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ORIGINAL RESEARCH

The Effect of Dexmedetomidine on Postoperative Acute Kidney Injury in High-Risk Partial Nephrectomy Patients: A Retrospective Cohort Study

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Background: Randomized controlled trial has shown that dexmedetomidine does not significantly reduce postoperative acute kidney injury (AKI) in general partial nephrectomy (PN) populations. However, evidence remains limited in patients with high susceptibility to renal ischemia, such as those with a solitary kidney or pre-existing chronic kidney disease (CKD).

Methods: We conducted a single-center retrospective cohort study including adult high-risk PN patients between 2015 and 2023. Eligible high-risk patients were those with a solitary kidney or pre-existing CKD. The study cohort was divided into dexmedetomidine-exposed and non-exposed groups. To balance baseline characteristics, inverse probability of treatment weighting (IPTW) was applied. The primary outcome was AKI incidence within 24 hours postoperatively, defined by KDIGO creatinine criteria.

Results: The study included 274 patients, with 82 assigned to the dexmedetomidine-exposed cohort and 192 to the non-exposed cohort. After IPTW adjustment, all baseline covariates were well balanced. Dexmedetomidine exposure was associated with significantly lower AKI incidence (23.9% versus 38.6%, P = 0.025), with a trend toward milder AKI staging. Intraoperative urine output was higher in the dexmedetomidine group (341 ± 183 versus 282 ± 188 mL, P = 0.022). Length of postoperative hospital stay, postoperative complications, ICU admission rate, percentage decrease in eGFR from baseline at 6-month follow-up, and incidence of a >20% decrease from baseline eGFR at 6-month follow-up did not differ significantly between the two groups.

Conclusion: In high-risk PN patients with a solitary kidney or pre-existing CKD, intraoperative dexmedetomidine was associated with a clinically meaningful reduction in postoperative AKI. These findings suggest a potential renoprotective role of dexmedetomidine in this vulnerable surgical population, although this early renal benefit did not translate into long-term improvements in renal function.

Keywords: dexmedetomidine, acute kidney injury, solitary kidney, chronic kidney disease, high-risk

Introduction

Partial nephrectomy (PN) is the preferred treatment for localized renal tumors, preserving renal parenchyma while maintaining oncologic efficacy.[1] However, the procedure inherently risks postoperative acute kidney injury (AKI), especially in patients with pre-existing renal compromise such as chronic kidney disease (CKD)[2] or solitary kidney.[3] These patients frequently experience prolonged renal ischemia, higher susceptibility to hemodynamic fluctuations, and reduced nephron reserve, all contributing to disproportionately high postoperative AKI incidence.[2,3]

Dexmedetomidine, a selective α2-adrenergic agonist, has been widely used in perioperative anesthesia for its sedative, analgesic, and sympatholytic properties.[4] Experimental studies suggested that dexmedetomidine mitigated renal ischemia-reperfusion injury primarily by reducing oxidative stress, inflammation, apoptosis, ferroptosis, and

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endoplasmic reticulum stress, as well as enhancing gap junction intercellular communication.[5] However, clinical data have been conflicting. Previous studies have demonstrated that dexmedetomidine confers a significant renoprotective effect across a broad spectrum of surgical settings, including cardiac surgery,[6] non-cardiac surgery,[7] liver transplantation,[8] and interventional procedures requiring contrast agents.[9] However, findings from our prior trial focusing on patients with abundant nephron reserve undergoing partial nephrectomy revealed no significant reduction in the incidence of postoperative AKI.[10] This observation raises the critical concern that dexmedetomidine-mediated renoprotection may be restricted to specific high-risk PN patient subgroups rather than the general population.

To date, no study has focused exclusively on high-risk PN patients with limited renal functional reserve. This population may uniquely benefit from dexmedetomidine due to its stabilization of hemodynamics,[8] attenuation of sympathetic stress response,[9] and potential protection against ischemic renal injury during hilar clamping.[10] Therefore, this study aimed to evaluate the association between intraoperative dexmedetomidine infusion and postoperative AKI in PN patients with preoperative CKD or solitary kidney using an inverse probability of treatment–weighted (IPTW) cohort design. We hypothesized that dexmedetomidine could reduce postoperative AKI incidence in these high-risk patients undergoing PN.

Methods

Study Design and Ethics

This was a single-center retrospective cohort study conducted at a tertiary hospital. The study protocol was approved by the institutional ethics committee (No.: 2025–1513) on October 24, 2025. Written informed consent was waived due to the retrospective nature of the study. All patient data were anonymized and handled in strict compliance with patient data confidentiality requirements. The study was reported in accordance with the Strengthening the Reporting of Cohort, Cross-Sectional, and Case-Control Studies (STROCSS) guidelines.

