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# Postoperative pulmonary complications after major abdominal surgery in elderly patients and its association with patient-controlled analgesia

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## Abstract

**Objectives** This study aims to identify the risk factors for postoperative pulmonary complications (PPCs) in elderly patients undergoing major abdominal surgery and to investigate the relationship between patient-controlled analgesia (PCA) and PPCs.

**Design** A retrospective study.

**Method** Clinical data and demographic information of elderly patients (aged ≥ 60 years) who underwent upper abdominal surgery at the First Affiliated Hospital of Sun Yat-sen University from 2017 to 2019 were retrospectively collected. Patients with PPCs were identified using the Melbourne Group Scale Version 2 scoring system. A directed acyclic graph was used to identify the potential confounders, and multivariable logistic regression analyses were conducted to identify independent risk factors for PPCs. Propensity score matching was utilized to compare PPC rates between patients with and without PCA, as well as between intravenous PCA (PCIA) and epidural PCA (PCEA) groups.

**Results** A total of 1,467 patients were included, with a PPC rate of 8.7%. Multivariable analysis revealed that PCA was an independent protective factor for PPCs in elderly patients undergoing major abdominal surgery (odds ratio = 0.208, 95% confidence interval = 0.121 to 0.358; $P < 0.001$). After matching, patients receiving PCA demonstrated a significantly lower overall incidence of PPCs (8.6% vs. 26.3%, $P < 0.001$), unplanned transfer to the intensive care unit (1.1% vs. 8.4%, $P = 0.001$), and in-hospital mortality (0.7% vs. 5.3%, $P = 0.021$) compared to those not receiving PCA. No significant difference in outcomes was observed between patients receiving PCIA or PCEA after matching.

**Conclusion** Patient-controlled analgesia, whether administered intravenously or epidurally, is associated with a reduced risk of PPCs in elderly patients undergoing major upper abdominal surgery.

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**Keywords** Postoperative pulmonary complications, Patient-controlled analgesia, Elderly patient, Upper abdominal surgery, Protective factor

## Introduction

With the global trend of aging, the proportion of elderly individuals is steadily increasing due to improved healthcare, declining fertility rates, and extended life expectancies [1]. This trend is leading to a significant rise in the number of elderly patients requiring surgical interventions, posing new challenges for healthcare systems worldwide [2]. In China, this trend is particularly pronounced. As of 2020, the elderly population over 60 years old accounted for 18.7% of the total population in China and exceeded the population of children for the first time [3]. The physiological changes brought about by aging may increase the risk of patients undergoing anesthesia and surgery, particularly for complex and lengthy surgeries [4, 5]. Upper abdominal surgery involves the diaphragm and abdominal wall muscles, impacting breathing and potentially leading to a prolonged postoperative recovery time [6, 7]. Effective perioperative planning and interventions during the period can improve the prognosis of elderly patients undergoing upper abdominal surgery [8].

Postoperative pulmonary complications (PPCs) are common after major abdominal surgery, directly related to delayed postoperative recovery, economic burden, and mortality rates. It was reported that PPCs occurred in 3–39.5% of adult patients [4, 9]. Identified risk factors of PPCs included older age [10, 11], high American Society of Anesthesiologists (ASA) classification [12, 13], and prolonged surgery [10, 13]. While intraoperative protective pulmonary ventilation and refraining from residual muscle relaxation were acknowledged to shorten the length of the hospital stay, their preventive value for PPCs was still under debate [14, 15]. Therefore, exploring and validating more controllable factors for preventing PPCs, especially in elderly patients undergoing upper abdominal surgery, is essential.

Postoperative pain in upper abdominal surgery patients has a significant impact on the recovery of effective spontaneous respiration [8]. However, there are limited studies directly analyzing the suitability and effectiveness of analgesic strategies on PPCs in elderly patients. Patient-controlled analgesia (PCA) based on opioids is a widely used technique for the management of postoperative pain in China [16], allowing patients to press the analgesic button to achieve effective analgesia while reducing adverse reactions, such as excessive sedation, respiratory depression, and difficulty in clearing sputum [17, 18]. Nevertheless, PCA relies on adequate analgesic education, personalized analgesia formulas, and timely adjustment of analgesic parameters. It was reported that PCA might not ensure proper analgesia [19], even delayed physical function recovery and increased the length of hospital stay in older patients undergoing orthopedic procedures [20]. Only moderate to low-quality evidence supports opioid-based intravenous PCA as an efficacious alternative to non-patient-controlled systemic analgesia for postoperative pain [21]. Therefore, while PCA stands out as an optimal choice for postoperative pain control, there is a need for further elucidation on the relationship between PCA and PPCs. This clarification is essential for enhancing the quality of analgesia and effectively preventing PPCs.

This study is designed to: (1) investigate whether the application of PCA was associated with reduced PPCs in elderly patients undergoing upper abdominal surgery; and (2) investigate the relationship between different analgesic methods and opioid drug doses and PPC incidence, thereby improving our ability to prevent PPCs.

## Materials and methods

### Study design

This single-center retrospective observational study was conducted at the First Affiliated Hospital of Sun Yat-sen University (FASU) in Guangzhou, China. The study's design and the waiver of informed consent were approved by the Ethics Committee of FASU (protocol# 2021−395).

### Setting and participants

The study included all elderly patients (age≥60) who received their initial upper abdominal surgery with general anesthesia at an academic medical center and teaching hospital in China between January 2017 and December 2019.

The exclusion criteria were: (1) patients receiving in-hospital pain treatment before the surgery or taking pain medication for an extended period before and after the onset of the illness; (2) unplanned PCA termination after surgery due to severe side effects (such as severe pruritus or nausea/vomit); (3) difficulty in determining the development of PPCs in patients.

### Anesthesia management

The anesthesia care followed our institute's management protocol. Typically, patients underwent general anesthesia through tracheal intubation using a combination of inhaled and intravenous anesthetics. During the surgery, volume-controlled mechanical ventilation was applied, with a tidal volume of 7-8 ml/kg of the ideal body weight and a fraction of inspired oxygen between 40% and 60%.

Intermittent recruitment maneuvers were performed during the surgery and before extubation. All patients received local anesthesia with ropivacaine at the wound site at the end of surgery. Flurbiprofen axetil and tramadol were the most commonly used analgesic drugs after surgery in our hospital, prescribed by the surgeon.

