International Urology and Nephrology (2019) 51:1553–1561
https://doi.org/10.1007/s11255-019-02171-9

UROLOGY - ORIGINAL PAPER

Determining whether dexmedetomidine provides a reno-protective effect in patients receiving laparoscopic radical prostatectomy: a pilot study

Shan Wu[1] · Hui Yao[1,2] · Nan Cheng[1] · Na Guo[1] · Jiaxin Chen[1,3] · Mian Ge[1] · Jun Cai[1]

Received: 28 February 2019 / Accepted: 13 May 2019 / Published online: 11 June 2019

Abstract

Purpose This study aims to determine whether perioperative treatment with dexmedetomidine (DEX) during laparoscopic radical prostatectomy (LRP) can provide a reno-protective effect.

Methods This pilot study enrolled 89 patients between 60 and 79 years old, who underwent LRP. These patients were randomly allocated into two groups: group D ($n=44$) and group C ($n=45$). For patients in group D, 1 μg/kg of DEX was intravenously administered within 10 min, followed by 0.5 μg/kg/h of DEX infusion during the operation. This was stopped at 30 min before the end of surgery. For patients in group C, saline was administered at the same doses. The primary outcome was the incidence of acute kidney injury (AKI), and secondary outcomes included other postoperative variables.

Results The incidence of AKI in group D and C was 4.5% and 13.3%, respectively ($P>0.05$). Compared with group C, patients in group D had significantly lower urea nitrogen levels at 6 h after surgery, lower creatinine levels at 6 and 48 h after surgery, and significantly lower CysC levels at 48 h after surgery. A significant decrease in VAS scores for pain and postoperative nausea and vomiting (PONV) at the second and third day after surgery was observed in patients in group D when compared to patients in group C.

Conclusion Intraoperative DEX does not reduce the incidence of AKI, but provides a potential reno-protective effect, and alleviates postoperative pain and PONV in patients undergoing LRP.

Keywords Acute kidney injury · Dexmedetomidine · Estimated glomerular filtration rate · Laparoscopic radical prostatectomy

Introduction

Elderly suffering from prostate cancer is increasing globally. In recent years, laparoscopic radical prostatectomy (LRP), which is a technique that aims to reduce the invasiveness of radical retropubic prostatectomy (RRP), has become a common procedure for patients with prostate cancer [1]. Nevertheless, LRP requires a longer operational time, the induction of pneumoperitoneum and a steep Trendelenburg position, and all of which result in worse outcomes, such as postoperative acute kidney injury (AKI) [2, 3]. This increase in risk might be associated with pathophysiological changes induced by the pneumoperitoneum and Trendelenburg position, leading to a reduction in glomerular filtration rate, renal blood flow and urine output decrease, and renal ischemia-reperfusion injury [4–6]. Eun-Young Joo et al. [7] reported that the incidence of AKI after RRP was 10.4%. Furthermore, according to our previous retrospective study,

Shan Wu and Hui Yao contributed equally to this work.

✉ Jun Cai
gzcaijun1970@163.com

Mian Ge
gemiansums@163.com

[1] Department of Anesthesiology, The Third Affiliated Hospital of Sun Yat-sen University, 600 Tianhe Road, Guangzhou 510630, Guangdong, China

[2] Department of Anesthesiology, Guangdong Second Provincial General Hospital, 466 Xingang Road, Guangzhou 510317, Guangdong, China

[3] Department of Anesthesiology, The Seventh Affiliated Hospital of Sun Yat-sen University, No. 628 Zhenyuan Road, Guangming District, Shenzhen 518107, Guangdong, China

the incidence of AKI after LRP was 12% in our hospital (data not published). Troublingly, there are few protection strategies to decrease the morbidity of AKI after LRP.

Dexmedetomidine (DEX) is a novel and highly selective α2-adrenoceptor (α2-AR) agonist [8] that has been widely used as an anesthetic adjuvant due to its sedative, analgesic and hemodynamic stabilizing ability [9]. The reno-protective effect of DEX has been reported in cardiac surgery [10]. In addition, Geng et al. [11]. revealed that DEX could inhibit mitochondrial damage and cell apoptosis, and thereby protect against renal I/R injury by upregulating SIRT3. In addition, the previous studies [12, 13] conducted by the investigators demonstrated that DEX inhibited Toll-like receptor 4 (TLR4)/NF-κB activation and reduced AKI after orthotopic autologous liver transplantation in rats. However, its impact on renal function during LRP remains unclear. Therefore, the aim of the present pilot study was to observe the impact of DEX on peri-operative renal function and the prognosis of patients who underwent LRP.

Patients and methods

In accordance with the CONSORT statement, the present pilot randomized controlled trial was approved by the appropriate Institutional Review Board (IRB) of the Third Affiliated Hospital of Sun Yat-sen University (IRB [2014]2-102, July 24, 2014), and written informed consent was provided by all patients. The trial was registered prior to patient enrollment in the Chinese Clinical Trial Registry at http://www.chictr.org (ChiCTR-TTRCC-14005144, Principal investigator: Jun Cai, Date of registration: August 3, 2014). The present study was carried out in the Third Affiliated Hospital of Sun Yat-sen University from August 23, 2014 to December 30, 2015.

