BMJ Open

Predicting risk factors for acute pain after hepatobiliary and pancreatic surgery: an observational case control study

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To cite: Zhang H, Yang YT, Jiang L, *et al*. Predicting risk factors for acute pain after hepatobiliary and pancreatic surgery: an observational case control study. *BMJ Open* 2024;**14**:e078048. doi:10.1136/bmjopen-2023-078048

► Prepublication history for this paper is available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2023-078048).

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Received 22 July 2023
Accepted 19 July 2024

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ABSTRACT

Background Inadequate postoperative analgesia is associated with increased risks of various postoperative complications, longer hospital stay, decreased quality of life and higher costs.

Objectives This study aimed to investigate the risk factors for moderate-to-severe postoperative pain within the first 24 hours and 24–48 hours after major hepatobiliary pancreatic surgery.

Methods Data of patients who underwent surgery at the Department of Hepatobiliary Surgery in Henan Provincial People's Hospital were collected from January 2018 to August 2020. Univariate and multivariate logistic regression analyses were used to identify the risk factors of postoperative pain.

Results In total, 2180 patients were included in the final analysis. 183 patients (8.4%) suffered moderate-to-severe pain within 24 hours after operation. The independent risk factors associated with moderate-to-severe pain 24 hours after procedures were younger age (OR, 0.97; 95% CI 0.95 to 0.98, p<0.001), lower body mass index (BMI) (OR, 0.94; 95% CI 0.89 to 0.98, p=0.018), open surgery (OR, 0.34; 95% CI 0.22 to 0.52, p<0.001), and postoperative analgesia protocol with sufentanil (OR, 4.38; 95% CI 3.2 to 5.99, p<0.001). Postoperative hospital stay was longer in patients with inadequate analgesia (p<0.05).

Conclusion Age, BMI, laparoscopic surgery, and different analgesic drugs were significant predictors of postoperative pain after major hepatobiliary and pancreatic surgery.

Trial registration ChiCTR2100049726.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study finally included more than 2000 cases over nearly 3 years.
⇒ The number of included cases was sufficient.
⇒ It is a single-centre retrospective study.
⇒ It is a risk factor analysis, and is insufficient for the development of a predictive model.

INTRODUCTION

Pain is an unpleasant, subjective, sensory and emotional experience. According to the current literature, approximately 30%–55% of patients suffered moderate or severe pain on the day after surgery.[1–3] The management of postoperative pain is an important aspect of patients' recovery after operation. Inadequate postoperative analgesia is connected with a high risk of pulmonary and cardiac complications, excessive opioid consumption, development of chronic pain, 30-day postoperative complications, prolonged hospital stay, patient dissatisfaction, re-admissions, reduced quality of life, and increased healthcare costs.[2–5] Effective pain management can reduce postoperative complications, improve patient satisfaction and promote patient recovery.

There are multiple reasons for postoperative pain, one of which is that some patients may have certain risk factors for developing more severe postoperative pain. Early identification of these risk factors for postoperative pain may facilitate personalised pain management strategies and prevent unintended distress in patients. Several literatures have reported factors contributing to severe postoperative pain, including demographic, psychosocial and various clinical factors.[4 5] However, few studies have analysed the associated risk factors for postoperative pain in major hepatobiliary pancreatic surgeries (excluding cholecystectomy alone). This study employed a retrospective case-control method to analyse the risk factors associated with moderate-to-severe postoperative pain at 24 hours and 24–48 hours after major hepatobiliary and pancreatic surgery in a hospital in China. Based on our findings, anaesthesiologists can be alerted to identify patients at high risk of experiencing moderate-to-severe pain after surgery, intervene proactively, and

closely monitor and manage postoperative pain to aid in patients' recovery.

METHODS

Written informed patient consent was waived by reason of the retrospective design and minimal intrusion to the privacy of the participants. The trial was registered at the Chinese Clinical Trial Registry (ChiCTR2100049726) on 08 August 2021. Our case-control study report followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[6] All data were extracted from electronic medical records and analysed anonymously. Patients who underwent surgery at the Department of Hepatobiliary Surgery in our hospital (Henan Provincial People's Hospital, Zhengzhou University People's Hospital) between January 2018 and August 2020 were included in this study.

The inclusion criteria were as follows: (1) Age between 18 years and 75 years, (2) American Society of Anesthesiologists (ASA) class I-III, and (3) Patients undergoing elective surgery under general anaesthesia. The exclusion criteria were as follows: (1) Patients with multiple surgeries, (2) Patients transferred to the intensive care unit (ICU) postoperatively, (3) Patients without patient controlled intravenous anaesthesia (PCIA) or with different analgesic regimens, and (4) Patients undergoing cholecystectomy exclusively.