### Data collection

The perioperative surgical and anesthesia records were reviewed for confirmation by two experienced clinicians via the Medicalsystem Health Electronic Database (Suzhou, China) and REHN analgesia database (Nantong, China). Data was then collected into a secure database, de-identified, and analyzed. General information (age, sex, weight, body mass index (BMI), ASA physical status classification, smoking history), preoperative comorbidities (GOLD [22] staging of pulmonary ventilation dysfunction, history of pulmonary diseases, history of chronic diseases) and surgical information (surgical site, surgical approach, length of surgery, conversion to open surgery, unplanned second surgery) were included as patient baseline variables.

As for missing data, general case information (such as age and sex) and surgery-related items (such as surgery duration and whether the surgery was open or not) are mandatory items in the registration system, and thus have no missing. For some numerical data (such as height and weight), there is less than 5% missing data, which we have imputed using the median value of the cohort. For important data related to exposure and outcome variables, such as analgesia plans, analgesic drugs, and their types, cases with missing data have been excluded from the study.

### Exposures

The major exposure in this study was the use of postoperative PCA. In general, PCA is typically used for patients experiencing moderate to severe postoperative pain. In our study, we included patients who underwent abdominal surgeries, which are known to cause significant pain in most cases. However, PCA would not be applied in the following conditions: (1) a patient has significant preoperative cognitive impairment or a related history, and cannot understand how to use the PCA device; (2) patients with a history of substance abuse or certain psychiatric conditions that were not suitable for opioids, such as severe renal or hepatic function damage, respiratory depression, or severe nausea and vomiting; and (3) patients refused to use PCA. More details about the PCA protocol of our hospital could refer to our previous publications [23, 24].

Patients were divided into two groups: those who received PCA and those who did not. For patients receiving PCA, the analgesia was initiated upon returning to the ward from the operating rooms. The PCA could be administered either intravenously (PCIA) or epidurally (PCEA). Predefined PCA parameters, including background dosage, bolus dosage, limited interval time, and hourly limits, were set by the attending anesthesiologists. Early education and postoperative adjustment of PCA parameters were provided to patients and their families, ensuring effective utilization of PCA for alleviating pain in elderly patients at rest or during activities (no or mild postoperative pain). For patients who did not receive PCA, pain relief was provided by surgeons/intensive care unit (ICU) doctors, such as non-steroidal anti-inflammatory drugs, tramadol, continuous intravenous opioid analgesia, etc., to ensure no or mild postoperative pain. Regardless of PCA or non-PCA management, the goal was to keep the Numeric Rating Scale (NRS) score under 4 for all patients.

### Endpoints

The primary endpoint of this study was the prevalence of PPCs. PPCs were diagnosed using the Melbourne Group Scale Version 2 (MGS-2) criteria [25, 26]. The MGS-2 is an assessment tool designed to detect PPCs and has been validated across various surgical populations, including post-upper abdominal surgery [26]. Information collected for PPC diagnosis included respiratory symptoms, pulmonary imaging, and functional examination (See Supplementary Table 1 for the criteria for diagnosing PPCs using MGS-2). If participants were discharged from the hospital within one week after surgery, it was assumed that they did not develop a PPC. This judgement is based on the discharge criteria at our hospital, which include: (1) infection indicators (PCT, WBC, N%) being either normal or showing a significant improvement trend on the day of discharge; (2) recovery of gastrointestinal function and dietary tolerance; (3) adequate pain control with oral analgesia to maintain a pain visual analog score below 5; (4) ability to perform self-care as before or having adequate post-discharge support; (5) no evidence of complications or untreated medical problems; and (6) patient willingness to leave. Therefore, if patients are able to be discharged within one week, we assume that they have no evidence of complications or untreated medical problems, including PPCs.

Secondary endpoints included other clinical outcomes, such as postoperative length of hospital stay (LHS), rate of unplanned postoperative ICU admissions, and in-hospital mortality. Additionally, postoperative pain management data (PCA routes, morphine milligram equivalents (MMEs) of opioid analgesics hours after surgery, total number of PCA pump presses, and effective press percentage) were reported.

### Quantitative variables

The total amount of opioids used for postoperative analgesia was converted to a daily intravenous morphine milligram equivalent dose according to the previous study [27].

### Statistical analysis

We did not perform a power analysis as we included all elderly patients undergoing upper abdominal surgeries in our hospital from 2017 to 2019. Continuous variables are expressed as the mean ± standard deviation or the median (interquartile range, IQR), while categorical variables are expressed as numbers and percentages. The t-tests or nonparametric tests were used to compare continuous variables, and $\chi 2$ tests were used to compare categorical variables.

We used a directed acyclic graph to identify the potential confounders, and guide the modeling strategy [28, 29]. For the primary analysis, the minimally sufficient adjustment variables were determined based on the directed acyclic graph (Fig. 1) using the "dagitty" package in R software. Multivariable logistic regression analysis with the minimally sufficient adjustment variables were used to investigate the risk factors of PPCs in elderly patients undergoing upper abdominal surgery and the association between the application of PCA and PPCs. A sensitivity multivariable analysis was also performed by including variables with a P-value less than 0.25 in univariate logistic regression analyses. If two continuous variables had an absolute Pearson's or Spearman's rank correlation coefficient greater than 0.5, we included only one variable to avoid collinearity [30]. In addition, we performed another sensitivity analysis using propensity score matching to verify the result of multivariable regression analysis.

Subgroup analysis was conducted by the following variables: age (60 to 70, 70 to 80, and 80 years or older), sex, body mass index (less than 25 vs. 25 or more), surgery site (stomach, liver/biliary tract, and pancreas), type of surgery (open vs. not open), preoperative pulmonary function, and length of surgery (less than 3 vs. 3 h or more). The heterogeneity of effects across subgroups was evaluated by testing the significance of the exposure-by-group interaction in the multivariable logistic regression models.

