Clinical Interventions in Aging

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CLINICAL TRIAL REPORT

Dexmedetomidine Attenuates Inflammation in Elderly Patients Following Major Hepatobiliary and Pancreatic Surgery: A Randomized Clinical Trial

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Background: Dexmedetomidine (Dex) may have anti-inflammatory properties and potentially reduce the incidence of postoperative organ injury.

Objective: To investigate whether Dex protects pulmonary and renal function via its anti-inflammatory effects in elderly patients undergoing prolonged major hepatobiliary and pancreatic surgery.

Design and Setting: Between October 2019 and December 2020, this randomized controlled trial was carried out at a tertiary hospital in Chongqing, China.

Patients: 86 patients aged 60–75 who underwent long-duration (> 4 hrs) hepatobiliary and pancreatic surgery without significant comorbidities were enrolled and randomly assigned into two groups at a 1:1 ratio.

Interventions: Patients were given either Dex or an equivalent volume of 0.9% saline (Placebo) with a loading dose of 1 μg kg^{-1} for 10 min, followed by 0.5 μg kg^{-1} hr^{-1} for maintenance until the end of surgery.

Main Outcome Measures: The changes in serum concentrations of interleukin-6 (IL-6) and tumour necrosis factor-α (TNF-α) were primary outcomes.

Results: At one hour postoperatively, serum IL-6 displayed a nine-fold increase ($P<0.05$) in the Placebo group. Administration of Dex decreased IL-6 to 278.09 ± 45.43 pg/mL (95% CI: 187.75 to 368.43) compared to the Placebo group ($P=0.019$; 432.16 ± 45.43 pg/mL, 95% CI: 341.82 to 522.50). However, no significant differences in TNF-α were observed between the two groups. The incidence of postoperative acute kidney injury was twice as high in the Placebo group (9.30%) compared to the Dex group (4.65%), and the incidence of postoperative acute lung injury was 23.26% in the Dex group, lower than that in the Placebo group (30.23%), although there was no statistical significance between the two groups.

Conclusion: Dex administration in elderly patients undergoing major hepatobiliary and pancreatic surgery reduces inflammation and potentially protects kidneys and lungs.

Registration: Chinese Clinical Trials Registry, identifier: ChiCTR1900024162, on 28 June 2019.

Keywords: dexmedetomidine, elderly patients, long-duration hepatobiliary and pancreatic laparotomy, perioperative renal function, perioperative pulmonary function

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Introduction

There is a growing trend in the number of surgical procedures being performed on elderly patients[1] and advancing age is associated with a high risk of perioperative complications.[2,3] It has been reported that the perioperative mortality rate in elderly patients is 4.4 times greater than that observed in young and middle-aged patients.[4,5] Notably, long-duration surgeries such as hepatobiliary and pancreatic surgery in elderly patients have a high risk of iatrogenic trauma and ischemia-reperfusion injury (IRI).[6] IRI produces inflammatory cytokines and damage-associated molecular pattern proteins (DAMPs), potentially leading to renal and pulmonary dysfunction postoperatively. This, in turn, results in prolonged hospital stays, elevated medical costs, and increased postoperative mortality.[7]

Dexmedetomidine (Dex) acts on α_2-adrenergic receptors in the nucleus locus coeruleus, suppressing the sympathetic nervous system while stimulating the vagus nerve, leading to sedative, hypnotic effects, and anti-inflammatory properties.[8–10] Our previous studies have suggested that Dex may confer renal and pulmonary protection by activating the PI3K/Akt and cholinergic anti-inflammatory signaling pathway, demonstrating renoprotective and pulmonary protective capabilities in a preclinical setting.[11] Previous clinical studies have also demonstrated that Dex suppresses cytokine release and mitigates against oxidative stress, thereby reducing inflammation. These mechanisms contribute to improved clinical outcomes, including a decreased incidence of acute kidney injury (AKI),[12,13] acute lung injury (ALI),[14] and neurologic complications[8] in critically ill and surgical patients. Furthermore, a previous randomized controlled trial reported that Dex administration alleviated lung dysfunction induced by lower limb extremity ischemia-reperfusion.[15] These findings suggest that Dex may potentially reduce the incidence of postoperative renal and pulmonary dysfunction, thereby enhancing patient surgical outcomes. This study, therefore, is investigating whether Dex exhibits anti-inflammatory effects and further protects pulmonary and renal function in elderly patients undergoing prolonged major hepatobiliary and pancreatic surgery.

Materials and Methods

This randomized trial was conducted at a tertiary hospital, the Southwest Hospital of Third Military Medical University (Army Medical University, China), between October 2019 and December 2020 with adherence to the Declaration of Helsinki. Written informed consent was obtained from all participating patients.