Anaesthesia and analgesia techniques

The protocol for anaesthesia was implemented in routine clinical practice. According to the preoperative fasting guidelines, patients fasted for both solids and fluids before surgery for at least 8 hours. A prophylactic antibiotic was administered 30 min prior to surgery. Upper extremity venous access was established, and blood pressure, ECG, heart rate, and pulse oximetry were routinely monitored. The anaesthesiologist decided whether to perform a single-shot ultrasound-guided nerve block with 30–40 mL of 0.25%–0.33% ropivacaine according to the site of surgery. The decision protocol is mainly based on the type of surgery, the patients' coagulation function, and the personal habits or preferences of the anaesthesiologist. The patients received premedication with 5 mg of dexamethasone and 0.5–1.0 mg of penehyclidine hydrochloride. All patients underwent general anaesthesia with the same type of medication. Anaesthesia was induced with 0.05 mg/kg of midazolam, 0.2–0.3 mg/kg of etomidate, 0.3–0.5 µg/kg of sufentanil and 0.15 mg/kg of cisatracurium or 0.6–0.9 mg/kg rocuronium. Mechanical ventilation was performed after tracheal intubation using a visual laryngoscope with a tidal volume of 6–8 mL/kg and 12 breaths/minute. During maintenance of anaesthesia, combined intravenous-inhalation anaesthesia with propofol (4–6 mg/kg/h), remifentanil (0.2–0.5 µg/kg/min), and sevoflurane (1%–3%) were administered to maintain the Bispectral Index between 40 and 60. The infusion of muscle relaxants was stopped and 5 mg of tropisetron was infused intravenously 30 min before the end of surgery. Patients were transferred to the postanaesthesia care unit for recovery after surgery. Neostigmine and tropine were used to antagonise residual neuromuscular block when necessary. The PCIA pump was attached to all the patients after surgery. It was mainly filled with 2.0–2.5 µg/kg of sufentanil or 8–10 mg of butorphanol with 1–1.5 µg/kg of dexmedetomidine and 10 mg of tropisetron. Additionally, 120–240 mg of ketorolac tromethamine was administered at the same time over the next 2 days. The background continuous rate was 2 mL/hour, and the bolus dose was 2 mL with a 15 min lockout interval. Patients with inadequate analgesia were advised to press the PCIA button, which was defined by a Visual Analogue Scale (VAS)≥4.

Data collection

Demographic characteristics (age, sex, body mass index (BMI) and educational level), comorbidities (hypertension, diabetes mellitus, coronary artery disease and

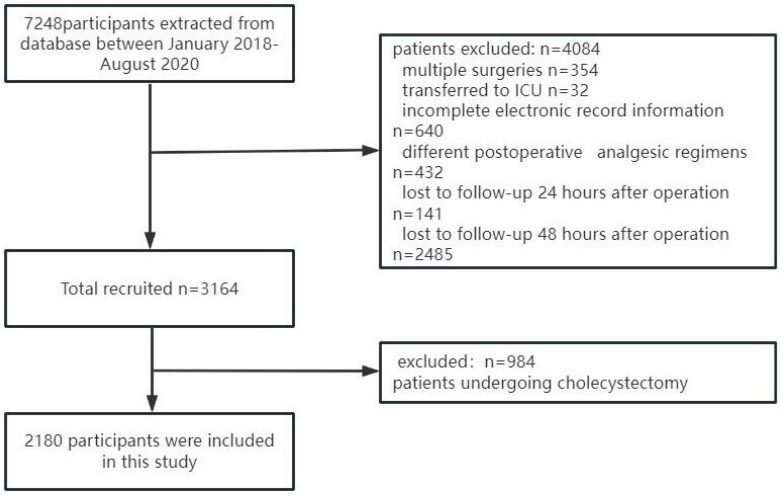

Figure 1 Flow chart detailing the selection process for patients included in this retrospective analysis. ICU, intensive care unit.

Table 1 Demographic characteristics of 2180 participating patients

Variables	Total (n=2180)	No moderate-severe pain within 24 hours (n=1997)	Moderate-severe pain within 24 hours (n=183)	P values
Gender, n (%)				0.15
Male	1265 (58.0)	1168 (58.5)	97 (53)	
Female	915 (42.0)	829 (41.5)	86 (47)	
Age (years)	55.4±11.5	55.8±11.3	51.1±12.5	<0.001
BMI (kg/m^2)	23.7±3.4	23.8±3.4	23.2±2.9	0.018
ASA				0.023
I	49 (2.2)	44 (2.2)	5 (2.7)	
II	1755 (80.5)	1596 (79.9)	159 (86.9)	
III	376 (17.2)	357 (17.9)	19 (10.4)	
Smoking, n (%)				0.4
No	1391 (63.8)	1269 (63.5)	122 (66.7)	
Yes	789 (36.2)	728 (36.5)	61 (33.3)	
Education level, n (%)				0.429
Preliminary school	968 (44.4)	895 (44.8)	73 (39.9)	
Middle school	762 (35.0)	696 (34.9)	66 (36.1)	
College degree	176 (8.1)	157 (7.9)	19 (10.4)	
Bachelor degree	105 (4.8)	98 (4.9)	7 (3.8)	
Postgraduate degree	169 (7.8)	151 (7.6)	18 (9.8)	
History of anaesthesia, n (%)				0.014
No	1161 (53.3)	1056 (52.9)	105 (57.4)	
Yes	805 (36.9)	753 (37.7)	52 (28.4)	
NA	214 (9.8)	188 (9.4)	26 (14.2)	
Hypertension, n (%)				0.005
No	1688 (77.4)	1531 (76.7)	157 (85.8)	
Yes	492 (22.6)	466 (23.3)	26 (14.2)	
Diabetes, n (%)				0.133
No	1900 (87.2)	1734 (86.8)	166 (90.7)	
Yes	280 (12.8)	263 (13.2)	17 (9.3)	
Coronary artery disease, n (%)				0.253
No	2099 (96.3)	1920 (96.1)	179 (97.8)	
Yes	81 (3.7)	77 (3.9)	4 (2.2)	
Cerebral complication, n (%)				0.605
No	2106 (96.6)	1928 (96.5)	178 (97.3)	
Yes	74 (3.4)	69 (3.5)	5 (2.7)	