In addition, we used propensity score matching to investigate the relationship between different analgesic methods (PCIA vs. PCEA) and opioid drugs (sufentanil vs. hydromorphone) in relation to PPC incidence. The same variables from the multivariable regression were

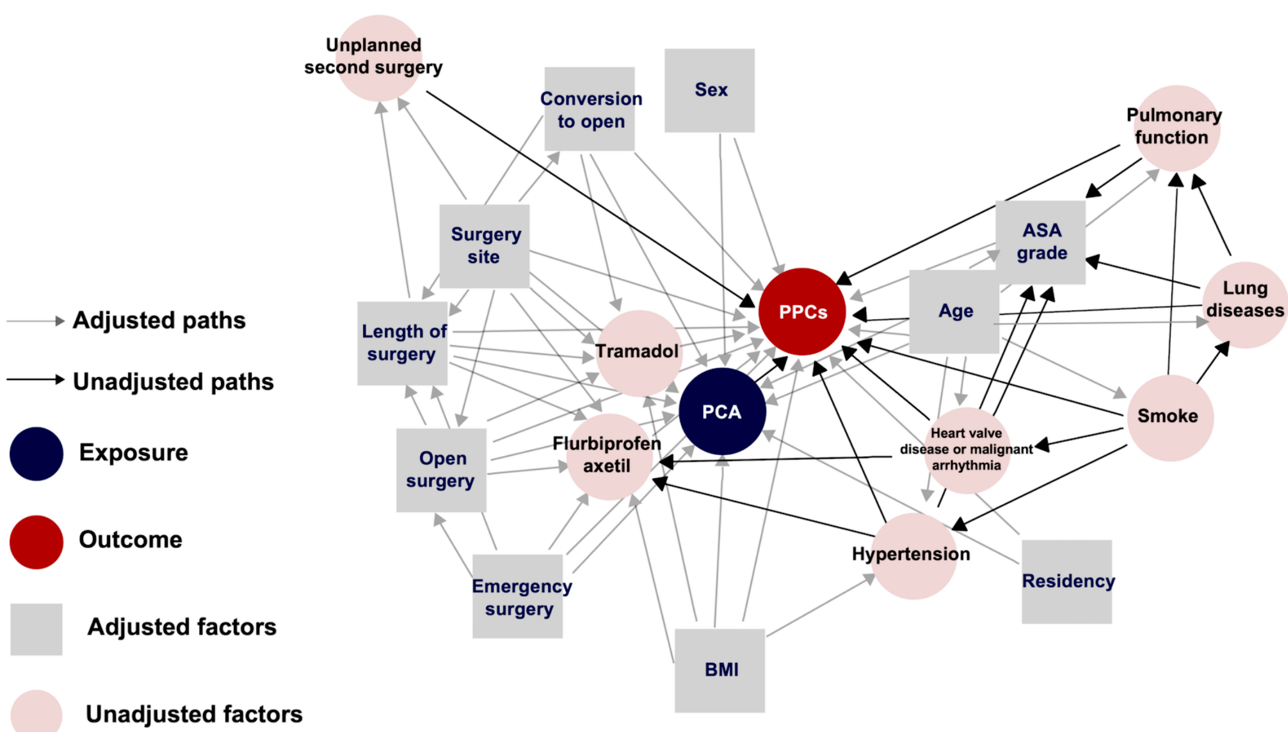


**Fig. 1** A directed acyclic graph represents associations between covariates and primary exposure and outcome. The adjusted arrows represent paths that are being adjusted for in the analysis, indicating confounding variables or backdoor paths that need to be controlled for to estimate the causal effect of interest. The unadjusted arrows represent paths that are not being adjusted for in the analysis, indicating direct effects or other relationships that do not require adjustment. PPCs, postoperative pulmonary complications; PCA, patient-controlled analgesia, BMI, body mass index; ASA, American Society of Anesthesiologists

included in the propensity score matching model. The balance between matched pairs was assessed using standardized differences, with a standardized difference < 10% regarded as indicative of balance. In cases where achieving a standardized difference below 10% for all variables was unfeasible, it was also deemed acceptable if only several variables exhibited a standardized difference below 20%.

P values less than 0.05 were considered statistically significant. All statistical analyses were conducted using R (version 4.3.1, R Foundation for Statistical Computing, Austria) and SPSS 26.0 (IBM, Armonk, NY, USA).

## Results

### Baseline data and PPCs

The final analysis included 1,467 patients, as depicted in the flowchart (Fig. 2). The median age of the patients was 66 years, with 70.4% being male. Among them, 127 patients (8.7%) were diagnosed with PPCs. The incidence and distribution of MGS-2 diagnostic items among patients with and without PPCs are illustrated in Supplementary Fig. 1. Detailed baseline characteristics of patients with or without PPCs are summarized in Table 1. Notably, patients diagnosed with PPCs exhibited an extended LHS and higher 90-day mortality rates (Table 1). Analysis of the thirteen deceased patients revealed that 31% (4 out of 13) had PPCs (Supplementary Table 1).

### The association between PCA and PPCs

PCA and other 18 variables were incorporated into the directed acyclic graph (Fig. 2). The minimally sufficient adjustment sets consisted of 10 confounders, including age, sex, ASA grade, BMI, surgical site, length of surgery, conversion to open surgery, open surgery, emergency surgery, and residency. These were included in the multivariable logistic regression model. The results showed that PCA was a significant beneficial factor for preventing PPCs (odds ratio [95% confidence interval], 0.208 [0.121 ~ 0.358], $P$ < 0.001; Table 2).

### Sensitivity analysis

The first sensitivity analysis was the multivariable logistic regression based on selected variables with P-value less than 0.25 in the univariate analyses (Supplementary Table 3). Consistent with the primary analysis, the sensitivity analysis also demonstrated that PCA was a significant beneficial factor for preventing PPCs (odds ratio [95% confidence interval], 0.187 [0.106 ~ 0.329], $P$ < 0.001; Supplementary Table 4). The second sensitivity analysis with propensity score generated two well balanced cohorts: one comprising 267 patients who received PCA and the other comprising 95 patients who did not receive PCA (Table 3). This analysis revealed a reduced incidence of PPCs in patients who received PCA (PCA vs. non-PCA, 23/267 [8.6%] vs. 25/95 [26.3%], $P$ < 0.001; Table 3).

### Subgroup analysis

The results of subgroup analysis are presented in Fig. 3. PCA was associated with a reduced risk of PPCs across age groups (60 ~ 70, 70 ~ 80, or over 80 years old; Fig. 3), but the effectiveness did not show significant difference across these groups (P for interaction = 0.729). The characteristics of patients in different age groups are detailed in Supplementary Table 5. The subgroup analysis also suggested that PCA was associated with significantly lower rate of PPCs in patients with a body mass index ≤ 24 (P for interaction = 0.033), receiving open surgery (P for interaction = 0.020), and without preoperative pulmonary decline (P for interaction = 0.045). In addition,