Patients

All patients scheduled for laparoscopic radical prostatectomy in the hospital were screened. Inclusion criteria: (1) patients between 60 and 79 years old, (2) patients with American Society of Anesthesiology (ASA) Physical Status I–III, (3) patients who provided written consent. Patients who met any of the following criteria were excluded from the study: (1) patients with renal insufficiency [estimated glomerular filtration rate (eGFR) of <60 ml/min/1.73 m^2]; (2) patients with heart diseases including sick sinus syndrome, bradycardia, and second and third degree atrioventricular block; (3) patients with serious renal, hepatic, or pulmonary diseases; (4) patients with long-term use of sedative drugs; (5) patients with neurologic or psychiatric illnesses. Furthermore, patients who met any of the following criteria were excluded from the statistical analysis: (1) patients who finally received RRP; (2) patients who had blood loss >3000 ml during surgery; (3) patients who died within 24 h after surgery; (4) patients with difficulties during the follow-up.

Randomization and masking

Before surgery, all patients were randomly allocated into two groups: group D and group C. The randomization sequence was computer generated. DEX or saline was prepared with the same 50-ml syringe by an anesthetist who was not involved in the management of anesthesia during surgery. To maintain blinding, patients, surgeons, investigators and statisticians were all blinded to the group allocation.

Intervention

Next, 200 μg of DEX was diluted in 50 ml of saline before infusion. In group D, patients were intravenously administered with 1 μg/kg (load dosage) of DEX using a micro pump within 10 min, followed by the infusion of 0.5 μg/kg/h (maintenance dosage) of DEX during the operation, and this was stopped at 30 min before the end of surgery [14, 15]. Patients in group C were given saline at the same infusion rate.

Procedures

After entering the operating room, the left hand radial artery and internal jugular vein of all patients were accessed by an anesthetist. Intraoperative monitoring, including electrocardiogram (ECG), heart rate (HR), invasive blood pressure (IBP), oxygen saturation (SpO_2) and end-tidal carbon dioxide tension ($etCO_2$) measurements, were standardized for all patients.

Patients received an induction of 0.05 mg/kg of midazolam, 0.3–0.4 μg/kg of sufentanil, 1.5–2.0 mg/kg of propofol and 0.2 mg/kg of cisatracurium, followed by tracheal intubation with artificial ventilation. Remifentanil, sevoflurane and cisatracurium were maintained, and the depth of anesthesia was evaluated by Narcotrend at 40–60 during surgery.

The systolic blood pressure levels of patients were kept higher than 90 mmHg. If these levels dropped below 80 mmHg, vasopressors were administered at the discretion of the anesthetist. If HR was lower than 50, atropine was administered. Patients with a hemoglobin concentration lower than 8 g/dl (measured by arterial blood gas) were given red blood cell transfusions.

Pneumoperitoneum was created by CO_2 insufflation (13–15 mmHg), and patients were positioned in the 30° steep Trendelenburg position. A single surgical team performed the surgery throughout the study period.