Participants

Adult patients who underwent PN (open, laparoscopic, or robot-assisted) between October 2015 and December 2023 were screened via the hospital's electronic medical record system. Eligible patients were those at high risk of postoperative renal injury, defined as meeting at least one of the following criteria: (i) solitary kidney, including congenital forms or those resulting from prior contralateral nephrectomy; (ii) pre-existing CKD, documented by preoperative medical records or preoperative estimated glomerular filtration rate (eGFR) <60 mL min $1.73m^{-2}$ calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.[11] Exclusion criteria were: (i) preoperative dialysis; (ii) concurrent other major surgeries; (iii) intraoperative conversion to radical nephrectomy; (iv) missing postoperative serum creatinine measurements; (v) total intraoperative dexmedetomidine dose less than 20 μg. A dose <20 μg was considered insufficient to achieve stable sedation and systemic sympatholysis, and thus unlikely to exert meaningful organ-protective effects.[12]

Exposure and Grouping

Patients were classified by intraoperative dexmedetomidine exposure into group DEX with a total dose ≥ 20 μg and group Non-DEX without any exposure. The decision to administer dexmedetomidine and the dosage were at the discretion of the attending anesthesiologist per clinical practice.

Data Collection

Data were extracted from electronic medical records by two independent investigators, with discrepancies resolved by consensus. Demographics included age, sex, and body mass index (BMI). Preoperative data included comorbidities (hypertension, diabetes mellitus, coronary heart disease, arrhythmia, chronic obstructive pulmonary disease, and stroke), renal conditions (solitary kidney, CKD, and R.E.N.A.L. score[13]), and laboratory tests (baseline serum creatinine, albumin, and hemoglobin). Intraoperative data included surgical approach, surgery duration, clamp time, blood loss, fluid volume, urine output, and intraoperative hemodynamics. Postoperative data included serum creatinine measurements, length of postoperative hospital stay, ICU admission, and complications (defined as Clavien-Dindo Grade II or higher). Patients were instructed to undergo a follow-up examination at the 6-month mark after surgery upon hospital discharge. Accordingly, serum creatinine

levels at 6 months postoperatively (ranging from 4 to 8 months after surgery) were retrieved from the Laboratory Information Management System of our hospital. Nevertheless, a minority of patients (24%) opted to have their follow-up examinations at other medical institutions, and telephone follow-ups were conducted to collect their serum creatinine data for the study.

Outcomes

The primary outcome was incidence of postoperative AKI within 24 hours, defined by KDIGO creatinine criteria:[14] absolute increase in serum creatinine >26.5 μmol/L, relative increase >50% from baseline, or new renal replacement therapy. Urine output criteria were not applied due to incomplete postoperative records, which may lead to underestimation of AKI incidence. Secondary outcomes were: (i) AKI stage (I to III), (ii) intraoperative urine output, (iii) length of postoperative hospital stay, (iv) ICU admission rate, (v) incidences of complications (Clavien-Dindo Grade II or higher), (vi) decreased rate of eGFR at postoperative 6-month follow-up, and (vii) incidence of >20% decrease from baseline eGFR at postoperative 6-month follow-up. Safety endpoints include bradycardia (heart rate <50 bpm), tachycardia (heart rate >100 bpm), hypotension (systolic blood pressure <90 mmHg), hypertension (systolic blood pressure >180 mmHg), hypoxemia (pulse oxygen saturation <92% requiring intervention), and delayed emergence (failure to extubate within 30 minutes of anesthetic discontinuation).

Missing Data Handling

Missing data were first manually verified. For variables with <10% missing values, missing data were addressed via multiple imputation with 10 imputed datasets using IBM SPSS Statistics (Version 26.0, IBM Corp., Armonk, NY, USA). After excluding non-imputed records, imputed values for each participant were aggregated into continuous variables by mean and categorical variables by mode. A single complete dataset was generated for subsequent analyses. Variables with >10% missing values were excluded.

Statistical Analysis

Inverse probability of treatment weighting (IPTW) based on the propensity score was performed to achieve balanced comparison between groups. Propensity scores were estimated using pre- and intraoperative variables associated with both treatment allocation and AKI. The covariates included age, sex, BMI, hypertension, diabetes mellitus, coronary artery disease, arrhythmia, chronic obstructive pulmonary disease, stroke, smoking status, ASA physical status classification, solitary kidney, CKD, R.E.N.A.L. score, baseline eGFR, serum albumin, hemoglobin, surgical approach, renal clamp time, surgery duration, intraoperative fluid infusion, and estimated blood loss. Covariate balance was assessed using the absolute standardized mean difference (ASD). An ASD < 0.10 was considered indicative of adequate balance. To comprehensively assess balance beyond mean differences and rule out residual distributional imbalance, we performed additional diagnostic checks. For continuous covariates, kernel density estimation plots were constructed to visually compare the full distributional profiles between groups after weighting. Between-group equality of variances was also assessed for key continuous variables. For categorical covariates, bar charts were used to confirm balanced frequency distributions. These complementary diagnostics ensured that balance was achieved in both central tendency and overall distribution.

Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range, IQR) based on the results of normality tests. Categorical variables were expressed as counts (percentages) and compared using the chi-square test or Fisher's exact test where appropriate. For continuous data, comparisons between two groups were performed with the independent samples *t*-test if normally distributed, or the Mann–Whitney *U*-test if the distribution was non-parametric. The relative differences for categorical variables were expressed as odds ratios (OR) and 95% confidence intervals (CI). Two-sided P<0.05 was considered statistically significant.

A post hoc analysis was conducted to evaluate the dose-dependent association of dexmedetomidine with postoperative AKI and the percentage reduction in eGFR from baseline at 6 months. Patients were stratified into three groups: no-dose, low-dose (20–50 μg), and high-dose (≥50 μg). Stabilized IPTW and overlap weighting were used to balance baseline characteristics. Owing to the reduction in sample size following dose stratification, some baseline variables remained with an ASD > 0.10 after weighting. These variables were included in multivariable weighted trend regression analyses to adjust for residual imbalance. Weighted trend regression was performed to estimate OR and 95% CI. A two-sided P-value < 0.05 was considered statistically significant.

Sensitivity analyses were performed to assess the robustness of the findings. First, to further evaluate the independent association between dexmedetomidine and postoperative AKI, a multivariable logistic or linear regression model was used to adjust for baseline confounding factors with an ASD >0.10 after IPTW. The magnitude of the effect was measured using OR and 95% CI. Second, the E-value was calculated to assess the impact of unmeasured confounders on the primary outcome.[15] Statistical analyses were performed using RStudio version 2024.12.0 (RStudio, Boston, MA, USA) and SPSS version 29.0 for Windows (IBM Corp., Armonk, NY, USA).

Results

Study Characteristics

A total of 4733 patients who underwent partial nephrectomy were initially identified. Among these, 4442 patients were excluded as they lacked preoperative CKD or a solitary kidney, leaving 291 patients for eligibility assessment. Subsequent exclusions included 3 patients who were converted to radical nephrectomy intraoperatively, 4 patients who received dialysis preoperatively, and 10 patients who received less than 20 μg of dexmedetomidine, resulting in 274 patients included in the final analysis (Figure 1). These patients were stratified into two cohorts, with 82 patients receiving intraoperative dexmedetomidine (Group DEX) and 192 patients not receiving it (Group Non-DEX).