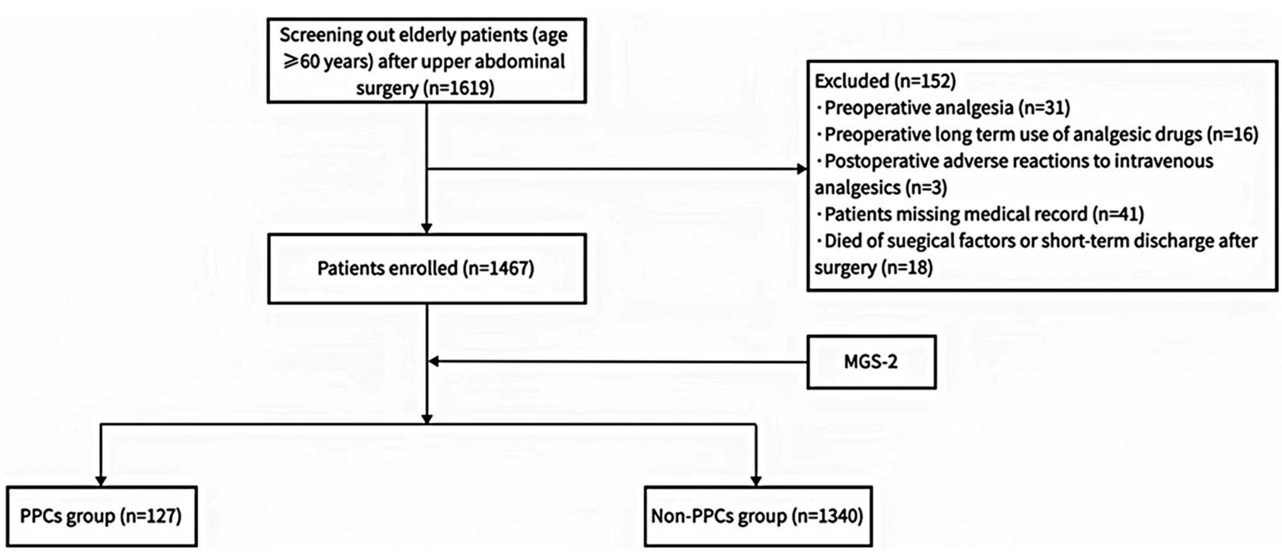


**Fig. 2** Patients enrolling flowchart. PPCs, postoperative pulmonary complications; MGS-2, Melbourne group scale Version 2

**Table 1** Baseline characteristics and clinical outcomes of all patients ($n = 1,467$)

| Variables | Total patients ($n = 1,467$) | Patients with PPCs ($n = 127$) | Patients without PPCs ($n = 1,340$) | *P* |
|---|---|---|---|---|
| **Baseline characteristics** | | | | |
| Age [years, M ($P_{25}$, $P_{75}$)] | 66 (60, 70) | 68 (63, 75) | 66 (62, 70) | 0.001 |
| 60 ~ 70 [n (%)] | 1,109 (75.6) | 76 (59.8) | 1,033 (77.1) | < 0.001 |
| 70 ~ 80 [n (%)] | 303 (20.7) | 36 (28.3) | 267 (9.9) | |
| > 80 [n (%)] | 55 (3.7) | 15 (11.8) | 40 (3.0) | |
| Male [n (%)] | 1033 (70.4) | 107 (84.3) | 926 (69.1) | 0.001 |
| Weight [kg, M ($P_{25}$, $P_{75}$)] | 59 (52, 66) | 59 (53, 64) | 58 (52, 66) | 0.619 |
| BMI [kg/$m^2$, M ($P_{25}$, $P_{75}$)] | 21.9 (19.8, 24.0) | 22.0 (20.0, 24.4) | 21.9 (19.8, 23.9) | 0.566 |
| Residency [n (%)] | | | | 0.737 |
| Urban | 904 (61.6) | 76 (59.8) | 828 (61.8) | |
| Rural | 563 (38.4) | 51 (40.2) | 512 (38.2) | |
| Smoke [n (%)] | 419 (28.6) | 46 (36.2) | 373 (27.8) | 0.058 |
| Pulmonary function [n (%)] | | | | < 0.001 |
| No decline | 1,376 (93.8) | 108 (85.0) | 1,268 (94.6) | |
| Moderate decline | 62 (4.2) | 9 (7.1) | 53 (4.0) | |
| Severe decline | 29 (2.0) | 10 (7.9) | 19 (1.4) | |
| Preoperative comorbidities [n (%)] | | | | |
| Lung diseases | 310 (21.1) | 49 (38.6) | 261 (19.5) | < 0.001 |
| Myasthenia gravis | 1 (0.1) | 0 (0.0) | 1 (0.1) | > 0.999 |
| Hypertension | 450 (30.7) | 54 (42.5) | 396 (29.6) | 0.003 |
| Heart valve disease or malignant arrhythmia | 94 (6.4) | 14 (11.0) | 80 (6.0) | 0.042 |
| ASA III/IV [n (%)] | 343 (23.3) | 58 (45.7) | 285 (21.3) | < 0.001 |
| Surgery site [n (%)] | | | | 0.075 |
| Stomach | 556 (37.9) | 60 (47.2) | 496 (37) | |
| Liver & Biliary tract | 715 (48.7) | 53 (41.7) | 662 (49.4) | |
| Pancreas | 196 (13.4) | 14 (11.0) | 182 (13.6) | |
| Open surgery [n (%)] | 1,108 (75.5) | 102 (80.3) | 1,006 (75.1) | 0.228 |
| Emergency surgery [n (%)] | 25 (1.7) | 13 (10.2) | 12 (0.9) | < 0.001 |
| Unplanned second surgery [n (%)] | 39 (2.6) | 18 (14.2) | 21 (1.6) | < 0.001 |
| Conversion to open surgery [n (%)] | 47 (3.2) | 6 (4.7) | 41 (3.1) | 0.451 |
| Length of surgery [min, M ($P_{25}$, $P_{75}$)] | 270 (200, 347) | 315 (240, 425) | 265 (200, 340) | < 0.001 |
| Length of surgery > 3 h [n (%)] | 1,185 (80.7) | 112 (88.2) | 1,073(80.1) | 0.036 |
| Postoperative PCA [n (%)] | 1,359 (92.7) | 94 (74.0) | 1,265 (94.4) | < 0.001 |
| PCEA | 125 (8.5) | 11 (8.7) | 114 (8.5) | > 0.999 |
| PCIA | 1,234 (84.1) | 83 (65.4) | 1,151 (85.9) | < 0.001 |
| Other postoperative analgesia | | | | |
| Flurbiprofen axetil, iv [n (%)] | 630 (42.9) | 69 (54.3) | 561 (41.9) | 0.009 |
| Tramadol, iv [n (%)] | 498 (33.9) | 61 (48.0) | 437 (32.6) | 0.001 |
| Total MME within postoperative 3 days [mg, M ($P_{25}$, $P_{75}$)] | 53.6 (32.4, 90.0) | 53.8 (36.1, 84.0) | 53.6 (32.3, 90.0) | 0.875 |
| Number of total bolus [number, M ($P_{25}$, $P_{75}$)] | 8 (3, 16) | 9 (3, 17) | 8 (3, 16) | 0.225 |
| Percentage of effective bolus [%, M ($P_{25}$, $P_{75}$)] | 91 (77, 100) | 89 (71, 100) | 92 (77, 100) | 0.091 |
| **Clinical outcomes** | | | | |
| Total LHS [days, M ($P_{25}$, $P_{75}$)] | 19.0 (15.0, 25.0) | 30.0 (23.0, 46.0) | 18.0 (14.0, 24.0) | < 0.001 |
| Postoperative LHS [days, M ($P_{25}$, $P_{75}$)] | 10.0 (8.0, 14.0) | 21.0 (14.0, 37.0) | 10.0 (8.0, 13.0) | < 0.001 |
| 30-day mortality [n (%)] | 8 (0.5) | 0 (0.0) | 8 (0.1) | 0.808 |
| 90-day mortality [n (%)] | 13 (0.9) | 4 (0.3) | 9 (0.1) | 0.019 |

