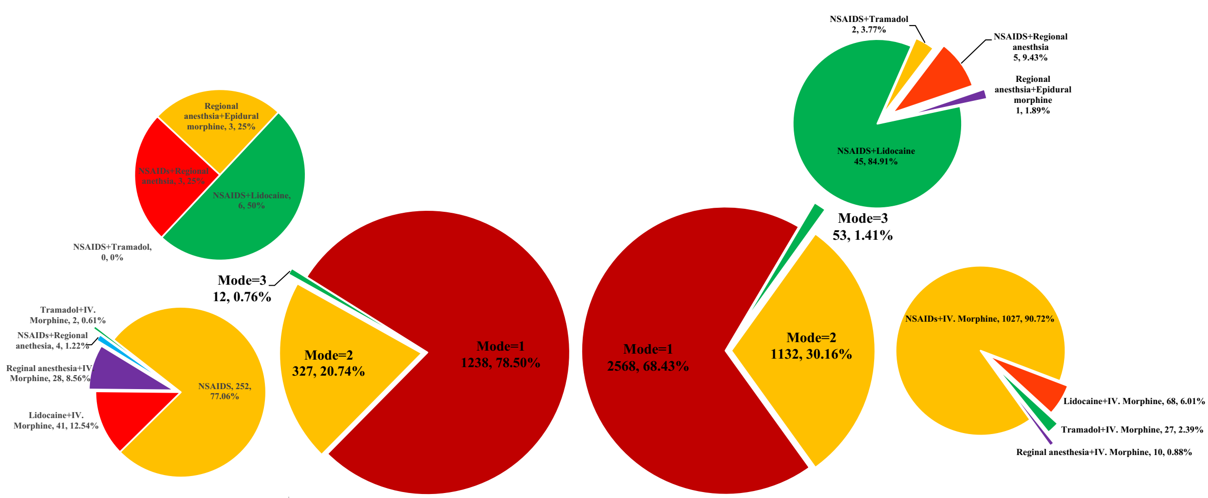

Fig. 1 Proportions and components of every analgesic mode: **A** pre-implementation group; **B** post-implementation group. (The texts in small pie chart: analgesic agents/techniques, number, percentage to the total number of respective analgesic modes; IV. Morphine was omitted from the analgesic agents/techniques in small pie chart of mode = 3). *NSAIDs* non-steroidal anti-inflammatory drugs; *IV.* intravenous

(4.47%) received three-mode analgesia, and 1132 patients (95.53%) received two-mode analgesia (Fig. 1B). No patients received analgesic mode more than three in both groups. The most frequently used non-opioids were NSAIDs, including flurbiprofen and parecoxib, with the highest proportion (1079 cases, 91.05%). The rest involved similar analgesic categories with the pre-implementation group but different proportions, which exhibited as intravenous lidocaine (113 cases, 9.54%), tramadol (29 cases, 2.45%), and regional anesthesia (16 cases, 1.35%), including paravertebral block and spinal anesthesia) (Fig. 2B).

For subgroup analysis, more patients from the post-implementation group received multiple analgesic mode than pre-implementation group in lung resection (31.5% post-implementation vs. 15.16% pre-implementation, $p < 0.001$) and radical mastectomy (45.63% post-implementation vs. 26.02% pre-implementation, $p < 0.001$) subgroups. However, for patients undergoing knee arthroplasty, the number of multiple analgesic mode was lower in post-implementation group than pre-