Ethics

Ethical approval for this study (approval No. KY2019106) was provided by the Ethics Committee and Institutional Review Board of the Third Military Medical University, Chongqing, China (Chairperson Prof Mao Qing) on 28 August 2019.

Trial Registration

The trial was registered at the Chinese Clinical Trials Registry (ChiCTR1900024162, on 28 June 2019).

Patients, Randomization, and Blinding

The inclusion criteria consisted of elderly patients between the ages of 60 and 75 who were scheduled to undergo major hepatobiliary and/or pancreatic surgery for a duration of more than 4 hours. Among these, certain patients underwent simultaneous liver, pancreatic, and biliary surgical interventions. Individuals with pheochromocytoma, severe heart block and/or ventricular insufficiency, or significant heart, lung, or kidney disease were excluded from the study. Detailed inclusion and exclusion criteria are presented in the Supplement 1. Between October 2019 and December 2020, 86 patients meeting the inclusion criteria were enrolled. Patients were randomized to either receive Dex or 0.9% saline using a 1:1 ratio via a random number generator (Supplement 1). Randomization was concealed using identical envelopes that were sealed until after the induction of surgery. If a patient was excluded due to inadequate surgical duration, the corresponding random number was replaced in a new envelope to subsequently enroll additional patients until 86 patients were included. Both patients and researchers were blinded to randomization.

Anesthesia and Postoperative Care

Patient characteristics, laboratory data, pre-operative respiratory function, Assess Respiratory Risk in Surgical Patients in Catalonia [ARISCAT (Canet)] score,[16] and the Child-Turcotte-Pugh (CTP) classification of liver function were recorded.[17] Intraoperative monitoring included electrocardiography, pulse oximetry, radial artery blood pressure, central venous pressure, stroke volume variations (SVV), bispectral index (BIS), and end-tidal carbon dioxide. After induction and tracheal intubation, anesthesia was maintained with a combination of sevoflurane, propofol, and remifentanil with the target BIS values between 40–60. A restricted fluid replacement strategy[18] and fluid pulse therapy guided by SVV > 13% were implemented. Blood transfusion therapy was provided as required, followed by perioperative transfusion guidelines. Postoperative pain was managed with a multimodal analgesia strategy including the use of bilateral oblique subcostal transversus abdominis plane (TAP) blocks and non-steroidal anti-inflammatory drug, parecoxib sodium. Pain management was in accordance with the PROSPECT recommendation[19] and previous studies.[20,21] Patients were transferred to the intensive care unit for 24 hrs after at least 1 hr of standard care in the post-anesthesia care unit.

Interventions and Outcomes

In the Dex group, an initial loading dose of Dex at 1 μg kg^{-1} was administered for 10 min immediately after the induction of anesthesia, followed by a maintenance dose of 0.5 μg kg^{-1} h^{-1} during surgery.[22] The placebo group received an intravenous equivalent volume of 0.9% saline. The administration of Dex or 0.9% saline was ceased upon completion of surgery. Blood samples were collected 5 min before anesthesia induction, 2 hrs after the start of the operation, and 1 hr and 1, 3, and 7 days after surgery to measure blood biomarkers.

Study Endpoint

The primary outcome was to evaluate the change in IL-6 and tumour necrosis factor-α (TNF-α) at various time intervals. Secondary outcomes included alterations in Crea, BUN, neutrophil gelatinase-associated lipocalin (NGAL), Horowitz Index (HI=PaO_2 FiO_2^{-1}), and lactate (cLac). Furthermore, blood cortisol (Cor), catecholamine (CA), and acetylcholine (Ach) levels were measured to assess the protective mechanisms associated with Dex. Other outcomes included assessing the incidence of acute kidney injury (AKI), acute lung injury (ALI), and various postoperative pulmonary complications, such as respiratory infection, pleural effusion, and atelectasis. The study also considered the duration of postoperative oxygen therapy, the length of postoperative hospitalisation, and the overall duration of hospitalisation.

Sample Size Estimation and Statistical Analysis

The sample size was determined from a previous study[23] that observed an increase in IL-6 and TNF-α to 146.1 ± 78.4 pg mL^{-1} and 26.8 ± 11.7 pg mL^{-1} in the placebo group and 102.7 ± 54.0 pg mL^{-1} and 19.8 ± 9.5 pg mL^{-1} in the Dex group at the end of surgery. To detect a significant difference with a power of 80% and an α-coefficient of 0.05, 39 patients were required in each group in this study. To account for a potential dropout rate of 10%, 43 patients were recruited in each group. The data were presented as mean ± standard deviation (SD), [95% confidence interval (CI)], median (IQR), or ratio as appropriate. Statistical analysis was performed using the Student's *T*-test and χ^2 test for comparisons between the two groups, or repeated measures analysis of variance (RMANOVA) followed by LSD test for multi-comparison. A *P* value of less than 0.05 was considered a significant difference. SPSS 26.0 statistical software (SPSS, Chicago, Illinois, USA) was used for the statistical analysis.