PPCs, postoperative pulmonary complications; BMI, body mass index; ASA, American Society of Anesthesiologists; PCA, patient-controlled analgesia; PCEA, patient-controlled epidural analgesia; PCIA, patient-controlled intravenous analgesia; iv, intravenous therapy drip; MME, morphine milligram equivalents; LHS, length of hospital stay

The continuous variables presented in this table did not follow normal distribution. Therefore, continuous data were presented as median (M), and interquartile range ($P_{25}$, $P_{75}$)

**Table 2** Results of multivariable logistic regression based on variables selected using the directed acyclic graph ($n=1,467$)

| | OR | 95% CI | *P* |
|---|---|---|---|
| PCA | 0.208 | 0.121 ~ 0.358 | < 0.001 |
| Confounder | | | |
| Age | 1.062 | 1.028 ~ 1.097 | < 0.001 |
| Male | 2.818 | 1.634 ~ 4.859 | < 0.001 |
| ASA III or IV | 2.057 | 1.334 ~ 3.172 | 0.001 |
| BMI | 1.071 | 1.007 ~ 1.139 | 0.028 |
| Surgical site | | | |
| Stomach | Ref. | Ref. | Ref. |
| Liver & Biliary tract | 0.724 | 0.468 ~ 1.121 | 0.148 |
| Pancreas | 0.537 | 0.270 ~ 1.068 | 0.076 |
| Length of surgery | 1.004 | 1.003 ~ 1.005 | < 0.001 |
| Conversion to open surgery | 1.117 | 0.423 ~ 2.949 | 0.823 |
| Open surgery | 1.702 | 1.031 ~ 2.808 | 0.038 |
| Emergency surgery | 3.984 | 1.354 ~ 11.72 | 0.012 |
| Residency | 0.851 | 0.565 ~ 1.283 | 0.442 |

OR, odds ratio; CI, confidence interval; PCA, patient-controlled analgesia; ASA, American Society of Anesthesiologists; BMI, body mass index. Ref., reference

patients who received PCA exhibited a lower rate of PPCs across different genders and surgical sites.

### The association between different analgesic methods and opioid drugs of PCA with PPCs

Further categorization of patients receiving PCA into distinct groups facilitated an exploration of the relationship between analgesic methods/opioid drugs and PPCs. Following propensity-score matching, patients receiving PCIA or PCEA exhibited balanced baseline characteristics (Supplementary Table 6). Results indicated no significant differences in PPCs, unplanned ICU transfers, postoperative LHS, or in-hospital mortality, irrespective of whether the patients received PCIA or PCEA (Table 4). Similarly, patients receiving hydromorphone or sufentanil demonstrated balanced baseline characteristics after propensity score matching (Supplementary Table 7). There were no differences in the aforementioned outcomes between patients who received hydromorphone or sufentanil postoperatively (Table 5).

## Discussion

### Key results

In this study, we observed a PPC incidence of 8.7% among elderly patients undergoing upper abdominal surgery. One in every five patients with PPCs required transfer to the ICU and reintubation. Based on multivariable analysis, we observed that PCA was associated with a reduced incidence of PPCs in elderly patients following upper abdominal surgery. The result was further validated by a sensitivity analysis using propensity score matching. Additionally, after categorizing patients receiving PCA into different groups, we observed no significant differences in PPCs, unplanned ICU transfers, postoperative LHS, or in-hospital mortality, regardless of the analgesic methods (PCIA vs. PCEA) and opioid drugs (hydromorphone vs. sufentanil).

### Interpretation

#### *Risk and beneficial factors for PPCs*

The study identified several factors influencing the occurrence of PPCs in elderly patients undergoing upper abdominal surgery. Consistent with previous findings [31], a history of preoperative pulmonary disease was an independent risk factor for PPCs [32]. At the medical center where this study was conducted, elderly patients undergoing upper abdominal surgery are required to undergo routine respiratory mechanics and pulmonary imaging (X-ray or CT) exams. We speculate that in the post-COVID era, the prevalence and detection rate of preoperative pulmonary disease screening will improve, aiding in the accurate preoperative diagnosis of pulmonary diseases, thereby enabling clinicians to take preventive measures against PPCs more promptly. In addition, age has consistently been a risk factor for PPCs [10, 12], with 80 years being a noteworthy threshold where the incidence of PPCs rapidly increases from 7.9 to 27.3% (≤80 vs. >80 years old), emphasizing the imperative to address controllable factors in order to mitigate PPC risk in elderly patients. Some of these factors are indeed controllable and adjustable, such as postoperative analgesia method, surgical duration, surgical approach, and secondary surgery.

#### *Interventions for PPC reduction*

Several established interventions may contribute to lowering the incidence of PPCs, including promoting enhanced recovery [33], epidural analgesia [34], prophylactic respiratory physiotherapy [35], goal-directed hemodynamic therapy [36], prophylactic sputum clearance, intraoperative lung-protective ventilation, and postoperative continuous positive airway pressure [37]. The combined use of the first four interventions has been shown to reduce the relative risk of PPCs by 25% [37]. In this study, we focused on the relationship between perioperative pain management strategies and the risk of PPCs.