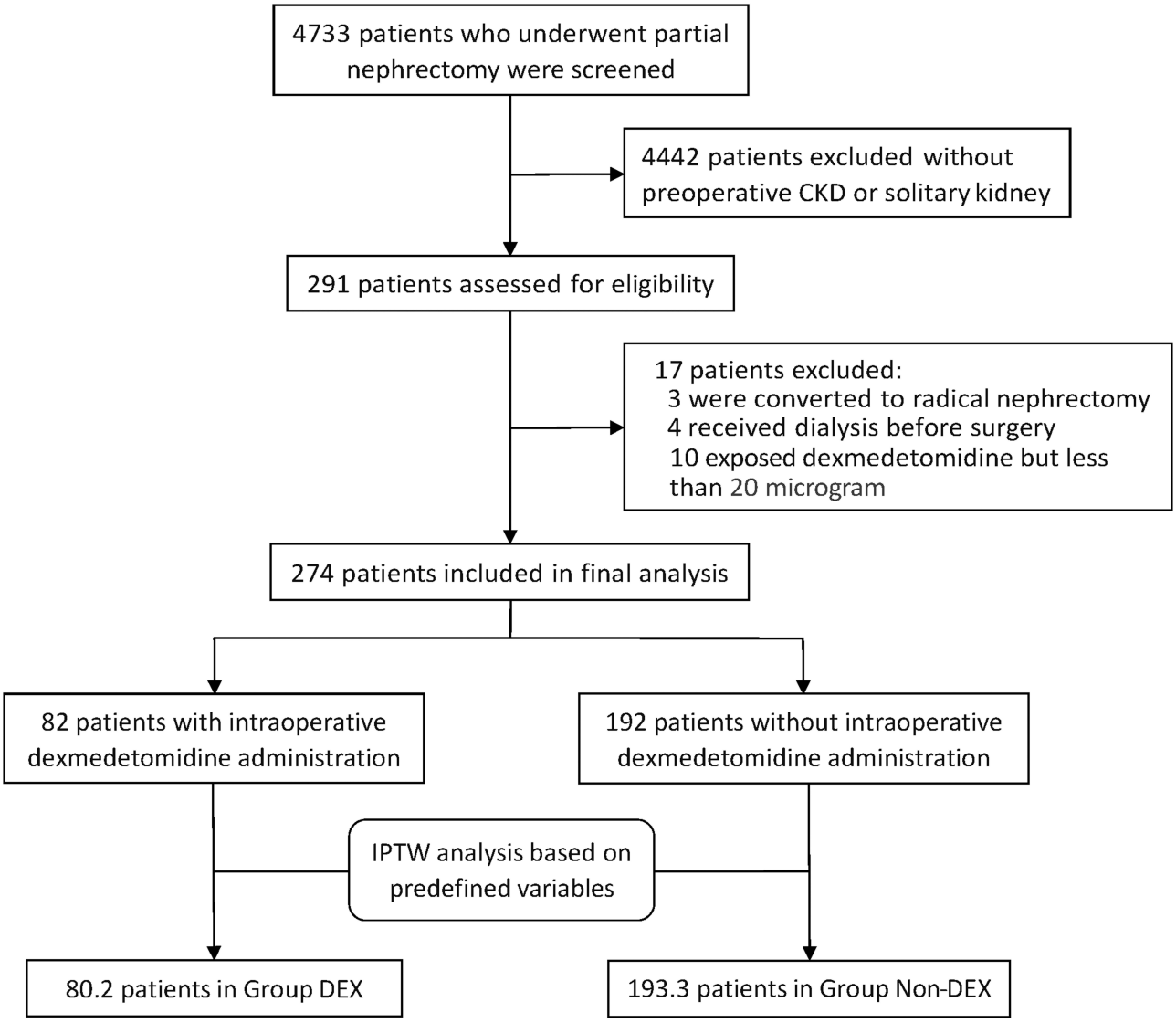

Figure 1 Flowchart of the study.
Abbreviations: CKD, chronic kidney disease; DEX, dexmedetomidine; IPTW, inverse probability of treatment weighting.

IPTW was utilized to account for confounding variables, generating weighted cohorts of 80.2 patients in the DEX group and 193.3 patients in the Non-DEX group for analysis. After IPTW weighting, all baseline and intraoperative characteristics were well balanced between the two groups, except for a minor imbalance in ASA classification (ASD = 0.101; Table 1). Kernel density plots and variance analyses confirmed that the distributions and variances of all key continuous covariates were well balanced between groups after IPTW weighting (Supplemental Figure 1). No significant between-group differences in variance were observed (all $P > 0.05$).

Table 1 Baseline and Intraoperative Data Used for IPTW

	Before IPTW			**After IPTW**		
	Group DEX (n = 82)	**Group Non-DEX (n = 192)**	**ASD**	**Group DEX (n = 80.2)**	**Group Non-DEX (n = 193.3)**	**ASD**
Demographics						
Age, year	59.2 ± 11.1	61.8 ± 10.0	**0.246**	61.0 ± 10.9	61.0 ± 10.2	0.004
Male gender	58 (70.7)	137 (71.4)	0.014	57.7 (71.9)	138.3 (71.5)	0.009
BMI, kg m^{-2}	25.7 ± 3.5	25.5 ± 3.2	0.050	25.8 ± 3.6	25.6 ± 3.2	0.064
Preoperative comorbidities						
Hypertension, n (%)	55 (67.1)	139 (72.4)	**0.116**	56.7 (70.7)	136.4 (70.5)	0.003
Diabetes mellitus, n (%)	23 (28.0)	61 (31.8)	0.081	23.2 (29.0)	58.0 (30.0)	0.023
Coronary heart disease, n (%)	11 (13.4)	30 (15.6)	0.063	12.2 (15.2)	28.5 (14.7)	0.012
Arrhythmia, n (%)	5 (6.1)	16 (8.3)	0.086	5.8 (7.2)	14.7 (7.6)	0.016
Chronic obstructive pulmonary disease, n (%)	1 (1.2)	5 (2.6)	**0.101**	1.5 (1.9)	4.2 (2.2)	0.021
Stroke, n (%)	7 (8.5)	17 (8.9)	0.011	6.9 (8.6)	17.0 (8.8)	0.005
Smoke, n (%)	16 (19.5)	38 (19.8)	0.007	17.3 (21.5)	38.3 (19.8)	0.042
ASA classification			**0.104**			**0.101**
II	50 (61.0)	115 (59.9)		47.4 (59.1)	116.4 (60.2)	
III	32 (39.0)	76 (39.6)		32.8 (40.9)	76.0 (39.3)	
IV	0 (0.0)	1 (0.5)		0.0 (0.0)	0.9 (0.5)	
Renal conditions						
Chronic kidney disease, n (%)	65 (79.3)	155 (80.7)	0.037	63.7 (79.5%)	155.4 (80.4)	0.023
Solitary kidney, n (%)	28 (34.1)	47 (24.5)	**0.214**	23.2 (29.0%)	54.5 (28.2)	0.018
R.E.N.A.L. score	6.4 ± 1.3	6.3 ± 1.3	**0.102**	6.3 ± 1.3	6.3 ± 1.3	0.041
Laboratory tests						
Base eGFR, mL $minute^{-1}$ $1.73m^{-2}$	56.3 ± 17.4	53.9 ± 17.7	**0.139**	55.6 ± 16.1	54.9 ± 18.2	0.040
Albumin, g l^{-1}	43.4 ± 3.9	43.8 ± 6.1	0.070	43.4±3.8	43.3 ± 3.9	0.025
Hemoglobin, g l^{-1}	138.1 ± 22.6	139.9 ± 17.1	0.091	140.0 ± 16.6	139.9 ± 17.0	0.002