Results

Baseline and Intraoperative Data

A total of 86 patients were enrolled in this study, and 43 patients assigned to each group were finally recruited between October 2019 and December 2020 (Figure 1). There were no significant differences between the two groups in terms of gender, age, height, weight, smoking history, ARISCAT scores, anticipated incidence of acute lung injury (ALI), CTP classification of liver function, hypertension, diabetes, and surgery type. The patients in the Dex group had a higher ASA grade (III) than the patients in the placebo group (*P*=0.044) (Table 1). Diuretics were more frequently administered

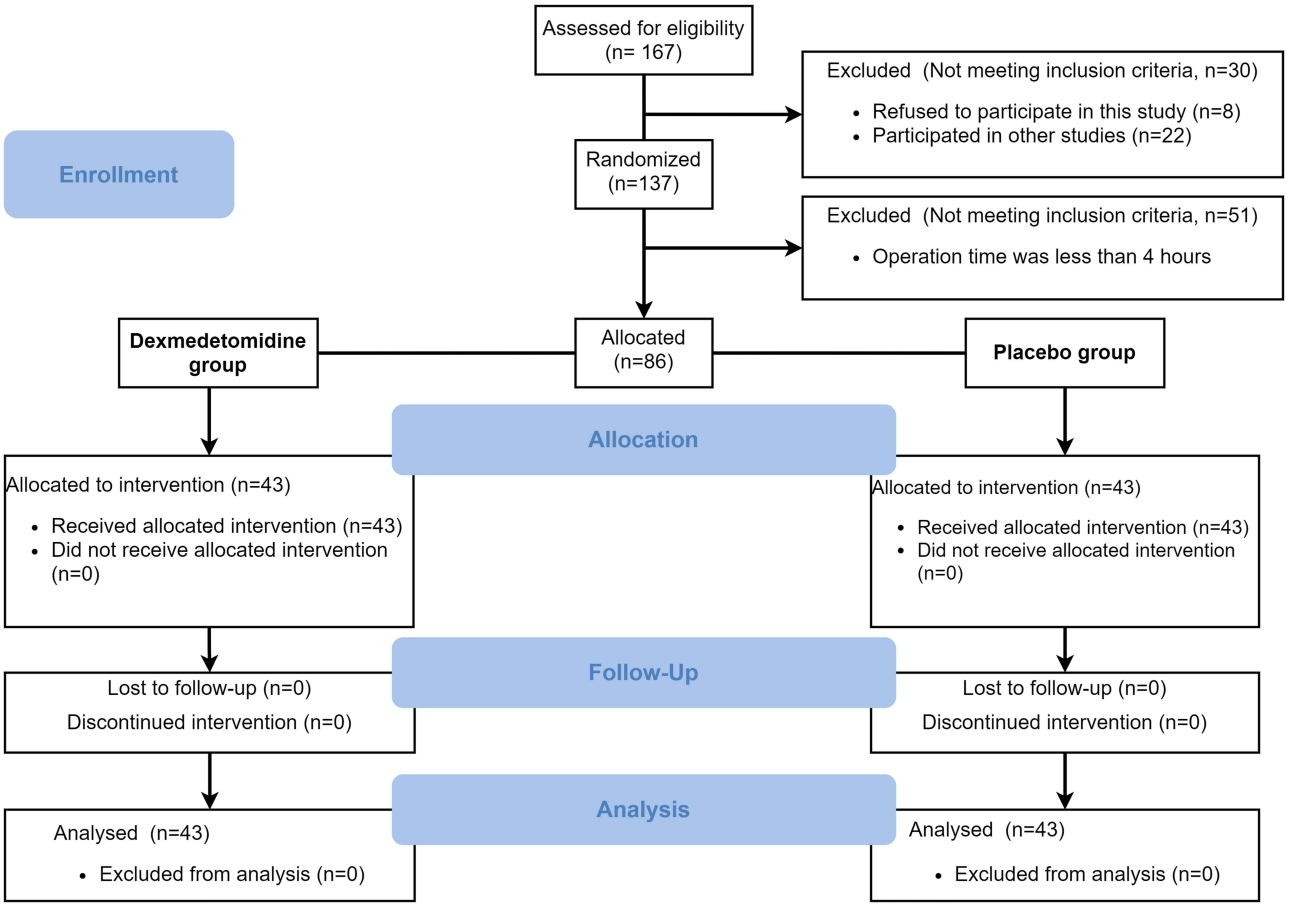

Figure 1 The CONSORT flow diagram.

during surgery in the placebo group (48.84%) than in the Dex group (18.61%) (P=0.003). Additionally, the Dex group received a higher proportion of dexamethasone (41.86%) compared to the placebo group (20.93%) (P=0.037). Hospital stay duration and other perioperative data demonstrated similar outcomes between the two groups (Table 2).