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

cerebral complications), ASA grade, history of anaesthesia, and smoking were retrospectively collected. In this study, patients were categorised as having a history of smoking if they had smoked daily for over 1 year, irrespective of whether they had quit around the time of surgery.[7] Intraoperative characteristics included the type of surgery, laparoscopic surgery, anaesthetic methods (with or without nerve block), types of nerve block, duration of operation, anaesthesia duration, intraoperative fluid volume, blood loss, urine volume, and blood transfusion. The postoperative days were also recorded. VAS scores during movement and at rest on postoperative day 1 and postoperative day 2 were assessed in our hospital, along with postoperative nausea and vomiting (PONV), and postoperative hospital stay days.

Postoperative pain assessment

Patients' pain was assessed by the acute pain services team members who were trained professionally, using a VAS at 24 hours and 48 hours postoperatively. A

Table 2 Perioperative characteristics of 2180 participating patients

Variables	Total (n=2180)	No moderate-severe pain within 24 hours (n=1997)	Moderate-severe pain within 24 hours (n=183)	P values
Types of surgery, n (%)				0.013
Hepatic resection	897 (41.1)	819 (41)	78 (42.6)	
Pancreatoduodenectomy	184 (8.4)	157 (7.9)	27 (14.8)	
Splenectomy and pancreatectomy	238 (10.9)	225 (11.3)	13 (7.1)	
Surgery for bile duct cancer and gall bladder cancer	187 (8.6)	169 (8.5)	18 (9.8)	
Choledocholithiasis	577 (26.5)	536 (26.8)	41 (22.4)	
Other surgery	97 (4.4)	91 (4.6)	6 (3.3)	
Laparoscopic surgery, n (%)				< 0.001
No	1436 (65.9)	1280 (64.1)	156 (85.2)	
Yes	744 (34.1)	717 (35.9)	27 (14.8)	
Postoperative analgesia protocol, n (%)				< 0.001
Butorphanol	1539 (70.6)	1468 (73.5)	71 (38.8)	
Sufentanil	641 (29.4)	529 (26.5)	112 (61.2)	
Preoperative Hb (g/dL)	126.1±21.2	126.0±21.4	127.9±19.4	0.238
Perioperative blood transfusion, n (%)				0.382
No	1720 (78.9)	1571 (78.7)	149 (81.4)	
Yes	460 (21.1)	426 (21.3)	34 (18.6)	
Anaesthesia duration (min)	249.7±106.7	248.5±106.9	262.1±103.6	0.099
Surgery duration (min)	235.2±105.7	234.0±105.9	248.0±103.0	0.085
Anaesthetic methods, n (%)				0.144
General anaesthesia	237 (10.9)	223 (11.2)	14 (7.7)	
General anaesthesia with nerve block	1943 (89.1)	1774 (88.8)	169 (92.3)	
Nerve block, n (%)				0.395
No	237 (10.9)	223 (11.2)	14 (7.7)	
Thoracic nerve block	1344 (61.7)	1217 (60.9)	127 (69.4)	
Quadratus lumborum block	281 (12.9)	261 (13.1)	20 (10.9)	
TAP	194 (8.9)	181 (9.1)	13 (7.1)	
Rectus sheath block	90 (4.1)	84 (4.2)	6 (3.3)	
Others	34 (1.6)	31 (1.6)	3 (1.6)	
Preoperative days (d)	5.5±3.8	5.5±3.9	5.2±3.2	0.232
Postoperative days (d)	11.5±5.7	11.4±5.7	12.7±6.0	0.004
VAS at rest	1.0 (0.0, 2.0)	0.0 (0.0, 1.0)	5.0 (4.0, 6.0)	< 0.001
VAS at movement	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	6.0 (5.0, 7.0)	< 0.001
Postoperative nausea, n (%)	50 (2.3)	41 (2.1)	9 (4.9)	0.033
Postoperative vomiting, n (%)	29 (1.3)	23 (1.2)	6 (3.3)	0.03

TAP, Transversus Abdominis Plane Block; VAS, Visual Analogue Scale.

score of 0 indicates no pain while a score of 10 indicates the highest level of pain on the VAS.