(*Continued*)

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Table 1 (Continued).

	Before IPTW			After IPTW		
	Group DEX (n = 82)	**Group Non-DEX (n = 192)**	**ASD**	**Group DEX (n = 80.2)**	**Group Non-DEX (n = 193.3)**	**ASD**
Intraoperative data						
Surgery duration, min	96.2 ± 35.5	103.5±42.7	**0.186**	99.6±37.1	101.3±41.3	0.044
Clamp time, minute	22.2 ± 10.4	23.1±10.0	0.094	22.9±11.8	22.9±9.9	<0.001
Blood loss, mL	89 ± 172	99 ± 297	0.042	94 ± 191	97 ± 282	0.013
Surgical approach			0.046			0.028
Laparoscopic surgery, n (%)	45 (54.9)	106 (55.2)		44.2 (55.1)	105.2 (54.4)	
Robotic surgery, n (%)	22 (26.8)	54 (28.1)		22.1 (27.6)	55.7 (28.8)	
Open surgery, n (%)	15 (18.3)	32 (16.7)		13.9 (17.3)	32.5 (16.8)	
Fluid infusion, mL	1619 ± 575	1667 ± 691	0.076	1647 ± 564	1669 ± 710	0.033

Note: Bold ASD values >0.100 indicate imbalance between groups.
Abbreviations: ASA, American Society of Anesthesiologists; ASD, absolute standardized difference; BMI, body mass index; DEX, dexmedetomidine; eGFR, estimated glomerular filtration rate; IPTW, Inverse Probability of Treatment Weighting.

Efficacy and Safety Outcomes

The incidence of postoperative AKI within postoperative 24 hours was significantly lower in Group DEX than in Group Non-DEX (23.9% vs. 38.6%; OR = 0.499, 95% CI: 0.271 to 0.921; P = 0.025) (Table 2). AKI severity tended to be milder in Group DEX, with AKI Stage I (19.2% versus 27.1%), Stage II (1.3% versus 6.0%), and Stage III (3.3% versus 5.5%), though the between-group difference did not reach statistical significance (P = 0.105). Intraoperative urine output was significantly higher in Group DEX (341 ± 183 mL versus 282 ± 188 mL, P = 0.022). There were no significant between-group differences in ICU admission, length of postoperative hospital stay, or incidence of postoperative complications (Table 2). At postoperative 6 months follow-up, percentage decrease in eGFR from baseline (8 ± 10 versus 11 ± 12, P = 0.094) and incidence of >20% decrease from baseline eGFR (10.4% versus 21.9%, P = 0.096) did not differ significantly between the two groups.

No significant differences in intraoperative and PACU safety events were noted between the two groups, including bradycardia (15.0% versus 8.3%, P = 0.112), tachycardia (1.2% versus 0.9%, P = 0.826), hypertension (12.8% versus 11.0%, P = 0.699), hypotension (9.8% versus 15.2%, P = 0.223), hypoxemia (1.1% versus 2.0%, P = 0.606), and delayed emergence (0% versus 0%) (Table 3).

Dose Subgroup Analysis

We performed a post hoc dose-response analysis to explore the association of dexmedetomidine with postoperative AKI and the percentage reduction in eGFR from baseline at 6 months using stabilized IPTW and overlap weighting. In multivariate weighted trend regression analyses, each incremental increase in dexmedetomidine dose was associated with a reduced risk of AKI via stabilized IPTW (OR = 0.414 [95% CI: 0.225–0.765], P = 0.005) and via overlap weighting (OR = 0.276 [95% CI: 0.134–0.568], P < 0.001); each incremental increase in dexmedetomidine dose was associated with a decreased percentage reduction in eGFR from baseline at 6 months via stabilized IPTW (OR = 0.471 [95% CI: 0.221–1.000], P = 0.051) and via overlap weighting (OR = 0.575 [95% CI: 0.284–1.166], P = 0.126) (Table 4).