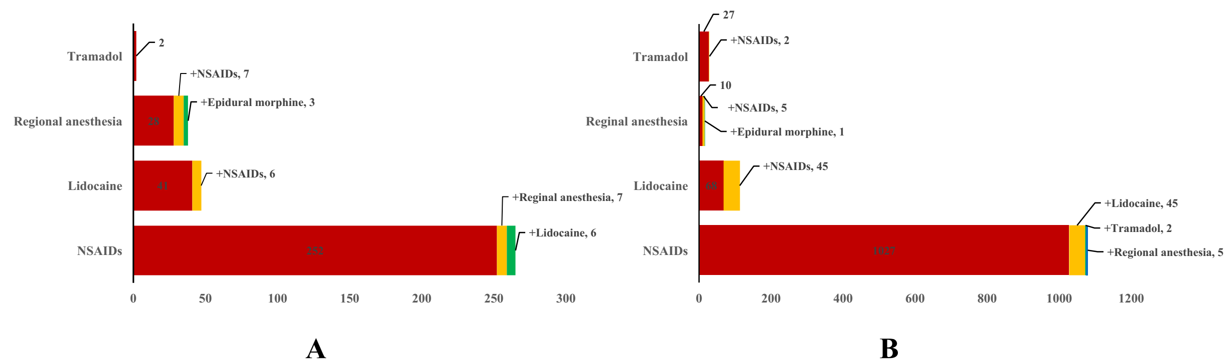

Fig. 2 Components of every non-opioid analgesic agents/techniques: **A** pre-implementation group; **B** post-implementation group. (The texts of every bar: additional analgesic agents/techniques, number). *NSAIDs* non-steroidal anti-inflammatory drugs

implementation group (11.50% post-implementation vs. 23.53% pre-implementation, $p < 0.001$) (Table 3).

To assess the intraoperative opioid consumption, hourly rated MME was collected and calculated. There was no difference between MME from post- and pre-implementation groups (0.402 vs. 0.456, $p = 0.995$). MME of multiple analgesic mode was significantly higher than single analgesic mode in both groups (post-implementation group: 0.412 vs. 0.398, $p < 0.05$; pre-implementation group: 0.503 vs. 0.443, $p < 0.05$). Furthermore, we performed subgroup analysis for MME and found MME from the post-implementation group was significantly increased than the pre-implementation group in lung resection (0.385 vs. 0.298, $p < 0.001$) and knee arthroplasty (0.298 vs. 0.275, $p < 0.05$). There was no

Table 4 Comparison of the hourly rated morphine equivalents

MME	Pre-implementation		*p* value[a]	Post-implementation		*p* value[a]
Total	0.456		/	0.402		0.995
	Mode = 1	Mode ≥ 2	0.002	Mode = 1	Mode ≥ 2	0.004
	0.443	0.503		0.398	0.412	
Lung resection	0.298		/	0.385		$p < 0.001$
	Mode = 1	Mode ≥ 2	0.729	Mode = 1	Mode ≥ 2	1.000
	0.395	0.362		0.299	0.287	
Knee arthroplasty	0.275		/	0.298		0.019
	Mode = 1	Mode ≥ 2	0.913	Mode = 1	Mode ≥ 2	0.376
	0.283	0.248		0.295	0.315	
Radical mastectomy	0.673		/	0.509		1.000
	Mode = 1	Mode ≥ 2	0.023	Mode = 1	mode ≥ 2	0.497
	0.659	0.714		0.513	0.504	

[a] $p < 0.05$ was considered significant

Table 5 Correlation between risk factors of persistent opioid use after surgery and analgesic mode

Factors	Coefficient (95% CI)	p value[a]
Age ≥ 50 years old	− 0.181 (− 0.324 to − 0.039)	0.013
Female	− 0.057 (− 0.199 to 0.084)	0.431
Tobacco use	− 0.179 (− 0.421 to − 0.061)	0.145
Alcohol drinking	0.118 (− 0.201 to 0.429)	0.463
Diabetes mellitus	0.105 (− 0.110 to 0.315)	0.335
ACEI	− 0.179 (− 0.388 to 0.026)	0.090
CPD	− 0.050 (− 0.420 to 0.302)	0.786
Mental disorder	0.443 (− 0.849 to 1.693)	0.490
Psychotic drugs	− 1.432 (− 2.896 to − 0.056)	0.047
Senior anesthesiologists (above attending)	0.674 (0.548–0.800)	< 0.001
Lung resection[b]	− 0.538 (− 0.695 to − 0.383)	< 0.001
Knee arthroplasty[c]	− 1.143 (− 1.366 to − 0.925)	< 0.001

CI confidence interval, *ACEI* angiotensin-converting enzyme inhibitor, *CPD* chronic pulmonary disease
[a] $p < 0.05$ was considered significant
[b] Lung resection was denoted as 1, and the rest of the surgeries were denoted as 0
[c] Knee arthroplasty was denoted as 1, and the rest of the surgeries were denoted as 0

difference between post-/pre-implementation groups in radical mastectomy (Table 4).