The patients were categorised into two groups based on the postoperative VAS Scores. The moderate-to-severe pain group (VAS Score ≥4 points), and the group without moderate-to-severe pain (VAS Score <4 points).

Patient and public involvement

None.

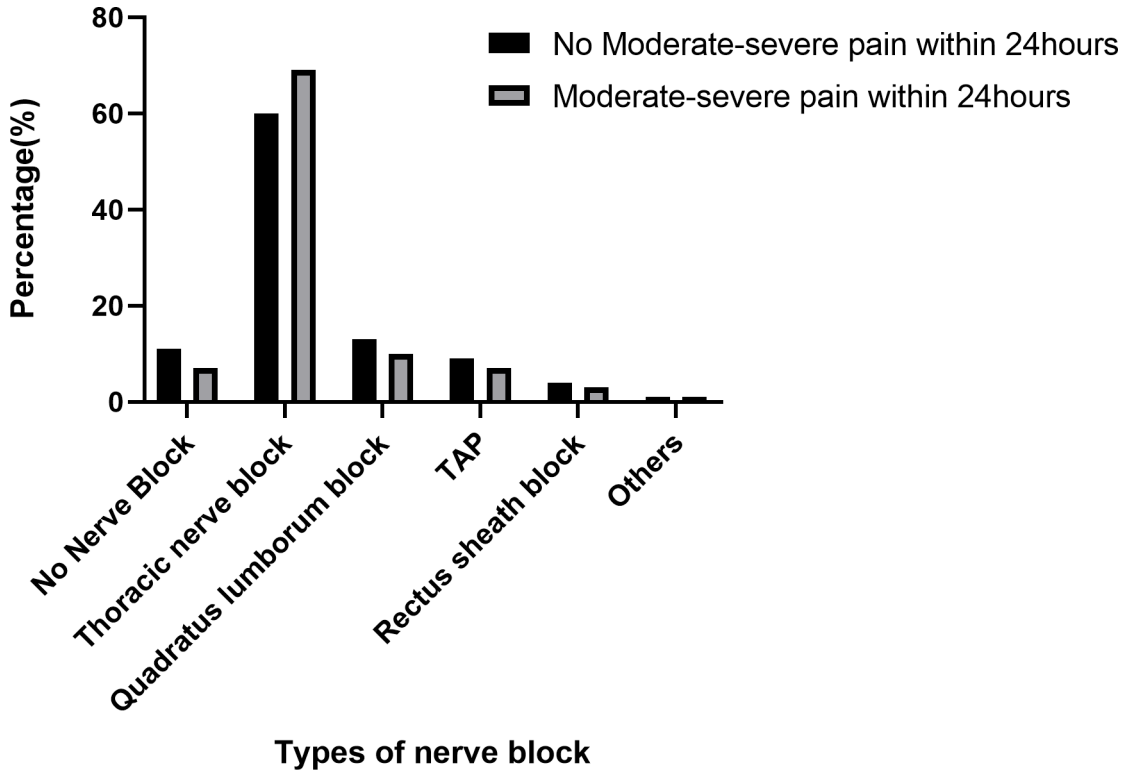

Figure 2 The constituent ratio of the different neural block types between groups of no moderate-severe pain and moderate-severe pain within 24 hours. There is no statistical difference in the two groups. Others means nerve block methods include serratus anterior plane, erector spinae plane block and so on, except the methods mentioned previously. TAP, Transversus Abdominis Plane Block.

STATISTICAL ANALYSIS

Data were reported as mean±SD or median (IQR) for continuous variables and as frequency and percentage for categorical variables. Missing data of outcome variables and those with a missing ratio of more than 20% were deleted. For continuous features, a few missing values were imputed using mean imputation, whereas categorical values were imputed with dummy variables. Continuous variables were analysed using unpaired Student's t-test for normally distributed data or the Mann–Whitney U test. Categorical variables were analysed using the χ^2 test or Fisher's exact test, as appropriate. Independent risk factors were identified using a multivariable logistic regression model that included preoperative and intraoperative variables with p<0.15 in the univariable analysis and ORs and 95% CIs were calculated. Statistical analyses were performed using the R Statistical Software (http://www. R-project. org, The R Foundation) and Free Statistics analysis platform, and p<0.05 was considered to be statistically significant.

RESULTS

A total of 7248 patients underwent hepatobiliary surgery during the study period. Among them, 354 patients were excluded due to multiple surgeries (n=354), incomplete electronic record information (n=640), transfer to the ICU after surgery (n=32), different postoperative analgesic regimens (n=432), no follow-up within 24 hours after operation (n=141), or no follow-up 48 hours after surgery (n=2485). Patients who underwent cholecystectomy alone were also excluded (n=984). Ultimately, 2180 patients were included in the analysis (figure 1).