Sensitivity Analysis

To ensure the robustness of the study findings, multivariable binary logistic regression was performed to adjust for the grouping variable and ASA physical status classification, as this variable exhibited an ASD > 0.10 after matching. The

Table 2 Endpoints of the Cohort After IPTW

	Group DEX (n = 80.2)	Group Non-DEX (n = 193.3)	OR or MD(95% CI)	*P* value
Primary endpoint				
Postoperative AKI, n (%)	19.2 (23.9)	74.6 (38.6)	OR = 0.499 (0.271 to 0.921)	**0.025**
Secondary endpoint				
AKI stage, n (%)				0.105
Stage I	15.4 (19.2)	52.4 (27.1)	OR = 0.625 (0.329 to 1.185)	
Stage II	1.1 (1.3)	11.5 (6.0)	OR = 0.177 (0.022 to 1.406)	
Stage III	2.7 (3.3)	10.7 (5.5)	OR = 0.585 (0.155 to 2.205)	
Intraoperative urine output, mL	341 ± 183	282 ± 188	MD = 58.85 (8.40 to 109.30)	**0.022**
ICU admitted, n (%)	14.4 (17.9)	39.5 (20.4)	OR = 0.851 = (0.424 to 1.712)	0.650
Length of postoperative hospital stay, days	4.8 ± 1.4	5.1 ± 1.7	MD = −0.28 (−0.69 to 0.12)	0.166
Postoperative complications, n (%) [a]	6.0 (7.5)	19.4 (10.0)	OR = 0.728 (0.289 to 1.835)	0.498
eGFR at 6 months, mL min $1.73m^{-2}$	50.7 ± 14.9	48.1 ± 15.3	MD 2.61 (−1.25 to 6.47)	0.185
Percentage decrease in eGFR from baseline at 6 months, %	8 ± 10	11 ± 12	MD = −2 (−5 to 0.4)	0.094
Incidence of >20% decrease from baseline eGFR at 6-month follow-up, n (%)	10.4 (13.0)	42.3 (21.9)	OR = 0.532 (0.251 to 1.129)	0.096

Notes: [a]Defined as Clavien–Dindo classification Grade II or higher. Bold P values <0.050 indicate statistically significant differences between groups.
Abbreviations: AKI, acute kidney injury; CI, confidence interval; DEX, dexmedetomidine; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; IPTW, Inverse Probability of Treatment Weighting; MD, mean difference; OR, odds ratio.

Table 3 Safety Endpoints of the Cohort After IPTW

Adverse Events[a]	Group DEX (n=80.2)	Group Non-DEX (n=193.3)	*P* value
Bradycardia, n (%)[b]	12.1 (15.0)	16.0 (8.3)	0.112
Tachycardia, n (%)[c]	0.9 (1.2)	1.7 (0.9)	0.826
Hypertension, n (%)[d]	10.3 (12.8)	21.3 (11.0)	0.699
Hypotension, n (%)[e]	7.9 (9.8)	29.5 (15.2)	0.223
Hypoxemia, n (%)[f]	0.9 (1.1)	3.8 (2.0)	0.606
Delayed emergence, n (%)[g]	0 (0.0)	0 (0.0)	NA

Notes: [a]Manifesting intraoperatively and in the post-anesthesia care unit period. [b]Defined as heart rate <50 bpm. [c]Defined as heart rate >100 bpm. [d]Defined as systolic blood pressure >180 mm Hg. [e]Defined as systolic blood pressure <90 mm Hg. [f]Defined as pulse oxygen saturation <92% and requiring intervention. [g]Defined as failure to extubate within 30 minutes of anesthetic discontinuation.
Abbreviations: DEX, dexmedetomidine; IPTW, Inverse Probability of Treatment Weighting.

results demonstrated that intraoperative dexmedetomidine administration remained an independent protective factor against postoperative AKI (OR = 0.497, 95% CI: 0.269 to 0.918, P = 0.026) (Supplemental Table 1).

The E-value for the association between dexmedetomidine and reduced AKI risk was 2.18, indicating that an unmeasured confounder would need to be associated with both dexmedetomidine use and AKI with an odds ratio of ≥2.18 to nullify the observed effect, suggesting moderate robustness to residual bias.