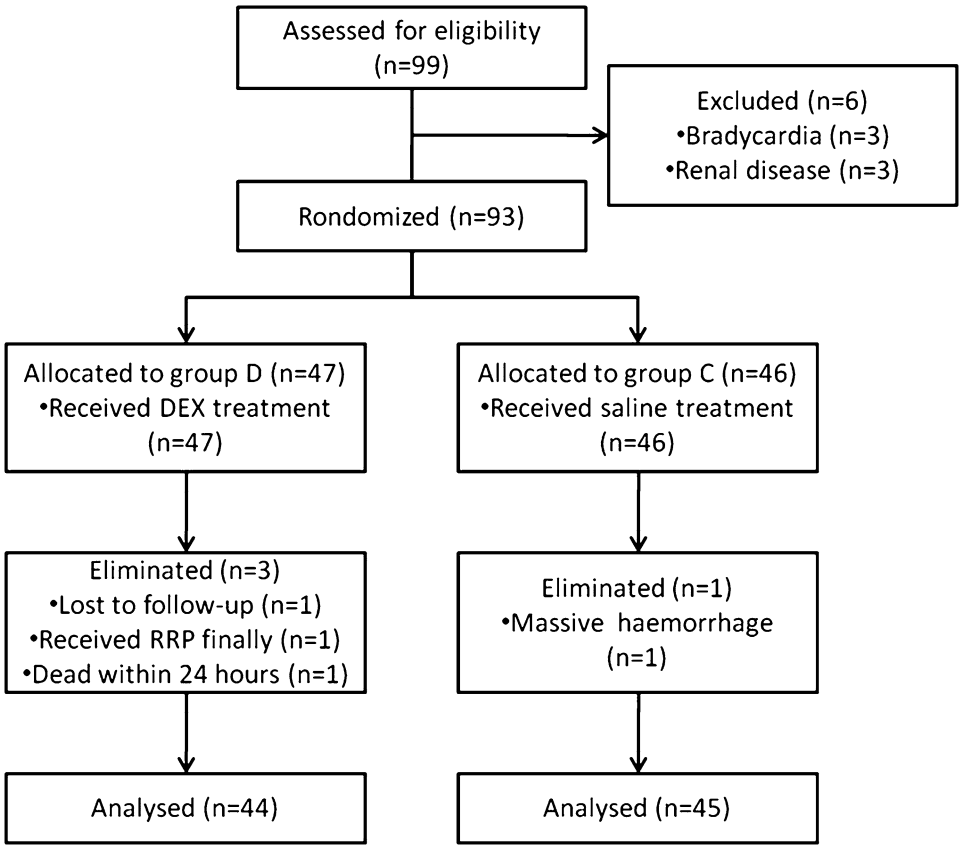

Fig. 1 CONSORT diagram showing the flow of participants

Data collection

Laboratory values, including blood urea nitrogen (BUN), serum creatinine (Scr), serum cystatin C (CysC) and β_2-microglobulin (β_2MG), were obtained at four time points: at baseline (T0, before surgery), and at 6 h (T6h), 24 h (T24h) and 48 h (T48h) after surgery. Blood samples were measured at the Central Laboratory of the Third Affiliated Hospital of Sun Yat-sen University using standard protocol.

Urine samples were collected at the same time points to measure *N*-acetyl-alpha-D-amino glycosidase enzymes (NAG) and urine creatinine.

Primary outcome

The primary outcome was the incidence of AKI, which was defined based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria [16] for AKI within 48 h after surgery [the presence of any of the following events: an increase in Scr by ≥ 0.3 mg/dl (≥ 26.5 μmol/l) within 48 h, an increase in Scr to ≥ 1.5 times the baseline levels within 1 week before surgery, or urine output < 0.5 ml/kg/h for 6 h]. In the present study, the urine output criterion was not included because urine output was measured on a daily basis, and not on an hourly basis.

Secondary outcomes

Secondary outcomes included the following: (1) kidney injury markers (Scr, BUN, CysC, β_2MG, and urine NAG/urine creatinine ratio); (2) eGFR, which was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [17]: $\text{eGFR} = 141 \times (\text{serum creatinine}/0.9)^{a} \times 0.993^{\text{age}}$, $a = -1.209$ when serum creatinine > 0.9 mg/dl, $a = -0.411$ when serum creatinine ≤ 0.9 mg/dl; (3) visual analogue scale (VAS) scores; (4) postoperative nausea and vomiting (PONV); (5) myocardial infarction diagnosed using an electrocardiogram; (6) acute respiratory distress syndrome (ARDS) diagnosed by chest X-ray; (7) other postoperative data [the consumption of analgesics, pain after urinary catheterization, urine volume, duration of ventilation, occurrence of delayed recovery, timing of flatus/removal of urinary catheter/removal of drainage tube, and length of stay (LOS)].

Statistical analysis

SPSS 22.0 software (SPSS Inc., Chicago, IL, USA) was used to perform the statistical analyses. Continuous data were analyzed through a normality test. All normally distributed data were presented as mean ± standard deviation (SD),

Table 1 Preoperative characteristics: continuous data were described as mean ± standard deviation (SD) or median (interquartile range), and categorical data were described as frequency or percentage

	Group D ($n=44$)	Group C ($n=45$)	P value
Age (years)	67	69	0.477
Weight (kg)	66.35 ± 10.46	64.96 ± 9.07	0.528
BMI (kg/m^2)	23.67 ± 3.65	23.24 ± 3.24	0.578
ASA classification			0.308
I	11 (25.00%)	17 (37.78%)	
II	22 (50.00%)	18 (40.00%)	
III	11 (25.00%)	10 (22.22%)	
Hypertension	20 (43.48%)	19 (44.19%)	0.759
DM	5 (11.63%)	3 (6.52%)	0.689
CAD	4 (9.30%)	6 (13.04%)	0.766
Cerebrovascular disease	5 (11.63%)	1 (2.17%)	0.195
COPD	1 (2.2%)	2 (4.44%)	1
Baseline hemoglobin (g/l)	138.44 ± 17.07	139.52 ± 10.62	0.725
The weight of prostate (g)	44.09 (22.40)	59.71 (34.02)	0.076
PSA (ng/ml)	10.63 (21.76)	13.81 (20.63)	0.14
Gleason score	7 (1)	7 (2)	0.194
Baseline renal function			
eGFR	88.20 ± 24.10	80.86 ± 20.77	0.131
BUN	5.52 ± 0.24	5.34 ± 0.22	0.577
Cr	82.55 ± 2.05	85.60 ± 1.95	0.469

BMI body mass index, *BUN* blood urea nitrogen, *ASA* American Society of Anesthesiologists, *DM* diabetes mellitus, *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease, *Cr* creatinine, *eGFR* estimated glomerular filtration rate, *PSA* prostate specific antigen

and compared between groups using independent t test. All non-normally distributed data were compared using the Mann–Whitney U test and were expressed as median with interquartile range (IQR). Categorical data were described as frequency or percentage, and analyzed using X^2-test or Fisher's exact test, as appropriate. All repeatedly measured data were analyzed by two-way repeated analysis of variance with Bonferroni correction for both within- and between-group comparisons. The differences were considered significant when the two-tailed P value was <0.05.