Primary analysis

The levels of IL-6 demonstrated a significant increase from baseline at all measured time points throughout the perioperative period in both groups (Figure 2A). Notably, Dex administration was associated with a significant reduction in IL-6 levels [278.09 ± 45.43, (95% CI 187.75 to 368.43) pg mL^{-1}] at postoperative 1 hr when compared to the Placebo group [432.16 ± 45.43, (95% CI 341.82 to 522.50) pg mL^{-1}], with a P value of 0.019. Furthermore, in the Dex group, the peak IL-6 level at 24 hrs postoperatively [108.49 ± 20.18, (95% CI 68.36 to 148.63) pg mL^{-1}] remained lower than that observed in the Placebo group [143.65 ± 20.18, (95% CI 103.52 to 183.79) pg mL^{-1}].

TNF-α levels were increased from the baseline in both groups post-surgery. Peak TNF-α levels were observed at 1 hr postoperatively in the Dex group [190.23 ± 17.68, (95% CI 155.08 to 225.39) pg mL^{-1}; P<0.001] and the placebo group [196.80 ± 17.68 (95% CI 161.65 to 231.96) pg mL^{-1}; P<0.001], with no significant differences between the two groups (Figure 2B).

Secondary Analysis and Others

Renal Function

On postoperative day 1, the Crea concentration increased from 65.55 ± 2.90, (95% CI 59.78 to 71.31) μmol l^{-1} at baseline to 71.07 ± 3.84, (95% CI 63.43 to 78.71) μmol l^{-1} (P=0.016, Figure 3A) in the placebo group while, in the Dex cohort, the Crea concentration increased from a baseline of 69.06 ± 2.90, (95% CI 63.29 to 74.83) μmol l^{-1} to 73.00 ±

Table 1 Comparisons of Baseline Information Between Two Groups

Items	Placebo Group (n=43)	Dex Group (n=43)	All Enrolled Patients (n=86)	*P* value
Patient's characteristics				
Male/Female, n	26/17	25/18	51/35	0.826
Age (years)	66.28 ± 3.76	67.42 ± 3.75	66.85 ± 3.78	0.163
Height (cm)	158.91 ± 8.17	159.95 ± 10.52	159.43 ± 9.38	0.608
Weight (kg)	57.33 ± 9.82	56.58 ± 11.25	56.95 ± 10.51	0.745
ASA classification (n, II/III)	41/2	35/8	76/10	0.044*
Smoking history, n (%)	13 (30.23%)	15 (34.88%)	28 (32.56%)	0.645
ARISCAT (Canet) scores (medium-/high- risk) and its anticipated incidence of ALI (%)	33/10, 23.26%	30/13, 30.23%	63/23, 27.71%	0.465
CTP classification of liver function (n, A level/B level)	31/12	38/5	69/17	0.058
Complications				
Hypertension (%)	16 (37.21%)	13 (30.23%)	29 (33.72%)	0.494
Diabetes (%)	7 (16.28%)	3 (6.98%)	10 (11.63%)	0.178
Involving surgery type, n (%)				
Liver surgery	19 (44.19%)	27 (62.79%)	46 (53.49%)	0.084
Biliary surgery	23 (53.49%)	19 (44.19%)	42 (48.84%)	0.388
Pancreatic surgery	18 (41.86%)	10 (23.26%)	28 (32.56%)	0.066

Notes: *Compared with the Control group, $P<0.05$. Data are expressed as mean ± standard deviation (SD), median (quartile), n (ratio, or rate). P values were results of comparisons between the Placebo group and the Dex group.
Abbreviations: Dex, Dexmedetomidine; ASA, American Society of Anesthesiologists; CTP, Child-Turcotte-Pugh; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia.

Table 2 Comparisons of Intraoperative Information Between Two Groups

Items	Placebo Group (n=43)	Dex Group (n=43)	All Enrolled Patients (n=86)	*P* value
Intraoperative information				
Operation time (minutes)	380.23 ± 116.52	376.16 ± 82.82	378.20 ± 100.51	0.852
Anesthesia time (minutes)	404.74 ± 110.95	397.63 ± 78.08	401.19 ± 95.43	0.732
Intraoperative fluid intake and output				
Crystalloid (mL)	1700 [1250 to 2200]	1700 [1300 to 2000]	1700 [1300 to 2000]	0.742
Colloid (mL)	500 [500 to 1000]	500 [500 to 1000]	500 [500 to 1000]	0.803
Urine output (mL)	700 [300 to 1000]	500 [400 to 1100]	600 [400 to 1000]	0.979
Blood loss volume (mL)	300 [300 to 600]	300 [200 to 400]	300 [275 to 425]	0.436
Blood transfusion rate, n (%)	17 (39.53%)	10 (23.26%)	27 (31.40%)	0.104
Diuretic usage, n (%)	21 (48.84%)	8 (18.61%)	29 (33.72%)	0.003*
Hepatic occlusion rate, n (%)	19 (44.19%)	10 (23.26%)	29 (33.72%)	0.084
Norepinephrine dosage (mg)	1 [0.5 to 2]	1 [1 to 2]	1 [0.875 to 2]	0.238
Dexamethasone usage rate, n (%)	9 (20.93%)	18 (41.86%)	27 (31.40%)	0.037*