Table 4 Weighted Trend Analysis of Dexmedetomidine with Outcomes

Outcomes	Statistical Models	Univariate			Multivariate[a]		
		OR	95% CI	P for Trend	OR	95% CI	P for Trend
Postoperative AKI	Stabilized IPTW	0.488	0.266–0.755	0.003	0.414	0.225–0.765	0.005
	Overlap Weighting	0.326	0.169–0.630	<0.001	0.276	0.134–0.568	<0.001
Percentage reduction in eGFR from baseline at 6 months	Stabilized IPTW	0.513	0.265–0.994	0.049	0.471	0.221–1.000	0.051
	Overlap Weighting	0.620	0.300–1.281	0.198	0.575	0.284–1.166	0.126

Notes: [a]Due to further reduction in sample size after stratification by dexmedetomidine dose, some baseline variables remained with ASD > 0.10 after weighting. Variables with ASD > 0.10 were included in the multivariable analysis to adjust for residual imbalance.

Abbreviations: AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; IPTW, Inverse Probability of Treatment Weighting; OR, odds ratio.

Discussion

In this IPTW-adjusted cohort of high-risk PN patients, intraoperative dexmedetomidine administration was associated with a significantly reduced incidence of postoperative AKI. This renal-protective association remained robust across sensitivity analyses and was accompanied by a trend toward milder AKI severity. These findings contrast with previous studies[10,16] in general PN populations but highlight the importance of patient selection and baseline renal vulnerability when evaluating renoprotective interventions.

Our previous study in patients with normal renal function demonstrated that the incidence of AKI with postoperative 48 hours after partial nephrectomy was 22.6%.[10] However, the incidence of AKI is substantially higher in high-risk patient populations, with incidences of 40% reported in patients with preexisting CKD[17] and 42–52% in those with a solitary kidney.[18,19] The development of postoperative AKI is significantly associated with poor long-term renal function outcomes in patients undergoing PN. Kälble et al[20] identified postoperative AKI caused chronic kidney disease progression after partial nephrectomy. Flammia et al[21] developed a nomogram for predicting 3-year CKD upstaging in patients who underwent robot-assisted partial nephrectomy, and this model achieved high predictive accuracy with a C-index of 84%. Notably, low baseline eGFR, solitary kidney status, and postoperative AKI are all associated with poor long-term renal outcomes.[21] Thus, for high-risk patients scheduled for partial nephrectomy, it is imperative to adopt preventive strategies to mitigate AKI occurrence, as this approach can yield favorable improvements in long-term renal outcome.

Dexmedetomidine exerts comprehensive renoprotective effects through interconnected biological processes supported by substantial evidence. It inhibits sympathetic overactivation to stabilize renal perfusion and alleviate hypercoagulability, thereby mitigating renal ischemia and hypoxia.[22,23] Dexmedetomidine also suppresses inflammatory responses by reducing immune cell infiltration and the release of pro-inflammatory mediators, while alleviating oxidative stress via enhancing antioxidant capacity.[24] Additionally, it protects renal function by inhibiting renal cell apoptosis, promoting autophagy to clear damaged cellular components, reducing ferroptosis-related lipid peroxidation, preserving the integrity of renal tubular epithelial cells, and inhibiting renal fibrosis to prevent chronic progression.[25,26] These synergistic effects collectively contribute to its protective role against perioperative AKI.

Three studies have investigated whether dexmedetomidine exerts a renoprotective effect in patients undergoing partial nephrectomy. A propensity score-matched retrospective cohort study by Wong et al[16] demonstrated that intraoperative dexmedetomidine infusion did not reduce the incidence of postoperative AKI (dexmedetomidine cohort: 31.3% versus non-dexmedetomidine cohort: 27.6%; P = 0.396). Kong et al[10] randomly assigned 290 participants to either the dexmedetomidine group or the placebo group, with the dexmedetomidine group receiving an intraoperative loading dose of 0.6 μg kg^{-1} followed by a continuous infusion at 0.4 μg kg^{-1} h^{-1} and 200 μg of dexmedetomidine as an adjuvant to sufentanil-based patient-controlled intravenous analgesia postoperatively; no significant differences were observed between the two groups in the incidence of postoperative AKI (22% versus 23%, P = 0.888), postoperative 2-day serum cystatin C and creatinine levels, or postoperative 6-month eGFR. In the Jiang et al[27] trial, patients undergoing partial nephrectomy received intravenous administration of dexmedetomidine at 0.6 μg kg^{-1} for 10 min immediately after unclamping the renal artery. Compared with the placebo group, the eGFR of the split affected kidney was significantly improved at postoperative 1 month, but this

improvement was not sustained until postoperative 6 months; this study did not evaluate the incidence of postoperative AKI. The aforementioned studies focused on low-risk patients with normal baseline renal function and abundant nephron reserve. For these patients, the limited benefits derived from dexmedetomidine-induced optimization of renal perfusion and suppression of perioperative inflammatory cascades may not be robust enough to alter the trajectory of clinical outcomes. In contrast, our study cohort comprised patients with solitary kidneys and CKD, whose limited renal reserve magnifies the clinical sequelae of intraoperative renal stress. For these patients, even minor reductions in ischemia-reperfusion injury or enhancements in renal perfusion may translate into measurable reductions in the incidence of postoperative AKI. Yet, there is a paucity of experimental and clinical research targeting CKD and solitary kidney populations, highlighting an urgent need for further investigations to verify this assumption.