A total of 183 patients (8.4%) experienced moderate-to-severe pain 24 hours after operation. The baseline characteristics of the study participants are presented in table 1. The demographic characteristics of patients with or without moderate-to-severe pain within 24 hours after surgery were compared (table 1). The average age of the entire group was 55.4±11.5 years with 58.0% of participants being male. In terms of gender, ASA status, smoking, education level, and preoperative complications including diabetes, coronary artery disease and cerebral complications, the two groups were similar (p>0.05). There were statistical differences between the two groups for age (55.8±11.3 vs 51.1±12.5) and BMI (23.8±3.4 vs 23.2±2.9). Furthermore, there was a disparity in the incidence of hypertension between the two groups (23.3% vs 14.2%). The perioperative characteristics of the participants in the two groups are presented in table 2. When considering the types of surgery, there were differences in the proportions between the two groups (p<0.05). Pancreatoduodenectomy was more frequent in the moderate-severe pain within 24 hours group (14.8% vs 7.9%), while for splenectomy and pancreatectomy, the proportions were reversed (7.1% vs 11.3%). The discrepancy between the two groups was significant concerning

Table 3 Univariate and multivariable analyses for moderate-severe postoperative pain within 24 hours

	Univariate analysis		Multivariable analysis	
Variable	OR_95 CI	P value	OR_95 CI	P value
Gender (female)	1.25 (0.92 to 1.69)	0.151	1.32 (0.96 to 1.83)	0.090
Age (years)	0.97 (0.96 to 0.98)	<0.001	0.97 (0.95 to 0.98)	<0.001
BMI (kg/m^2)	0.94 (0.9 to 0.99)	0.018	0.94 (0.89 to 0.98)	0.016
ASA				
I	Reference			
II	0.88 (0.34 to 2.24)	0.784		
III	0.47 (0.17 to 1.32)	0.15		
Smoking				
No	Reference			
Yes	0.87 (0.63 to 1.2)	0.401		
Education level				
Preliminary school	Reference			
Middle school	1.16 (0.82 to 1.65)	0.395		
College degree	1.48 (0.87 to 2.53)	0.146		
Bachelor degree	0.88 (0.39 to 1.95)	0.746		
Postgraduate	1.46 (0.85 to 2.52)	0.171		
History of anaesthesia, n (%)	1.05 (0.99 to 1.11)	0.104		
Hypertension	0.54 (0.35 to 0.83)	0.005		
Diabetes	0.68 (0.4 to 1.13)	0.136		
CHD	0.56 (0.2 to 1.54)	0.26		
Cerebral complication	0.78 (0.31 to 1.97)	0.606		
Types of surgery, n (%)			0.92 (0.84 to 1.01)	0.086
Hepatic resection	Reference			
Pancreatoduodenectomy	1.81 (1.13 to 2.89)	0.014		
Splenectomy and pancreatectomy	0.61 (0.33 to 1.11)	0.106		
Surgery for bile duct cancer and gall bladder	1.12 (0.65 to 1.92)	0.684		
Choledocholithiasis	0.8 (0.54 to 1.19)	0.275		
Other surgery	0.69 (0.29 to 1.63)	0.401		
Laparoscopic surgery, n (%)	0.31 (0.2 to 0.47)	<0.001	0.34 (0.22 to 0.52)	<0.001
Perioperative blood transfusion, n (%)	0.84 (0.57 to 1.24)	0.383		
Preoperative days (d)	0.97 (0.93 to 1.02)	0.23		
Anaesthesia duration (min)	1 (1 to 1)	0.099		
Surgery duration (min)	1 (1 to 1)	0.086		
Postoperative analgesia protocol, n (%)			4.23 (3.10 to 5.93)	<0.001
Butorphanol	Reference			
Sufentanil	4.38 (3.2 to 5.99)	<0.001		
Anaesthetic methods, n (%)				
General anaesthesia	Reference			
General anaesthesia with nerve block	0.66 (0.38 to 1.16)	0.146		
Nerve block, n (%)				
No	Reference			
Thoracic nerve block	1.66 (0.94 to 2.94)	0.081		

Continued

Table 3 Continued

Variable	Univariate analysis		Multivariable analysis	
	OR_95 CI	P value	OR_95 CI	P value
Quadratus lumborum block	1.22 (0.6 to 2.47)	0.58		
TAP	1.14 (0.52 to 2.5)	0.735		
Rectus sheath block	1.14 (0.42 to 3.06)	0.798		
Others	1.54 (0.42 to 5.67)	0.515		

ASA, American Society of Anesthesiologists; BMI, body mass index; CHD, Coronary Heart Disease; Hb, haemoglobin; TAP, Transversus Abdominis Plane Block.

whether laparoscopic surgery was performed (p<0.05). For anaesthesia duration, surgery duration, anaesthetic methods, composition of nerve block types and preoperative days were similar in the two groups (p>0.05). The group experiencing moderate-to-severe pain within 24 hours had a longer postoperative hospital stay (12.7±6.0 days vs 11.4±5.7 days). Regarding the nerve block variable, the distribution of different types between the groups with no moderate-to-severe pain and those with moderate-to-severe pain within 24 hours is illustrated in figure 2.The incidence of moderate-to-severe pain in the patients was 8.4% during the first 24 postoperative hours with a mean VAS Score of 5 (4, 6), whereas patients without moderate-to-severe pain had a mean VAS Score of 0 (0, 1). The incidence of moderate-to-severe pain was 2.8% (60) during the 24–48 postoperative hours. The incidences of PONV were significantly different between patients with and without insufficient analgesia 24 hours after surgery (p<*0.05*). For PONV, the two groups showed significant difference (p<0.05).