Notes: *Compared with the Control group, $P<0.05$. Data are expressed as mean ± standard deviation (SD), median (quartile), n (ratio, or rate). P values were results of comparisons between the Placebo group and the Dex group.
Abbreviations: Dex, Dexmedetomidine; ASA, American Society of Anesthesiologists; CTP, Child-Turcotte-Pugh; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia.

3.84, (95% CI 65.36 to 80.64) μmol l^{-1} (P=0.082, Figure 2A). There were no statistically significant changes in BUN between the two groups (Figure 3B). Additionally, in the placebo group, NGAL levels significantly increased from a baseline of 142.95 ± 11.48, (95% CI 120.11 to 165.78) ng mL^{-1} to 163.71 ± 12.79, (95% CI 138.27 to 189.15) ng mL^{-1} at 2 hrs postoperatively (P=0.001) and 152.71±12.24, (95% CI 128.38 to 177.05) ng mL^{-1} (P=0.043) at 24 hrs postoperatively. No significant increase in NGAL was observed in the Dex group (Figure 3C). The incidence of

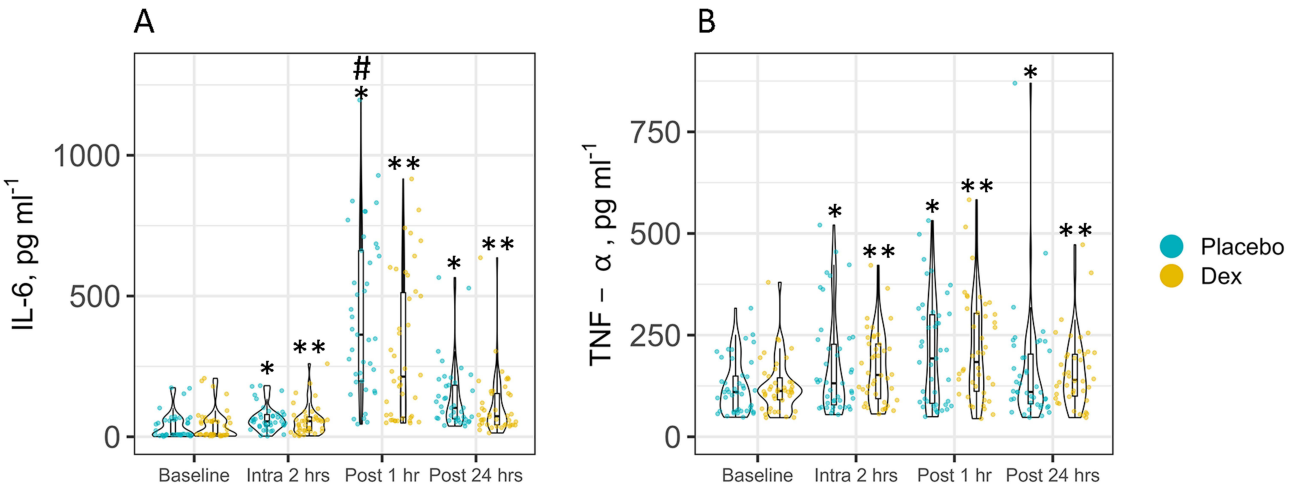

Figure 2 Changes in interleukin-6 (IL-6) and tumour necrosis factor-α (TNF-α) levels (primary outcomes).
Notes: The distribution of (**A**) IL-6 and (**B**) TNF-α in the placebo group (blue points) and the Dex group (yellow points) of all individuals are shown with violin plots (n=43 patients per group). Data are presented as violin plots with overlaid box plots. The bounds of the box show the interquartile range, and the centre line of the box shows the median. Vertical endpoints represent the 5th and 95th percentiles. Data are analyzed with the repeated measures analysis of variance (RMANOVA) followed by the LSD test for multi-comparison. *Significant difference with $P<0.05$ compared with the baseline in the Placebo group. **Significant difference with $P<0.05$ compared with the baseline in the Dex group. #Significant difference with $P<0.05$ compared with the Dex group at the corresponding time.

postoperative AKI was twice as high in the placebo group (9.30%) compared to the Dex group (4.65%), although this difference was not statistically significant (P=0.393, Table 3).