Previous studies have demonstrated the role of PCA in alleviating postoperative pain and facilitating postoperative mobility [38, 39]. PCA may also reduce respiratory muscle dysfunction and enhance ventilatory efficiency [40], potentially preventing PPCs. However, the effectiveness of PCA depends on adequate analgesic education and timely adjustment of analgesic parameters. Improperly use of PCA may cause respiratory depression and decrease minute ventilation, contributing to PPCs [19]. Although prior studies indicated that PCA may reduce PPCs, these studies were limited by sample sizes and

**Table 3** Sensitivity analysis: the impact of PCA on clinical outcomes before and after propensity-score matching

| Variables | Pre-PSM (*n* = 1,467) | | | Post-PSM (*n* = 372) | | |
|---|---|---|---|---|---|---|
| | PCA (*n* = 1,359) | Non-PCA (*n* = 108) | SMD | PCA (*n* = 267) | Non-PCA (*n* = 95) | SMD |
| **Baseline data** | | | | | | |
| Age [years, M ($P_{25}$, $P_{75}$)] | 66.0 (62.5, 70.0) | 65.0 (62.0, 72.0) | 0.129 | 66.0 (62.5, 71.5) | 65.0 (62.0, 71.5) | 0.014 |
| Male [n (%)] | 955 (70.3) | 78 (72.2) | 0.043 | 187 (70.0) | 69 (72.6) | 0.057 |
| Weight [kg, M ($P_{25}$, $P_{75}$)] | 59.0 (52.0, 66.0) | 58.0 (51.8, 64.0) | 0.071 | 60.0 (53.0, 66.0) | 58.0 (52.1, 65.0) | 0.029 |
| BMI [kg/m$^2$, M ($P_{25}$, $P_{75}$)] | 21.9 (19.8, 24.0) | 21.6 (19.6, 24.0) | 0.022 | 22.2 (20.6, 24.4) | 22.3 (20.3, 24.4) | 0.038 |
| Residency [n (%)] | | | | | | |
| Urban | 839 (61.7) | 65 (60.2) | 0.032 | 178 (66.7) | 59 (62.1) | 0.095 |
| Rural | 520 (38.3) | 43 (39.8) | | 89 (33.3) | 36 (37.9) | |
| Smoke [n (%)] | 389 (28.6) | 30 (28.0) | 0.019 | 80 (30.0) | 28 (29.5) | 0.011 |
| Pulmonary function [n (%)] | | | 0.209 | | | 0.100 |
| No decline | 1,278 (94.1) | 98 (90.7) | | 256 (95.9) | 89 (93.7) | |
| Moderate decline | 57 (4.2) | 4 (3.7) | | 7 (2.6) | 4 (4.2) | |
| Severe decline | 23 (1.7) | 6 (5.6) | | 4 (1.5) | 2 (2.1) | |
| Preoperative comorbidities [n (%)] | | | | | | |
| Lung diseases | 287 (21.1) | 23 (21.5) | 0.209 | 52 (19.5) | 16 (16.8) | 0.068 |
| Myasthenia gravis | 1 (0.1) | 0 (0.0) | 0.038 | 1 (0.4) | 0 (0.0) | 0.087 |
| Hypertension | 410 (30.2) | 40 (37.4) | 0.146 | 94 (35.2) | 34 (35.8) | 0.012 |
| Heart valve disease/ malignant arrhythmia | 88 (6.5) | 6 (5.6) | 0.039 | 12 (4.5) | 4 (4.2) | 0.014 |
| ASA III/IV [n (%)] | 300 (22.1) | 42 (39.3) | 0.391 | 88 (33.0) | 35 (36.8) | 0.076 |
| Surgery site [n (%)] | | | 0.068 | | | 0.084 |
| Stomach | 512 (37.7) | 43 (40.2) | | 88 (33.0) | 35 (36.8) | |
| Liver & Biliary tract | 664 (48.9) | 51 (47.7) | | 142 (53.2) | 47 (49.5) | |
| Pancreas | 182 (13.4) | 13 (12.1) | | 37 (13.9) | 13 (13.7) | |
| Open surgery [n (%)] | 1,039 (76.5) | 68 (63.6) | 0.277 | 156 (58.4) | 58 (61.1) | 0.054 |
| Emergency surgery [n (%)] | 11 (0.8) | 13 (12.1) | 0.494 | 5 (1.9) | 5 (5.3) | 0.184 |
| Unplanned second surgery [n (%)] | 37 (2.7) | 2 (1.9) | 0.058 | 3 (1.1) | 0 (0.0) | 0.151 |
| Conversion to open surgery [n (%)] | 42 (3.1) | 5 (4.7) | 0.080 | 9 (3.4) | 5 (5.3) | 0.093 |
| Length of surgery [min, M ($P_{25}$, $P_{75}$)] | 270 (200, 345) | 265 (193, 378) | 0.038 | 265 (195, 373) | 275 (185, 378) | 0.022 |
| Length of surgery > 3 h [n (%)] | 1,103 (81.2) | 81 (75.7) | 0.151 | 214 (80.1) | 71 (74.7) | 0.130 |
| Other postoperative analgesia | | | | | | |
| Flurbiprofen axetil, iv [n (%)] | 585 (43.0) | 45 (41.7) | 0.028 | 110 (41.2) | 43 (45.3) | 0.082 |
| Tramadol, iv [n (%)] | 839 (61.7) | 65 (60.2) | 0.152 | 87 (32.6) | 41 (43.2) | 0.219 |
| **Clinical outcomes** | **PCA** (*n* = 1,359) | **Non-PCA** (*n* = 108) | ***P*** | **PCA** (*n* = 267) | **Non-PCA** (*n* = 95) | ***P*** |
| PPCs [n (%)] | 94 (6.9) | 33 (30.6) | < 0.001 | 23 (8.6) | 25 (26.3) | < 0.001 |
| Unplanned transfer to ICU [n (%)] | 20 (1.5) | 10 (9.3) | < 0.001 | 3 (1.1) | 8 (8.4) | 0.001 |
| Postoperative LHS [day, M ($P_{25}$, $P_{75}$)] | 10 (8, 14) | 10 (7, 17) | 0.973 | 11 (8, 15) | 10 (7, 16) | 0.572 |
| In-hospital mortality [n (%)] | 8 (0.6) | 5 (4.6) | < 0.001 | 2 (0.7) | 5 (5.3) | 0.021 |

PCA, patient-controlled analgesia; PSM, propensity-score matching; SMD, standardized mean difference; BMI, body mass index; ASA, American Society of Anesthesiologists; PPCs, postoperative pulmonary complications; ICU, intensive care unit; LHS, length of hospital stay; SMD, standard mean difference

The covariates we used for propensity score method include: age, male, smoke, BMI, surgical site, lung diseases, heart valve disease/ malignant arrhythmia, ASA III/IV grade, open surgery, emergency surgery, length of surgery, unplanned second surgery, hypertension, and pulmonary function. We used a caliper width of 0.1 of the standard deviation of logit of propensity score

specific types of surgery (such as cardiac or thoracic surgery) [41–43]. The role of PCA in reducing PPCs in elderly patients has not been fully explored.