There were no significant interactions between all variables (VIF age: 1.182, gender: 1.864, tobacco use: 1.811, alcohol drinking: 1.304, diabetes mellitus: 1.065, ACEI: 1.066, CPD: 1.009, mental disorder: 3.053, psychotic drug: 3.054, anesthesiologists: 1.042, thoracic surgery: 1.605, knee surgery: 1.326). Therefore we included all variables into logistic regression model. For the patients' characteristics of persistent opioid use after surgery, only two factors (age ≥ 50 years old and psychotic drugs) were found to have correlations with analgesic mode. However, age ≥ 50 years old (coefficient, − 0.181, CI, − 0.324 to − 0.039, $p < 0.05$) and psychotic drugs (− 1.432, − 2.896 to − 0.056, $p < 0.05$) were associated with the decreased analgesic mode. Furthermore, the positional level of anesthesiologists and surgery type also showed association with analgesic mode. According to the Chinese medical training system, we defined attending doctors as junior anesthesiologists and above attending as senior anesthesiologists. They all have completed residency training and are eligible to practice independently in anesthesia. We found the senior anesthesiologists would like to choose more analgesic modes (0.674, 0.548–0.800, $p < 0.001$). It appeared that lung resection (− 0.538, − 0.695 to − 0.383, $p < 0.001$) and knee arthroplasty (− 1.143, − 1.366 to − 0.925, $p < 0.001$) were related with fewer analgesic modes. All analysis results of all involved factors are presented in Table 5.

DISCUSSION

Anesthesiologists are on the front line of defense against surgical pain. However, anesthesiologists cannot obtain pain scores directly through interviewing patients intraoperatively. Therefore proper understanding and application of MMA and ERAS should be initiated and strengthened in anesthesiologists' minds to sufficiently relieve surgical pain. Also, supervision and feedback of anesthesiologists' behavior should be conducted simultaneously. However, there is no research focusing on evaluating the intraoperative analgesic behavior of anesthesiologists. Secondly, the previous study does not assess patients' and anesthesiologists' characteristics, such as patients' demographic features, medical history, and positional level, which may influence the final analgesic decision. On the other hand, research focusing on assessing the quality of ERAS intervention does not allow adequate time to establish a new paradigm, leading to misleading results entirely. These are deficiencies needing further improvement.

The observational study relies on data in which physician preferences and patient characteristics decide clinical treatment. Although it is not as efficient as a prospective randomized study to reveal the effectiveness of the intervention, the observational study can provide information on the real-world situation and what is essential to healthcare decision-makers [17]. Therefore, our retrospective observational study was chosen to evaluate the actual intraoperative implementation of MMA by anesthesiologists and what factors influence the decisions. Previous studies reveal the overall adherence to perioperative multimodal analgesia is 82.39–89.2% [3, 15]. However, this research is prospective or retrospective for a short term (3 years after initiation). In our study, we chose the maximal interval (5 years) after MMA initiation to evaluate the performance of anesthesiologists, and the overall adherence was 31.57% from our study. Therefore, the adherence can be much lower than expected without proper supervision, especially with time flying. However, this result is still below our expectations.

Furthermore, several studies revealed the burnout of anesthesiologists worldwide [29, 30]. Our study observed that surgery needing complicated preparation and maintenance such as lung resection and knee arthroplasty would inhibit more analgesic mode. Therefore intensive workload and burnout of anesthesiologists might be factors influencing MMA application. Furthermore, reimbursement rules of Chinese medical insurance might impact intraoperative analgesic regimens. Some analgesic agents and techniques, including NSAIDs and neuraxial blocks, are not covered by Chinese basic medical insurance in some circumstances. Therefore anesthesiologists prefer to avoid using these items.