Other Biomarkers and Postoperative Pulmonary Complications

The mean HI in both groups did not drop below 300 mmHg at any time point, with no significant differences observed between the two groups (Figure 3D). In the Dex group, lactate increased from a baseline of 1.28 ± 0.63, (95% CI 0.03 to 2.53) mmol l^{-1} to 2.41 ± 0.73, (95% CI 0.96 to 3.87) mmol l^{-1} (P<0.001) at 1 hr postoperatively. Similar changes in lactate were also observed in the placebo group, with no statistically significant difference between the two groups (Figure 3E). The anticipated incidence of postoperative ALI was 23.26% in the placebo group and 30.23% in the Dex group, according to ARISCAT scores (Table 1). However, the actual incidence of ALI was 23.26% in both groups (Table 3), indicating potential pulmonary protective effects of Dex, although no statistically significant differences were observed between the two groups. The incidence of pulmonary complications exceeded 70% in both groups, with no significant difference (P=0.451, Table 3) observed. In addition, there were no differences between the two groups in terms of postoperative and total days of hospitalization, as well as the duration of postoperative oxygen therapy (Table 3).

Corticosteroids (Cor), catecholamines (CA) and acetylcholine (Ach)

No significant differences were observed in Cor levels between the two groups (Figure 3F). Similarly, no significant differences were noted in the levels of CA or Ach within or between the two groups (Figure 3G and H).

Discussion

In this trial, the anti-inflammatory and organoprotective effects of Dex were assessed in elderly patients undergoing prolonged major hepatobiliary and pancreatic surgery. Dex administration was associated with significantly lower levels of IL-6, while TNF-α levels remained unaffected. The effects of Dex on Cor, CA, and Ach demonstrated no significant differences between the Dex and the Placebo group. In addition, Dex administration lowered the incidence of AKI and ALI within 24 hrs post-surgery. However, there were no significant differences in postoperative pulmonary function, oxygen therapy, complications, or total hospital stay.

This study demonstrated that IL-6 and TNF-α increased 1 hr after surgery, indicating an inflammatory state in elderly patients following long-duration surgery. In addition, lactate levels peaked at 1 hr postoperatively, indicating tissue damage and underlying organ dysfunction.[24] Dex administration was associated with lower IL-6 levels 1 hr after surgery