In univariate analysis, moderate-to-severe pain 24 hours after operation was associated with younger age, lower BMI, open surgery, hypertension, pancreatoduodenectomy and postoperative analgesia with sufentanil (table 3). In multivariable analysis, the independent risk factors associated with moderate-to-severe pain 24 hours after operation included younger age (OR, 0.97; 95% CI 0.95 to 0.98, p<0.001), lower BMI (OR, 0.94; 95% CI 0.89 to 0.98, p=0.018), open surgery (OR, 0.34; 95% CI 0.22 to 0.52, p<0.001), and postoperative analgesia with sufentanil (OR, 4.38; 95% CI 3.2 to 5.99, p<0.001). As shown in table 4, the independent risk factors for moderate-to-severe acute pain 24–48 hours after surgery were almost the same, except that BMI (OR, 0.93; 95% CI 0.85 to 1.01, p=0.708) was not included (table 4).

The incidence of moderate-to-severe acute postoperative pain, observed 24 hours after surgery, significantly decreased with advancing age among patients categorised into four quartile age groups. Furthermore, 24 hours after surgery, the incidence of pain was higher in the group with BMI < 25 kg/m^2 as compared with those with BMI ≥25 kg/m^2 (figure 3).

The occurrence of moderate-to-severe pain within 24 hours was associated with an increased incidence of nausea or vomiting in early postoperative outcomes, but this association was not observed within 24–48 hours. Patients with inadequate analgesia had a longer postoperative hospital stay (table 5).

DISCUSSION

In recent years, laparoscopy is frequently used in various procedures. It could relieve postoperative pain and benefit the patients' recovery. However, hepatobiliary and pancreatic surgery (without cholecystectomy) are still considered the more traumatic types of abdominal surgeries. Existing literature on pain indicates moderate-to-severe pain intensities of 42% on day 1 and 33% on day 2 after living donor hepatectomy.[8] Another study reported a 64.8% incidence of postoperative pain following urological and hepatobiliary operations.[9] In our retrospective cohort study, the occurrence rate of moderate-to-severe pain was 8.4% in the postoperative period of major hepatobiliary and pancreatic surgeries. This may be attributed to varying population characteristics, types of operations, postoperative analgesia and the analgesic drugs administered. In addition, the relevant literature was reviewed from several years ago, at which time enhanced recovery after surgery and multimodal analgesia programmes were not implemented. Therefore, the incidence of postoperative acute pain would be higher.

In this study, we included surgeries for both the liver and pancreas, since they are performed by the same department in our centre. Additionally, there are studies that investigate postoperative pain in various types of surgeries. Exploring research that can be applied to multiple surgical types may enhance the representativeness and generalisability of our findings. This consideration guided our decision to include a wider range of surgical types. We categorised the patients into two groups based on their experience of moderate-to-severe pain (VAS≥4 points) after surgery. We found that the distribution of surgical types was consistent between the groups, leading us to conclude that the surgical method did not affect our outcomes.

The main finding of this study is that age, BMI, laparoscopy and different postoperative analgesic drugs are significant risk factors for postoperative pain following these surgeries.

Table 4 Univariate and multivariable analysis for moderate-severe postoperative pain within 24–48 hours