Elderly patients are inherently frail and more sensitive to opioids compared to younger people, making them more susceptible to opioid-related side effects such as respiratory depression, dizziness, drowsiness, and hypotension. Our study emphasizes the role of PCA in elderly patients undergoing abdominal surgery, and observed the effectiveness of PCA in reducing PPCs in different age groups of elderly patients. Given the severity and humanitarian concerns of pain in upper abdominal surgery, 92.6% of elderly patients received PCA. Although there was a significant imbalance in the number of patients between the PCA and non-PCA groups in the entire population, this discrepancy does not imply frailty or more comorbidities in the non-PCA group. In fact, non-PCA patients often declined PCA due to economic reasons (postoperative analgesia not fully covered by medical insurance in China) and fear of side effects of analgesics

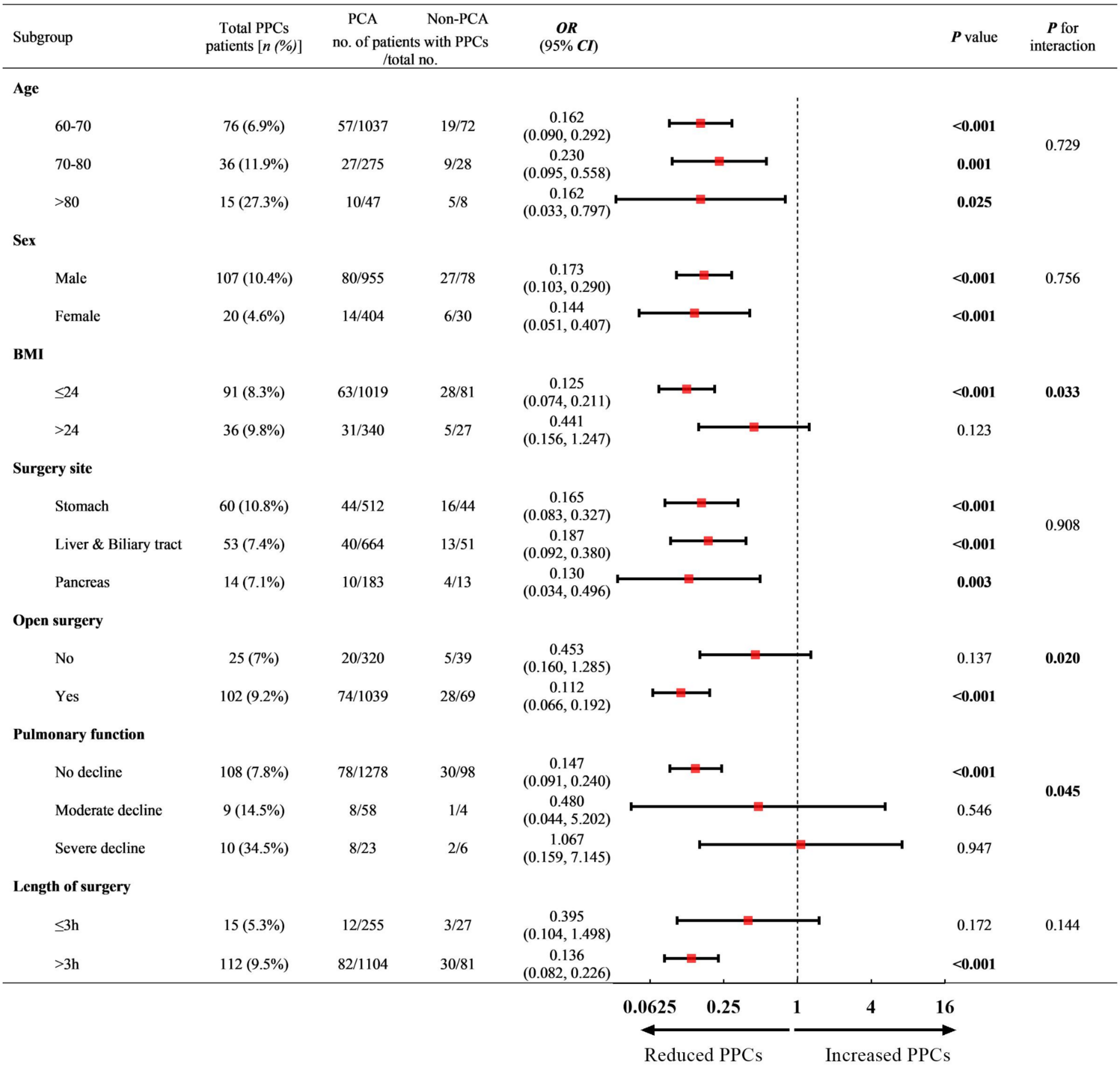


**Fig. 3** Results of subgroup analysis. PPCs, postoperative pulmonary complications; PCA, patient-controlled analgesia; OR, odds ratio; BMI, body mass index

**Table 4** The impact of type of PCA on clinical outcomes before and after propensity-score matching

| Variables | Pre-PSM ($n=1,359$) | | | Post-PSM ($n=491$) | | |
|---|---|---|---|---|---|---|
| | PCIA ($n=1,234$) | PCEA ($n=125$) | *P* | PCIA ($n=367$) | PCEA ($n=124$) | *P* |
| PPCs [n (%)] | 83 (6.7) | 11 (8.8) | 0.493 | 27 (7.4) | 11 (8.9) | 0.726 |
| Unplanned transfer to ICU [n (%)] | 17 (1.4) | 3 (2.4) | 0.607 | 6 (1.6) | 3 (2.4) | 0.860 |
| Postoperative LHS [d, M ($P_{25}$, $P_{75}$)] | 10 (8, 14) | 11 (8, 15) | 0.038 | 11 (8, 15) | 11 (8, 15) | 0.727 |
| In-hospital mortality [n (%)] | 8 (0.6) | 0 (0) | 0.772 | 4 (1.1) | 0 (0) | 0.556 |

PCA, patient-controlled analgesia; PSM, propensity-score matching; PCIA, patient-controlled intravenous analgesia; PCEA, patient-controlled epidural analgesia; PPCs, postoperative pulmonary complications; ICU, intensive care unit; LHS, length of hospital stay