Results

Among the 99 consecutive patients screened for inclusion, six patients were excluded due to bradycardia and renal insufficiency. In addition, four patients were excluded from the statistical analysis. Finally, 89 patients were enrolled for analysis. Among these patients, 44 patients were assigned in group D, while 45 patients were assigned in group C (Fig. 1).

Patient characteristics

As presented in Table 1, there were no significant differences in age, weight, body mass index (BMI), preexisting clinical conditions [hypertension, diabetes mellitus, cerebrovascular disease, chronic obstructive pulmonary disease (COPD), and coronary artery disease (CAD)], American Society of Anesthesiologists (ASA) classification, preoperative use of nephrotoxic drugs, diagnostic groups [the size of the prostate, prostate-specific antigen (PSA), and Gleason scores], or levels of preoperative hemoglobin between patients with or without DEX.

As presented in Table 2, DEX administration reduced HR, but not MAP, during surgery, when compared with placebo. In addition, MAP was lower at 1 h after pneumoperitoneum in group D, when compared to group C. This finding might be correlated to the possibility that DEX could reduce stress response resulting from pneumoperitoneum. There were no significant differences in other parameters between these two groups.

Incidence of AKI

Among all patients, AKI occurred in eight patients (8.99%) within the first 48 h after LRP. Among these AKI patients, two (4.5%) patients were from group D, while six (13.3%) patients were group C. There were no significant differences between these two groups (Table 3).

Postoperative renal function of patients

Figure 2a–f presents the postoperative renal function analytic results. In categorizing patients with an eGFR of <60 ml/min/1.73 m^2 as renal insufficiency, it was found that five patients in group D and 11 patients in group C suffered from renal insufficiency ($P<0.05$). Furthermore, compared with patients in group D, patients in group C had significantly higher BUN at T6h (3.91 ± 0.92 vs. 4.57 ± 1.54 mmol/l, $P<0.05$), significantly higher Scr at T6h (78.62 ± 13.17 vs. 85.13 ± 16.13 μmol/l, $P<0.05$) and T48h (82.77 ± 7.04 vs. 89.68 ± 5.31, $P<0.05$), and significantly higher CysC at T48h (0.764 ± 0.207 vs. 0.86 ± 0.46 mg/l, $P<0.05$).

Postoperative variables of patients

Table 4 presents the postoperative variables of the study participants. There was a significant decrease in VAS scores for pain at the second [2 (1) vs. 3 (1), $P<0.05$] and third day [2 (1.25) vs. 2 (2), $P<0.05$] after surgery, and a decrease in

Table 2 Intraoperative characteristics: continuous data were presented as mean ± standard deviation (SD) or median (interquartile range), and categorical data were presented as frequency or percentage

	Group D ($n=44$)	Group C ($n=45$)	P value
Surgical approach			0.758
Extraperitoneal	33 (75.00%)	35 (77.78%)	
Intraperitoneal	11 (25.00%)	10 (22.22%)	
Duration of surgery (min)	208 (55)	210 (84)	0.844
Duration of pneumoperitoneum (min)	177.5 (64)	173.0 (92)	0.812
Pressure of pneumoperitoneum (mmHg)	13 (0)	13 (0)	0.405
Totally output (ml)	1550 (1475)	1375 (903)	0.172
Intraoperative fluids administered (ml)	3500 (1100)	3200 (875)	0.056
Colloid	1000 (300)	1000 (150)	0.057
Crystalloid	2250 (825)	2200 (700)	0.054
Intraoperative transfusions	5 (11.36%)	6 (13.04%)	0.778
Hemoglobin < 90 g/l or decrease > 30%	20 (45.45%)	15(33.33%)	0.242
Vasopressor agents	30 (72.73%)	29 (64.44%)	0.4
Dopamine (mg)	7 (26)	6 (13)	0.35
Norepinephrine (μg)	460 (740)	400 (755)	0.395
Phenylephrine (μg)	100 (50)	75 (50)	0.229
Atropine	21 (47.73%)	13 (28.89%)	0.067
Bradycardia	21 (47.73%)	13 (28.89%)	0.067
MAP (mmHg)			
Baseline	96 ± 12	93 ± 10	0.341
Loading dose of DEX	92 ± 11	93 ± 10	0.955
One hour after pneumoperitoneum	73 ± 8#,*	82 ± 12	0.013
Two hours after pneumoperitoneum	73 ± 9#	76 ± 9	0.32
End of surgery	72 ± 8#	77 ± 10	0.9
HR (beats/min)			
Baseline	77 ± 11	74 ± 12	0.394
Loading dose of DEX	65 ± 10#,*	74 ± 10	< 0.0001
One hour after pneumoperitoneum	68 ± 11#	72 ± 10	0.091
Two hours after pneumoperitoneum	68 ± 11#	70 ± 10	0.326
End of surgery	66 ± 9#	69 ± 8	0.15