Variable	Univariate analysis		Multivariable analysis	
	OR_95 CI	P value	OR_95 CI	P value
Gender (female)	0.86 (0.5 to 1.45)	0.563		
Age (years)	0.97 (0.95 to 0.99)	0.002	0.97 (0.95 to 0.99)	0.010
BMI (kg/m^2)	0.93 (0.86 to 1.01)	0.077	0.93 (0.85 to 1.01)	0.708
ASA				
I	Reference			
II	0.45 (0.14 to 1.49)	0.192		
III	0.29 (0.07 to 1.16)	0.081		
Smoking	1.27 (0.75 to 2.13)	0.372		
Education level				
Preliminary school	Reference			
Middle school	1.17 (0.66 to 2.09)	0.584		
College degree	1.56 (0.67 to 3.67)	0.306		
Bachelor degree	0.73 (0.17 to 3.14)	0.675		
Postgraduate	0.68 (0.2 to 2.28)	0.534		
History of anaesthesia	1.06 (0.96 to 1.17)	0.221		
Hypertension	0.45 (0.2 to 0.99)	0.046		
Diabetes	1.2 (0.59 to 2.47)	0.613		
CHD	0.43 (0.06 to 3.15)	0.408		
Cerebral complication	0.48 (0.07 to 3.47)	0.464		
Types of surgery, n (%)				
Hepatic resection	Reference			
Pancreatoduodenectomy	1.87 (0.85 to 4.09)	0.117		
Splenectomy and pancreatectomy	1.1 (0.47 to 2.59)	0.823		
Surgery for bile duct cancer and gall bladder	1.21 (0.49 to 2.99)	0.687		
Choledocholithiasis	0.77 (0.38 to 1.56)	0.471		
Other surgery	0.77 (0.18 to 3.29)	0.72		
Laparoscopy surgery, n (%)	0.42 (0.22 to 0.82)	0.011	0.47 (0.24 to 0.91)	0.026
Perioperative blood transfusion, n (%)	1 (1 to 1)	0.399		
Preoperative days (d)	0.99 (0.93 to 1.07)	0.876		
Anaesthesia duration(min)	1 (1 to 1)	0.072		
Surgery duration(min)	1 (1 to 1)	0.067		
Postoperative analgesia protocol, n (%)			2.50 (1.48 to 4.21)	<0.001
Butorphanol	Reference			
Sufentanil	2.65 (1.58 to 4.43)	<0.001		
Anaesthetic methods, n (%)				
General anaesthesia				
General anaesthesia with nerve block	0.91 (0.39 to 2.14)	0.826		
Nerve block, n (%)				
No	Reference			
Thoracic nerve block	1.24 (0.52 to 2.95)	0.624		
Quadratus lumborum block	0.84 (0.27 to 2.64)	0.765		
TAP	0.81 (0.23 to 2.91)	0.748		

Continued

Table 4 Continued

Variable	Univariate analysis		Multivariable analysis	
	OR_95 CI	P value	OR_95 CI	P value
Rectus sheath block	0.88 (0.17 to 4.42)	0.872		
Others	0 (0 to Inf)	0.984		

ASA, American Society of Anesthesiologists; BMI, body mass index; CHD, Coronary Heart Disease; TAP, Transversus Abdominis Plane Block.

Although many studies have confirmed that postoperative pain decreases with age,[10 11] some have found no age-related differences.[12] Therefore, it is unclear whether postoperative pain is associated with age. This study supported that younger individuals are more likely to experience postoperative pain, and the incidence of postoperative pain decreased by 3% with increasing age (OR, 0.97; 95% CI 0.95 to 0.98). Furthermore, comparisons of groups with IQRs also showed consistent conclusions. This may be related to changes in the inflammatory response, immune system, pain processing, autonomic nervous system and pain regulation.[13 14] Moreover, the thermal and mechanical thresholds measured on the skin using quantitative sensory testing were found to be increased in the elderly.[15 16]Furthermore, elderly patients may have a higher pain threshold and show increased sensitivity to opioids, which is related to pharmacokinetic and psychosocial mechanisms.[17 18] In comparison to articles with differing conclusions, the variations may be attributed to the different types of procedures and the small sample size in that literature.

Currently, the impact of BMI on postoperative pain remains uncertain. Some studies suggest that patients with a high BMI are more prone to postoperative pain,[19–21] while others indicate no significant correlation.[22 23] Notably, there is a lack of research on the association between BMI and postoperative pain following major hepatobiliary pancreatic surgery. The findings of this study indicate a higher incidence of postoperative pain in patients with low BMI. A one-unit increase in BMI was linked to a 6% reduction in the risk of postoperative pain (OR, 0.94; 95% CI 0.89 to 0.98, p=0.018), and the rate of pain incidence was higher in the group with BMI<25 kg/m^2 24 hours postsurgery. Individuals with a healthy body fat percentage may exhibit a heightened metabolic rate, increased enzymes activity within the body and accelerated metabolism of analgesics. Individuals with a lower BMI are often linked with frailty and have a higher propensity for experiencing postoperative complications, which can result in postoperative pain. Subsequent research should aim to elucidate potential mechanisms and establish causal relationships in this context.

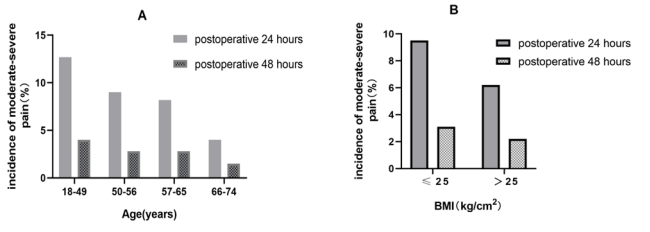

Figure 3 The incidence of moderate-severe acute pain in different age (A) and body mass index (BMI) (B) groups. Ages of the four quartile groups (quartiles, left) were ≤49 years, 50–56 years, 57–65 years and ≥66 years and pain significantly declines with age in (A). BMI of value 25 and pain significantly increased in the group of ≤25years in (B).