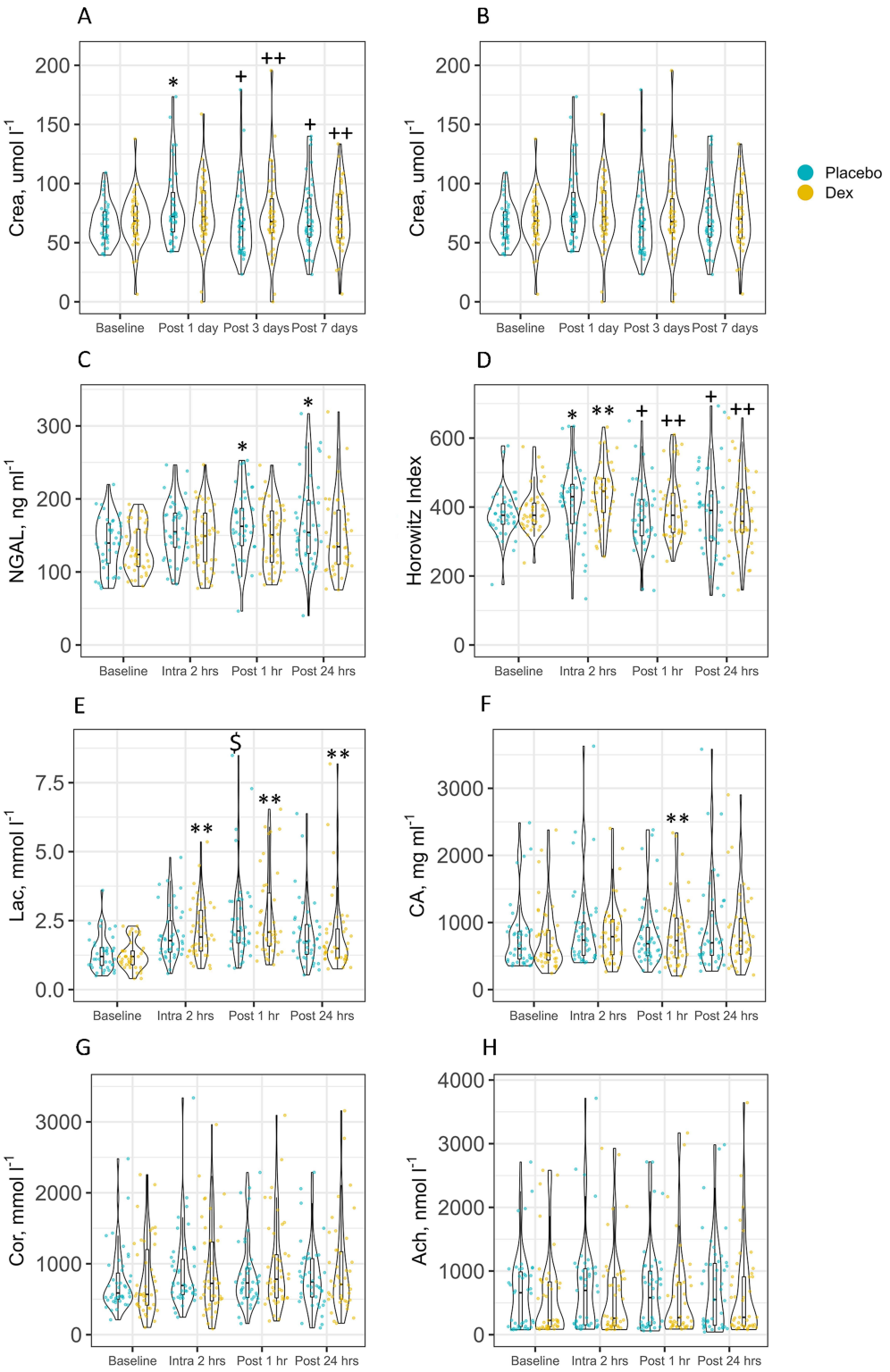

Figure 3 Assessment of renal function, pulmonary complications, and other biomarkers.

Notes: The distribution of (**A**) Crea, (**B**) BUN, (**C**) NGAL showing renal function, and (**D**) Horowitz Index and (**E**) cLac reflecting pulmonary complications, as well as other biomarkers of (**F**) CA, (**G**) Cor, and (**H**) Ach in the placebo group (blue points) and the Dex group (yellow points) of all individuals are shown with violin plots (n=43 patients per group). Data are presented as violin plots with overlaid box plots. The bounds of the box show the interquartile range, and the centre line of the box shows the median. Vertical endpoints represent the 5th and 95th percentiles. Data are analysed with the repeated measures analysis of variance (RMANOVA) followed by the LSD test for multi-comparison. *Significant difference with $P<0.05$ compared with the baseline in the placebo group. **Significant difference with $P<0.05$ compared with the baseline in the Dex group. $^{+}$Significant difference with $P<0.05$ compared with the placebo group at the corresponding time. $^{++}$Significant difference with $P<0.05$ compared with the Dex group at the corresponding time. $^{\$}$Significant difference with $P<0.05$ compared with the other 3 time points (Baseline, Intra 2 hrs, and Post 24 hrs) in the Placebo group.

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Table 3 Postoperative Clinical Outcomes in the Two Groups

Items	Placebo Group (n=43)	Dex Group (n=43)	All Enrolled Patients (n=86)	*P* value
Postoperative oxygen therapy time (days)	4 [3 to 8]	4 [2 to 5]	4 [3 to 6]	0.265
Postoperative pulmonary complications, n (%)	34 (79.07%)	31 (72.09%)	65 (75.58%)	0.451
Pleural effusion, n (%)	34 (79.07%)	30 (69.77%)	64 (74.42%)	0.323
Atelectasis, n (%)	9 (20.93%)	5 (11.63%)	14 (16.28%)	0.243
Respiratory infection, n (%)	12 (27.91%)	13 (30.23%)	25 (29.07%)	0.812
Incidence of postoperative ALI, n (%)	10 (23.26%)	10 (23.26%)	20 (23.26%)	>0.999
Incidence of postoperative AKI, n (%)	4 (9.30%)	2 (4.65%)	6 (6.98%)	0.338
Total hospital stays (days)	25 [17 to 36]	23 [17 to 29]	23 [17 to 30]	0.337
Postoperative hospital stays (days)	15 [11 to 23]	15 [11 to 18]	15 [11 to 22]	0.343

Notes: Data are expressed as median (quartile), and n (ratio). P values were results of comparisons between the Placebo group and the Dex group.

than the placebo group, suggesting that Dex mitigates against surgery-associated inflammation and potentially reduces the incidence of systemic inflammatory response syndrome. Preclinically, Dex has exhibited an inhibitory effect on inflammation, protecting both renal and pulmonary function, which may be through the activation of the PI3K/Akt signalling pathway via α_2AR[11,15] and inhibition of the cholinergic anti-inflammatory pathway.[13]

In addition, we did not find any difference in corticosteroid (Cor), catecholamine (CA) and acetylcholine (Ach) levels between the two groups, even though Dex is known to inhibit norepinephrine release and promote acetylcholine release.[25] Several factors may contribute to these findings. Firstly, hepatobiliary and pancreatic surgery involves prolonged operating times, requiring substantial doses of norepinephrine to maintain stable hemodynamics, thereby influencing serum concentrations of Ach and CA. Secondly, prolonged surgery may lead to an imbalance between sympathetic and parasympathetic drive. Thirdly, the intraoperative use of dexamethasone in the Dex group may have interfered with the results.