MAP mean arterial pressure, *HR* heart rate, *DEX* dexmedetomidine

#$P < 0.05$ vs. baseline, *$P < 0.05$ vs. group C

Table 3 Incidence of AKI: data were presented as percentages

	Group D ($n=44$)	Group C ($n=45$)	P value
AKI	2 (4.55%)	6 (13.33%)	0.281
Non-AKI	42 (95.45%)	39 (86.67)	

AKI acute kidney injury

occurrence of PONV (4.55% vs. 22.22%, $P < 0.05$) in patients in group D, when compared to patients in group C. However, there were no significant differences in the incidence of bradycardia, analgesics consumption, severity of pain after urinary catheter, fever, postoperative urine volume, duration of ventilation, delayed recovery, time of flatus/removing urinary catheter/drainage tube, and LOS between patients with or without DEX. Furthermore, none of the participants suffered from ARDS or myocardial infarction in either of the groups.

Discussion

A previous study reported a postoperative AKI incidence of 5.5% after robot-assisted laparoscopic radical prostatectomy (RALP) and 10.4% after RRP [7]. However, the incidence of postoperative AKI after LRP has not been well-described. According to the experience of our hospital, the incidence of AKI after LRP was 12% (data not published), which was higher than RALP or RRP. Consequently, there is an urgent need to develop preventive and treatment strategies to reduce such event.

This prospective, randomized, double-blinded controlled trial demonstrated that intraoperative DEX use does not reduce the incidence of AKI. In the present study, AKI was defined based on the KDIGO criteria [16]. Previous studies [18] have identified that the KDIGO criteria exhibits higher sensitivity, when compared to the "Risk, Injury, Failure,

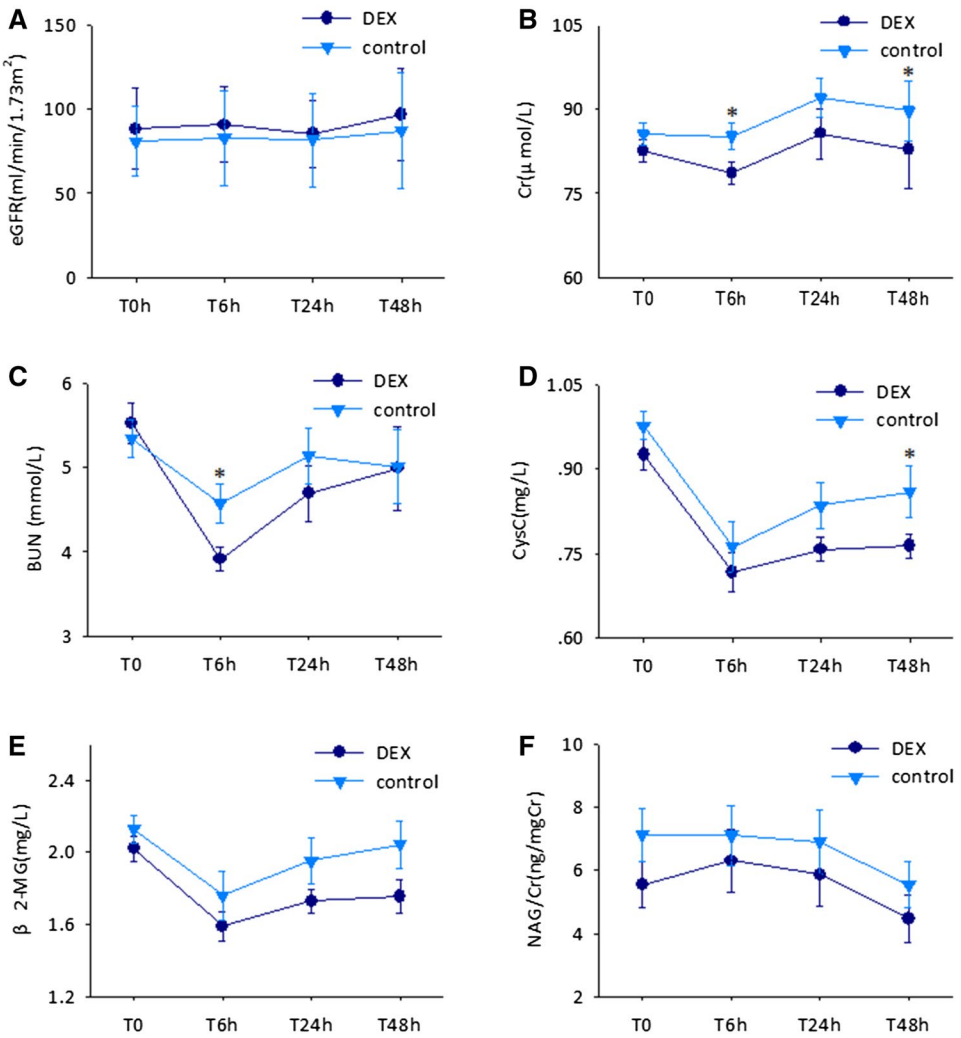

Fig. 2 Biomarkers of kidney function: **a** eGFR; **b** Serum Cr; **c** Serum BUN; **d** Serum CysC; **e** β2-MG; **f** urine NAG/urine Cr. Data were presented as mean ± standard deviation (SD). *$P < 0.05$ vs. group C