**Table 5** The impact of type of analgesics on clinical outcomes before and after propensity-score matching

| Variables | Pre-PSM (*n* = 1,042) | | | Post-PSM (*n* = 964) | | |
|---|---|---|---|---|---|---|
| | Hydromorphone (*n* = 781) | Sufentanil (*n* = 261) | *P* | Hydromorphone (*n* = 705) | Sufentanil (*n* = 259) | *P* |
| PPCs [n (%)] | 55 (7.0) | 20 (7.7) | 0.843 | 44 (6.2) | 20 (7.7) | 0.501 |
| Unplanned transfer to ICU [n (%)] | 12 (1.5) | 3 (1.1) | 0.877 | 8 (1.1) | 3 (1.2) | > 0.999 |
| Postoperative LHS [day, M ($P_{25}$, $P_{75}$)] | 10 (8, 14) | 10 (8, 14) | 0.473 | 10 (8, 14) | 10 (8, 14) | 0.663 |
| In-hospital mortality [n (%)] | 5 (0.6) | 3 (1.1) | 0.684 | 5 (0.7) | 3 (1.2) | 0.779 |

PSM, propensity-score matching; PPCs, postoperative pulmonary complications; ICU, intensive care unit; LHS, length of hospital stay

[44–46]. To minimize the bias from this imbalance, we matched baseline data for patients in both PCA and non-PCA groups and found that postoperative PCA was still associated with a lower risk of PPCs in elderly patients undergoing major upper abdominal surgery.

Continuous thoracic epidural analgesia (TEA) was once considered the best analgesic method after abdominal surgery [34, 47], achieving effective analgesia by blocking visceral and somatic pain signals to the spinal cord. However, recent high-quality studies have shown that TEA increases the risk of hypotension and arrhythmias after thoracic surgery [48, 49]. TEA may also impair postoperative lung function by paralyzing respiratory muscles such as intercostal or abdominal muscles [50]. At the center where this dataset was collected, thoracic segment PCEA is mainly used for patients undergoing upper abdominal surgery via laparotomy. However, with the increased adoption of laparoscopic minimally invasive techniques over the years, the proportion of patients experiencing moderate to severe pain after upper abdominal surgery has significantly decreased. Additionally, with the development of multimodal analgesia, auxiliary analgesic measures including local infiltration anesthesia at the wound site, early initiation of oral NSAIDs, traditional Chinese acupuncture, and family-like accompaniment, the demand for traditional opioid analgesics in elderly patients has gradually decreased. Therefore, even low-dose opioid-based patient-controlled intravenous analgesia can achieve effective analgesic effects while reducing interference with respiration and effective coughing [51]. This may explain why there was no difference in the incidence of PPCs between the PCEA and PCIA groups in this dataset whether confounding factors were matched or not, as well as the choice between the water-soluble opioid (hydromorphone) and the lipophilic opioid (sufentanil) in PCIA did not show a significant association with the occurrence of PPCs. From another perspective, compared to the operational difficulty of epidural puncture in elderly patients, PCIA may serve as a more achievable alternative to PCEA for anesthesiologist.

### Generalizability

One of the strengths of our study was the focus on a high-risk population. Preventing PPCs in elderly patients posed greater challenges and clinical significance compared to younger patients. Reducing the delayed discharge rates and mortality associated with PPCs significantly impacted the acceleration of recovery of life quality in elderly patients and alleviated societal burdens. Additionally, pain following upper abdominal surgery is typically more severe [52], with movement pain notably impacting respiratory function [53, 54]. This study concentrated on the effects of PCA on PPCs in elderly patients.

However, it is essential to consider the limitations in generalizing our findings. Our sample primarily consists of elderly patients who underwent upper abdominal surgery, which may not represent all elderly patients or those undergoing different types of surgeries because the severity of postoperative pain and PCA's side effect can vary significantly depending on the surgical procedure and patient demographics. Although an increasing number of surgeons and pain specialists have recognized the importance of PCA in controlling excessive stress in patients undergoing major surgery and in protecting organ functions, few studies have directly correlated postoperative analgesia with adverse outcomes, possibly due to the heterogeneity of analgesic regimens across different studies. Therefore, caution should be exercised when extrapolating these results to other populations or surgical contexts. Further studies with diverse cohorts and standardized analgesic protocols are needed to validate our results and enhance the generalizability of our conclusions.

### Limitations

The results of this study should be interpreted in light of its limitations. One limitation is the sourcing of patient data from a single center, which limits the extrapolation and scalability of our findings over time and impedes the external validation of the discovered results. Secondly, several factors may influence the application of PCA but the information could not be collected in this retrospective study, such as the income of patients, pre- and postoperative cognitive decline assessments, or anxiety. Third, unobserved or latent variables associated with PPCs might have been missing, such as prophylactic respiratory physiotherapy, goal-directed hemodynamic therapy, the specific days required to start standing and walking postoperatively, and postoperative pain intensity. Although strategies were employed to minimize the impacts of these limitations, the inherent limitations of this retrospective study could not be completely eliminated. Fourth, we judged a patient who was discharged from the hospital within one week after surgery, as not having PPC. Although this judgement is based on the discharge criteria at our hospital, we cannot entirely rule out the possibility that some patients may develop PPCs after discharge. Hence, the existing results should be carefully interpreted in further research with longer follow-up.

## Conclusion

Elderly patients undergoing upper abdominal surgery should take measures to prevent the PPCs. PCA may be beneficial, whether through intravenous or epidural. However, the specific mechanisms and effects of PCA required further prospective research.

## Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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**Author contributions**
Z.X. Wang and Q.L. He designed the study. Z.Y. Lai, S.Y. Peng and G.H Mo. collected and collated the data. Q.L. He, S.Y. Peng and X. Zhao performed statistical analysis and data interpretation. Q.L. H, Z.Y. Lai and Xu Zhao wrote the main manuscript text and prepared the figures and Tables 1, 2, 3, 4 and 5. S.Y. Peng and X. Zhao prepared all the supplemental tables. S.Q. Lin and Z.X. Wang provided guidance for data analysis and the discussion section of the main text. All authors reviewed the manuscript.

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**Data availability**
Data are available upon reasonable request, provided by the corresponding author of the manuscript (Z.X. Wang; E-mail: wzhxing@mail.sysu.edu.cn).

## Declarations

**Ethical approval**
This retrospective study was approved by the ethics committees of the First Affiliated Hospitals of Sun Yat-sen University according to the China Good Clinical Practice (GCP) guidelines and the tenets of the Declaration of Helsinki. The requirement for written consent was waived by the Institutional Review Board of the First Affiliated Hospitals of Sun Yat-sen University (No. 2021 – 395, approval date: Jun 3rd, 2021).

**Consent for publication**
Not applicable.

**Patient and public involvement**
Patients or the public were not involved in setting the research agenda.

**Competing interests**
The authors declare no competing interests.

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