AKI is a prevalent postoperative complication,[26] and postoperative AKI induces a fourfold increased risk of mortality,[27] particularly after major abdominal surgery.[28] In this study, postoperative AKI was diagnosed according to the KDIGO Clinical Practice definition, and renal function was assessed alongside changes in serum NGAL. The overall incidence of postoperative AKI was 6.98%, lower than previously reported.[29] This can be potentially attributed to patients who had adequate renal function before surgery, effective intraoperative management to maintain renal perfusion, avoidance of nephrotoxic drugs, and a strict fluid management regimen. NGAL is now recognized as an early diagnostic marker for AKI, which is more precise and sensitive than serum Crea.[30–32] In this study, NGAL levels increased at 1 and 24 hrs after the surgery in the placebo group but remained unaffected in the Dex group. The higher occurrence of postoperative AKI in the placebo group (9.30%) compared to the Dex group (4.65%) may explain this observation, indicating that Dex may have renoprotective effects.

Respiratory complications, with a frequency ranging from <1% to 23% after major surgery,[33] significantly increase hospitalization rates and postoperative mortality.[34] Patients experiencing pulmonary complications after major surgery face a 14–30% mortality risk within 30 days.[33] Following the European Perioperative Clinical Outcome (EPCO) consensus,[35] this study monitored pulmonary complications, including respiratory infection, respiratory failure, pleural effusion, bronchospasm, pneumothorax, atelectasis, and aspiration pneumonia. Following long-duration hepatobiliary and pancreatic surgery in elderly patients, pulmonary complications exceeded 70%, with a median hospital stay of 15 days and a postoperative ALI incidence of 23.26%, consistent with previous studies.[16] The pre-operative ARISCAT score categorized patients into low-, intermediate-, and high-risk groups, correlating with postoperative pulmonary complications (PPC) of 1.6%, 13.3%, and 42.2%, respectively. In this study, 10 patients (23.26%) in the placebo group and 13 patients (30.23%) in the Dex group had high-risk pre-operative ARISCAT scores. However, the actual incidence of ALI in the Dex group was 23.26%, which is lower than anticipated (30.23%), suggesting a potential role for Dex in lung protection.

Clinical Implications and Limitations

This study presents the potential clinical benefits of Dex use in major abdominal surgery for elderly patients with renal or pulmonary dysfunction. The aim is to prevent organ injury and failure, as well as improve surgical outcomes, although further research is necessary to confirm these findings. However, the limitations of our study must be considered. Firstly, although the study achieved statistically significant results with IL-6 as the primary outcome, it is important to further investigate the clinical implications of the observed differences with a larger sample size. Secondly, the lack of a standardized protocol for intraoperative administration of diuretics and dexamethasone, which is typically used in procedures requiring portal venous pressure control and portal occlusion technology, confers a challenge in interpreting the Ach, CA and Cor data, as well as the anti-inflammatory effects of Dex. Thirdly, in the current study, the ASA classification assessed preoperatively was higher in the Dex group which may negate the protective effects of Dex. Additionally, it is prudent to note that, whilst the inflammatory response that occurs after surgery can lead to organ damage, it is important to consider other factors such as pre-existing co-morbidities, surgical duration and techniques, and post-operative care, which may also contribute to complications and deleterious patient outcomes.

Conclusions

The findings of our study indicate that the administration of Dex in elderly patients who have undergone prolonged major hepatobiliary and/or pancreatic surgery has the potential to reduce the inflammatory response and provide direct organ protection. These factors likely contribute to a decrease in the incidence of AKI and ALI, although this warrants further investigation.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

Ethical approval for this study (approval No. KY2019106) was provided by the Ethics Committee and Institutional Review Board of the Third Military Medical University, Chongqing, China (Chairperson Prof Mao Qing) on 28 August 2019, and written informed consent was obtained from all patients that participated in the study. This study has been prospectively registered in the Chinese Clinical Trials Registry (ChiCTR1900024162, on 28 June 2019). All methods performed in this study were in accordance with the relevant guidelines and regulations. All procedures performed in this study involving human participants were in accordance with the Ethical Standards of the Institutional Ethics Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent for Publication

All authors have read and approved the manuscript in its current state and have approved the manuscript for publication.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests.

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