Loss of kidney function, and End-stage kidney disease" (RIFLE) classification and Acute Kidney Injury Network (AKIN) criteria. The incidence of postoperative AKI in patients who underwent LRP in group D was 4.5%, which is lower than that in patients in group C (13.3%), but there were no significant statistical differences between these two groups. This is probably due to the fact that the sample size was not based on the incidence of postoperative AKI, and that there was no existing research about LRP. In addition, one of the KDIGO criteria for AKI is urine output (< 0.5 ml/kg/h for 6 h), and urine output was not measured in the present study due to its inaccuracy. This might have led to the under diagnosis of AKI. Furthermore, for patients in cardiac surgery trials who received a continuous infusion of DEX at 0.4 μg/kg/h without a loading dose intraoperatively and within the first 24 h postoperatively, the duration of DEX administration was shorter and the cumulative DEX dose was significantly lower, when compared to patients involved in cardiac surgery in previous studies [10, 19]. Finally, the present study merely analyzed 89 patients, which may partially contribute to these negative findings.

DEX is a novel and highly selective α_2-adrenoceptor (α_2-AR) agonist, which has been widely used as an anesthetic adjuvant due to its sedative, analgesic and hemodynamic stabilizing ability [9]. A number of researches [8, 10, 14, 15] have demonstrated that DEX exhibits organ-protective effects in vivo and in vitro, and the mechanisms involved might be associated with its anti-inflammatory, antioxidative and anti-apoptotic effects. Geng et al. [11] revealed that DEX could inhibit mitochondrial damage and cell apoptosis, and thereby protect against renal I/R injury by upregulating SIRT3. The previous study conducted by the investigators [12, 13] revealed that DEX inhibits Toll-like receptor 4 (TLR4)/NF-κB activation and reduces AKI after orthotopic autologous liver transplantation in rats. However, little is known on the perioperative reno-protective effect of DEX. Cho et al. [19] reported that perioperative DEX use reduced the incidence and severity

Table 4 Postoperative outcome variables: continuous data were presented as mean ± standard deviation (SD) or median (interquartile range), and categorical data were presented as frequency or percentage

	Group D ($n=44$)	Group C ($n=45$)	P value
VAS score			
First day	3 (1)	4 (2)	0.127
Second day	2 (1)	3 (1)	0.008
Third day	2 (1.25)	2 (2)	0.039
The requirement of analgesic	17 (38.64%)	25 (55.56%)	0.11
PONV	2 (4.55%)	10 (22.22%)	0.033
Pain after urinary catheter	7 (15.91%)	8 (17.78%)	0.814
Fever	18 (40.90%)	20 (44.44%)	0.736
Urine volume (ml)			
First day	1620 (800)	1400 (1245)	0.371
Second day	3162.42 ± 1533.45	2886.86 ± 1051.29	0.403
Third day	3559.94 ± 1157.94	3600.94 ± 1066.02	0.883
Forth day	3443.04 ± 849.59	3428.93 ± 1114.76	0.958
Total urine volume	11,677.77 ± 2594.07	11,440.89 ± 2927.36	0.755
Duration of ventilation (h)	55 (30)	45 (32.5)	0.164
Delayed recovery	5 (11.36%)	5 (11.11%)	0.97
Time of flatus (h)	47 (24)	44 (39)	0.861
Removing drainage tube (day)	5 (4)	6 (3)	0.137
Removing urinary catheter (day)	11 (5)	11 (7)	0.44
Length of stay (day)	13 (7)	12 (5)	0.255
ARDS	0	0	
Myocardial infarction	0	0	

VAS visual analogue scale, *PONV* postoperative nausea and vomiting, *ARDS* acute respiratory distress syndrome

of AKI following valvular heart surgery. Nevertheless, the reno-protective effect of DEX in LRP has not been well-described, and the present findings provide evidence for this phenomenon.

It has been shown that DEX decreased Scr, BUN and CysC levels in patients who underwent LRP, when compared to patients who received a placebo. This finding strongly supports the theory that DEX administration during LRP could provide renoprotection. However, the levels of postoperative BUN, CysC and β2-MG were lower than preoperative levels. This is probably because the renal injury during LRP is milder when compared to that developed during cardiac surgery (18.9–49%) [20–22] or liver transplantation (3.97–70%) [23, 24]. Furthermore, approximately 3500 ml of fluids were administered during the surgery, and this would potentially lead to a dilution effect. In addition, the hematocrit levels at different time points were have analyzed, and the present data support this theory.