On the other hand, multimodal analgesia primarily focuses on the concurrent use of non-opioid analgesics to decrease opioid use. Therefore, a combination of analgesics to assure analgesic effectiveness and opioid-sparing are two critical components of MMA [4]. Our study found that multiple analgesic mode was more often used during the post-implementation period, which indicated that more patients received a combination of different analgesics in this circumstance. However, the intraoperative opioid consumption showed no difference between the two groups. Furthermore, multiple analgesic modes consumed more opioids than single analgesic modes, disobeying the opioid-sparing principle. At the same time, the average MME of the post-implementation group increased compared to the pre-implementation period. The evidence above indicates that anesthesiologists use multiple analgesics to relieve more pain rather than decrease opioid consumption. Especially after MMA implementation, a strong emphasis was put on postsurgical pain control; therefore, anesthesiologists might behave actively in pain management. However, in multiple analgesic mode, we observed that most cases only involved two analgesic modes: intravenous opioids and NASAIDs. As discussed above, under intensive workload, anesthesiologists might prefer convenient administering routes and familiar analgesics. On the other hand, insufficient understanding and mastering of MMA principles and analgesic techniques such as regional anesthesia could result in this circumstance. In general, we can conclude that the complete adherence to the MMA principle is poor.

The goal of MMA is not only to avoid the adverse events of opioids perioperatively but also to help prevent and deal with the worldwide opioid crisis on anesthesiologists' part. As reported previously, tremendous cases of opioid abuse originate from iatrogenic causes [31]; therefore, anesthesiologists who are qualified to prescribe opioids are in a unique position to minimize opioid exposure and prevent persistent opioid use after surgery [7, 32]. Identifying patient-level risk factors for prolonged opioid use after surgery is essential in this circumstance. Our study involved several patients-level risk factors of persistent opioid use after surgery, which are identifiable easily. However, the results revealed that anesthesiologists' decisions of analgesic mode were not associated with these risk factors. Some factors (age $\geq$ 50 years old and psychotic drugs) even harmed analgesic mode. As we know, the intervention window during the perioperative period for anesthesiologists is short; in this case, our anesthesiologists need to focus more on the opportunity.

Furthermore, senior anesthesiologists in our hospital tend to use more analgesic modes. From an informal interview of ten anesthesiologists (five senior and five junior anesthesiologists), we collected more reasons for not adhering to MMA from junior anesthesiologists such as medical reimbursement, long-term adverse effect, time-consumption, inadequate experience, negative attitude to the impact of MMA, follow-up problem, and inconvenient coordination with the surgical team. While for senior anesthesiologists, medical reimbursement and contraindication were considered chiefly. Therefore it seems senior anesthesiologists are more experienced and skilled with the analgesic techniques of MMA protocol and with the collaboration in the perioperative team. Moreover, complicated surgery such as lung resection and knee arthroplasty would inhibit more analgesic mode. Therefore, future efforts might be put into training anesthesiologists to master analgesic techniques and skills in multidisciplinary collaboration, and improvement of analgesics such as developing extended-release and combined-release analgesics might help simplify MMA practice.

Due to the nature of the retrospective study, the data in our study might be less accurate and consistent than that achieved with a prospective study design. Therefore, a prospective observational study can be conducted in the future to overcome this limitation. Next, our study only involved patients from three specific types of surgeries, which cannot represent anesthesiologists' performance in other surgeries anesthesia. Also, our study data were collected from a single center; the general representativeness of results is limited. For the data analysis, we modeled all variables as categorical variables and performed logistic regression with the assumption of linearity. However, this assumption was not strict enough since the actual relationship between predictors and response variables was unknown. An ensemble modeling technique for predicting the relationship between predictors and response variables was created by Zhongheng Zhang and his/her colleagues [33]. This technique was based on machine-learning algorithms and required no strict assumption of linearity. Therefore it could be employed in this case after systemic training.

Another limitation of our study is that we did not involve the analgesic agents and techniques administered by other medical staff, such as surgeons. As we know, wound infiltration, intraarticular injection, etc., are components of multimodal analgesia but are performed by surgeons [4, 34]. However, from the data extraction of the pilot study, the overall rate of analgesic techniques by surgeons was quite low ($\sim$ 2.74%) and showed huge heterogeneity among surgery types. Therefore we did not incorporate it into analysis to avoid false-positive results. These analgesic components might influence the decision of anesthesiologists and can be included to help comprehensive analysis in the future prospective study.

CONCLUSIONS

Although more analgesic modes were implemented intraoperatively after the initiation of MMA, no differences in opioid consumption were observed, which indicates the poor adherence to MMA by anesthesiologists. Moreover, patients at risk of persistent opioid use after surgery were not identified and provided with the proper analgesic decision. Furthermore, future improvements can focus on specific training for junior anesthesiologists and developing analgesics to simply the process.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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