In the current trial, the use of sufentanil for postoperative analgesia increased the risk of postoperative pain by 4.38 times (OR, 4.38; 95% CI 3.2 to 5.99, p<0.001) as compared with butorphanol. Additionally, butorphanol is an opioid agonist-antagonist that mainly induces analgesia through κ-receptor agonists. Similar to traditional opioids, butorphanol inhibits the uploading of noxious stimuli in the spinal dorsal horn and activates the pain control circuit transmitted from the midbrain to the spinal dorsal horn via the rostral ventromedial region, thereby producing analgesic effects. Moreover, patients undergoing hepatobiliary surgery typically experience visceral pain resulting from laparoscopic peritoneal stretching, intraoperative visceral pull and visceral ischaemia. Butorphanol proves to be more effective in alleviating visceral pain, with a lower incidence of associated adverse effects such as vomiting, nausea, dizziness and respiratory depression compared with purely α-receptor agonists.[24 25]

In this study, cholecystectomy alone was excluded, mainly because the trauma, operation time, postoperative analgesia type and postoperative pain incidence rate of this surgery were significantly different as compared with other surgery types. Therefore, the data for major hepatobiliary and pancreatic surgeries except cholecystectomy were analysed.

Although women report greater postoperative pain in various procedures than men, this phenomenon was not observed in the present cohort. Factors such as diabetes, educational level and the anaesthesia method were not found to be associated with postoperative pain.

In previous studies, neuraxial anaesthesia has been shown to be beneficial for postoperative pain. Nerve block is known to provide a protective effect for postoperative analgesia. However, in our study, the combination of general anaesthesia and nerve block did not result in a superior postoperative analgesic effect. The distribution ratio of different types between groups with

Table 5 Relationship between moderate-severe pain and postoperative outcomes

	Moderate-severe acute pain within 24 hours			Moderate-severe acute pain within 24–48 hours		
	Yes	No	P value	Yes	No	P value
Postoperative nausea	9 (4.9)	41 (2.1)	0.033	3 (5)	54 (2.5)	0.205
Postoperative vomiting	6 (3.3)	23 (1.2)	0.03	0 (0)	11 (0.5)	1
Postoperative days	12.7±6.0	11.4±5.7	0.004	13.0±6.2	11.5±5.7	0.043

no moderate-to-severe pain and groups with moderate-severe pain within 24 hours was similar. Furthermore in the univariate analysis, nerve block was not found to be associated with postoperative analgesia ($p > 0.05$). Considering that nerve block was administered as a single injection without continuous tube insertion and was typically carried out prior to surgery in our centre, the duration of the block's effect was insufficient to last for 24 hours postsurgery. There may have been a rebound tenderness effect, thus negating any inherent advantage in the VAS Score 24 hours postsurgery. It is essential to conduct relevant prospective trials to ascertain the specific effects of nerve block.

The overall incidence of PONV among patients was relatively low, primarily attributed to the comprehensive measures implemented at our centre such as volume repletion, and avoidance of dexamethasone and tropisetron usage, and other interventions. Nonetheless, the incidence was observed to be higher in patients experiencing moderate-to-severe pain, possibly linked to laparoscopic surgery, opioid administration, motion sickness and various other factors. Consistent with prior research, our study indicated that moderate-to-severe postoperative pain correlated with extended hospitalisation postoperatively.

This study had some limitations. First, it was retrospective in nature. Confounding variables of pain such as relevant psychological disorders were not included in our study. Second, postoperative pain is an individual experience that involves psychosocial, environmental and genetic factors. These limitations should be considered when attempting to predict pain.

CONCLUSION

In summary, age, BMI, surgical approach, and various analgesic drugs were significant predictors of postoperative pain after major hepatobiliary and pancreatic surgeries. Based on these results, more personalised postoperative pain management strategies should be considered early on, particularly in younger patients with a lower BMI. Additionally, laparoscopic surgery should be preferred whenever feasible.

Acknowledgements The authors thank all the individuals who participated in this study. The authors also thank Wenjing Dong and Zhiguang Ping for their technical assistance in data extraction and analysis. The authors also thank Editage (www.editage.cn) for English language editing.

Contributors HZ conceived the study. HZ and YY substantially contributed to conception and design, and analysed and interpreted data. JZ and LZ revised the manuscript critically for important intellectual content. LJ and XX contributed to the materials/analysis tools. HZ acquired, analysed and interpreted most of the data and drafted the article. JZ and LZ revised the manuscript. All authors read and approved the final manuscript. JZ is the guarantor.

Funding This study was supported financially by National Natural Science Foundation of China (grant number: 82201364), Henan Natural Science Foundation (grant number: 222300420360) and Henan Province Medical Science and Technology Joint Construction Project (grant number: LHGJ20220066).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This single-centre, retrospective study was approved by the Medical Ethics Committee of Henan Provincial People's Hospital (Ethics approval number: (2021) lun shen (100)), an academic tertiary hospital in Zhengzhou, China. Written informed patient consent was waived by reason of the retrospective design and minimal intrusion to the privacy of the participants, which was approved by the Medical Ethics Committee of Henan Provincial People's Hospital. All methods were carried out in accordance with the ethical standards of the Declaration of Helsinki 1964 and its later amendments.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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