The enhanced recovery after surgery (ERAS) protocol is a multimodal perioperative care pathway designed to achieve early recovery after surgical procedures. The key elements of ERAS protocols are standardized analgesia and the recovery of gastroenteric function [25, 26]. Despite the fact that LRP is a minimally invasive surgery, it remains as an invasive procedure that induces postoperative pain and PONV. DEX has been shown to have the ability to be neuromodulative and modify the biosynthesis of neurotransmitters and is involved in substance P, 5-HT and other neurotransmitter transmissions [27]. These neurotransmitters are well-known for their roles in mediating the pain, nausea and vomiting pathway. In addition, treatment with DEX reduces the amount of intra-operative and postoperative opioids, and inhaled anesthetics used [28]. In the present study, there was a significant decrease in VAS scores for pain at the second and third day, and in the occurrence of PONV after surgery in group D, when compared to group C ($P<0.05$). This is compatible with previous researches.

Limitations

There were several limitations in the present study. First, different dosages of DEX should be used to investigate the relationship between the renoprotection effect of DEX and its dosage. Second, the long-term outcomes of using DEX were not monitored. Third, the absence of urine output data might have resulted in the under diagnosis of AKI. Finally, follow-up data was absent in non-survivors, and the approach of excluding those with massive bleeding, which is a major risk factor of AKI, might have contributed to selection bias.

Conclusion

In conclusion, intraoperative DEX use does not reduce the incidence of AKI, but provides a potential reno-protective effect, and alleviates postoperative pain and PONV in patients undergoing LRP.

Acknowledgements The authors thank Doctor Qianqian Zhu for the guidance of the statistics analyses in this manuscript, and we also thank Medjaden Bioscience Limited for editing and proofreading our manuscript.

Author contributions SW and HY contributed to this work equally. SW and HY: clinical data collection, writing up of the first draft of the paper and data analysis; NC, NG and JXC: clinical anaesthesia for the patients; MG and JC: study design.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

References

1. Heidenreich A, Bellmunt J, Bolla M, Joniau S, Mason M, Matveev V, Mottet N, Schmid HP, van der Kwast T, Wiegel T, Zattoni F, European Association of U (2011) EAU guidelines on prostate cancer. Part 1: screening, diagnosis, and treatment of clinically localised disease. Eur Urol 59(1):61–71. https://doi.org/10.1016/j.eururo.2010.10.039
2. Lee BR, Cadeddu JA, Molnar-Nadasdy G, Enriquez D, Nadasdy T, Kavoussi LR, Ratner LE (1999) Chronic effect of pneumoperitoneum on renal histology. J Endourol 13(4):279–282. https://doi.org/10.1089/end.1999.13.279
3. Miki Y, Iwase K, Kamiike W, Taniguchi E, Sakaguchi K, Sumimura J, Matsuda H, Nagai I (1997) Laparoscopic cholecystectomy and time-course changes in renal function. The effect of the retraction method on renal function. Surg Endosc 11(8):838–841
4. Chekan EG, Nataraj C, Clary EM, Hayward TZ, Brody FJ, Stamat JC, Fina MC, Eubanks WS, Westcott CJ (1999) Intraperitoneal immunity and pneumoperitoneum. Surg Endosc 13(11):1135–1138
5. Miyano G, Nakamura H, Seo S, Sueyoshi R, Okawada M, Doi T, Koga H, Lane GJ, Yamataka A (2016) Pneumoperitoneum and hemodynamic stability during pediatric laparoscopic appendectomy. J Pediatr Surg 51(12):1949–1951. https://doi.org/10.1016/j.jpedsurg.2016.09.016
6. Sodha S, Nazarian S, Adshead JM, Vasdev N, Mohan SG (2016) Effect of pneumoperitoneum on renal function and physiology in patients undergoing robotic renal surgery. Curr Urol 9(1):1–4. https://doi.org/10.1159/000442842
7. Joo EY, Moon YJ, Yoon SH, Chin JH, Hwang JH, Kim YK (2016) Comparison of acute kidney injury after robot-assisted laparoscopic radical prostatectomy versus retropubic radical prostatectomy: a propensity score matching analysis. Medicine (Baltimore) 95(5):e2650. https://doi.org/10.1097/MD.0000000000002650
8. Chen Q, Yi B, Ma J, Ning J, Wu L, Ma D, Lu K, Gu J (2016) alpha2-Adrenoreceptor modulated FAK pathway induced by dexmedetomidine attenuates pulmonary microvascular hyper-permeability following kidney injury. Oncotarget 7(35):55990–56001. https://doi.org/10.18632/oncotarget.10809
9. Kunisawa T, Nagata O, Nagashima M, Mitamura S, Ueno M, Suzuki A, Takahata O, Iwasaki H (2009) Dexmedetomidine suppresses the decrease in blood pressure during anesthetic induction and blunts the cardiovascular response to tracheal intubation. J Clin Anesth 21(3):194–199. https://doi.org/10.1016/j.jclinane.2008.08.015
10. Soliman R, Hussien M (2017) Comparison of the renoprotective effect of dexmedetomidine and dopamine in high-risk renal patients undergoing cardiac surgery: a double-blind randomized study. Ann Card Anaesth 20(4):408–415. https://doi.org/10.4103/aca.ACA_57_17
11. Si Y, Bao H, Han L, Chen L, Zeng L, Jing L, Xing Y, Geng Y (2018) Dexmedetomidine attenuation of renal ischaemia-reperfusion injury requires sirtuin 3 activation. Br J Anaesth 121(6):1260–1271. https://doi.org/10.1016/j.bja.2018.07.007
12. Yao H, Chi X, Jin Y, Wang Y, Huang P, Wu S, Xia Z, Cai J (2015) Dexmedetomidine inhibits TLR4/NF-kappaB activation and reduces acute kidney injury after orthotopic autologous liver transplantation in rats. Sci Rep 5:16849. https://doi.org/10.1038/srep16849
13. Yu X, Chi X, Wu S, Jin Y, Yao H, Wang Y, Xia Z, Cai J (2016) Dexmedetomidine pretreatment attenuates kidney injury and oxidative stress during orthotopic autologous liver transplantation in rats. Oxid Med Cell Longev 2016:4675817. https://doi.org/10.1155/2016/4675817
14. Lee SH, Lee CY, Lee JG, Kim N, Lee HM, Oh YJ (2016) Intraoperative dexmedetomidine improves the quality of recovery and postoperative pulmonary function in patients undergoing video-assisted thoracoscopic surgery: a CONSORT-prospective, randomized, controlled trial. Medicine (Baltimore) 95(7):e2854. https://doi.org/10.1097/MD.0000000000002854
15. Wang ZX, Huang CY, Hua YP, Huang WQ, Deng LH, Liu KX (2014) Dexmedetomidine reduces intestinal and hepatic injury after hepatectomy with inflow occlusion under general anaesthesia: a randomized controlled trial. Br J Anaesth 112(6):1055–1064. https://doi.org/10.1093/bja/aeu132
16. Khwaja A (2012) KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract 120(4):c179–c184. https://doi.org/10.1159/000339789
17. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, Coresh J, Ckd EPI (2009) A new equation to estimate glomerular filtration rate. Ann Intern Med 150(9):604–612
18. Luo X, Jiang L, Du B, Wen Y, Wang M, Xi X, Beijing Acute Kidney Injury Trial w (2014) A comparison of different diagnostic criteria of acute kidney injury in critically ill patients. Crit Care 18(4):R144. https://doi.org/10.1186/cc13977
19. Cho JS, Shim JK, Soh S, Kim MK, Kwak YL (2016) Perioperative dexmedetomidine reduces the incidence and severity of acute kidney injury following valvular heart surgery. Kidney Int 89(3):693–700. https://doi.org/10.1038/ki.2015.306
20. Fuhrman DY, Kellum JA (2017) Epidemiology and pathophysiology of cardiac surgery-associated acute kidney injury. Curr Opin Anaesthesiol 30(1):60–65. https://doi.org/10.1097/ACO.0000000000000412
21. Hoste EAJ, Vandenberghe W (2017) Epidemiology of cardiac surgery-associated acute kidney injury. Best Pract Res Clin Anaesthesiol 31(3):299–303. https://doi.org/10.1016/j.bpa.2017.11.001
22. Wang Y, Bellomo R (2017) Cardiac surgery-associated acute kidney injury: risk factors, pathophysiology and treatment. Nat Rev Nephrol 13(11):697–711. https://doi.org/10.1038/nrnephh.2017.119

23. Chen X, Ding X, Shen B, Teng J, Zou J, Wang T, Zhou J, Chen N, Zhang B (2017) Incidence and outcomes of acute kidney injury in patients with hepatocellular carcinoma after liver transplantation. J Cancer Res Clin Oncol 143(7):1337–1346. https://doi.org/10.1007/s00432-017-2376-8
24. Hilmi IA, Damian D, Al-Khafaji A, Planinsic R, Boucek C, Sakai T, Chang CC, Kellum JA (2015) Acute kidney injury following orthotopic liver transplantation: incidence, risk factors, and effects on patient and graft outcomes. Br J Anaesth 114(6):919–926. https://doi.org/10.1093/bja/aeu556
25. Pedziwiatr M, Pisarska M, Major P, Grochowska A, Matlok M, Przeczek K, Stefura T, Budzynski A, Klek S (2016) Enhanced recovery after surgery protocol (ERAS) combined with laparoscopic colorectal surgery diminishes the negative impact of sarcopenia on short-term outcomes. Clin Nutr ESPEN 12:e49. https://doi.org/10.1016/j.clnesp.2016.02.061
26. Soeters PB (2017) The enhanced recovery after surgery (ERAS) program: benefit and concerns. Am J Clin Nutr 106(1):10–11. https://doi.org/10.3945/ajcn.117.159897
27. Whittington RA, Virag L (2006) Dexmedetomidine-induced decreases in accumbal dopamine in the rat are partly mediated via the locus coeruleus. Anesth Analg 102(2):448–455. https://doi.org/10.1213/01.ane.0000195234.07413.5a
28. Blaudszun G, Lysakowski C, Elia N, Tramer MR (2012) Effect of perioperative systemic alpha2 agonists on postoperative morphine consumption and pain intensity: systematic review and meta-analysis of randomized controlled trials. Anesthesiology 116(6):1312–1322. https://doi.org/10.1097/ALN.0b013e31825681cb