An intriguing finding of our study was that patients receiving dexmedetomidine had significantly higher intraoperative urine output compared with the control group. This observation is consistent with our previous clinical trial in patients undergoing PN (200 [150–350] vs 300 [200–500], P = 0.001)[28] and major non-cardiac surgery (600 [300–900] vs 400 [250–700], P<0.001).[29] Multiple mechanisms may underlie this effect. First, dexmedetomidine providesstable hemodynamic control by attenuating sympathetic overactivation, maintaining consistent renal perfusion pressure, and reducing renal vasoconstriction caused by surgical stress.[30] Second, dexmedetomidine has been shown to inhibit arginine vasopressin secretion, thereby reducing water reabsorption in the collecting duct and increasing free water clearance, which directly contributes to increased urine output.[31] Third, experimental studies have demonstrated that dexmedetomidine protects renal tubular epithelial cells against ischemia-reperfusion injury via α_2-adrenoceptor-mediated activation of pro-survival signaling pathways, which may preserve tubular function and contribute to improved urine production during the perioperative period.[32,33] Accordingly, we postulate that inclusion of the urine output criterion in the diagnostic criteria for postoperative acute kidney injury would likely amplify the statistically significant renoprotective effect detected in our study.

Consistent with our results, studies confirm that dexmedetomidine provides dose-dependent renal protection—higher doses yield stronger benefits. A randomized trial found that high-dose dexmedetomidine reduced postoperative NGAL levels more effectively than low-dose or placebo.[34] A meta-analysis showed that higher initial doses (>0.5 μg kg^{-1}) and administration were associated with more pronounced renoprotective effects after cardiac surgery.[35] Animal study also demonstrated dose-dependent protection against renal ischemia-reperfusion injury.[36] These findings support our conclusion that dexmedetomidine protects against postoperative AKI in a dose-dependent manner.

Our findings are consistent with previous studies investigating the long-term renal effects of dexmedetomidine. Park et al[37] reported that intraoperative dexmedetomidine infusion was associated with favorable short-term renal changes but did not improve eGFR at 3 or 6 months after kidney transplantation. Similarly, Jiang et al[27] demonstrated that dexmedetomidine exerted significant early renoprotection in patients undergoing laparoscopic partial nephrectomy, yet the beneficial effect was not sustained at 6 months postoperatively, with comparable GFR between groups. Possible reasons why dexmedetomidine exerts beneficial short-term renal effects but fails to improve long-term renal outcomes may include the following. First, dexmedetomidine only provides transient pharmacological effects limited to the perioperative period, mainly by attenuating ischemia–reperfusion injury, reducing inflammatory responses, stabilizing hemodynamics, and improving renal microcirculation, which can alleviate early acute kidney injury but cannot modify persistent chronic pathophysiological processes that determine long-term renal function. Second, long-term renal function is predominantly determined by baseline renal status, preoperative comorbidities, disease progression, and sustained systemic risk factors, which far outweigh the transient perioperative renoprotection provided by dexmedetomidine. Finally, limited sample size may reduce statistical power and lead to failure in detecting potential mild long-term renal benefits.

Regarding the side effects of dexmedetomidine, bradycardia and hypotension are the most common ones.[38] In the present study, although the incidence of bradycardia was numerically higher in the DEX group than in the Non-DEX group (15.0% vs. 8.3%), this difference did not reach statistical significance. Nonetheless, this trend constitutes a potential safety signal that warrants appropriate caution, particularly in patients with pre-existing bradycardia or those receiving concomitant negative chronotropic medications. There were no significant between-group differences in the incidence of hypertension, hypotension, or tachycardia. In addition, no significant delay in emergence from anesthesia was observed in either group.

There are several limitations that should be clarified. First, as a retrospective study, residual confounding cannot be fully eliminated, even with IPTW adjustment. Second, the incidence of AKI may have been underestimated primarily due to the absence of urine output criteria for AKI diagnosis. Moreover, no significant differences were observed between the two groups at the 6-month postoperative follow-up, and a larger sample size may be required to detect potential intergroup variations. Nevertheless, our study is the first to explore the renoprotective effect of dexmedetomidine in high-risk PN patients, and the findings warrant validation through future RCTs.

Conclusion

In high-risk partial nephrectomy patients with a solitary kidney or pre-existing CKD, intraoperative dexmedetomidine infusion was associated with a significantly reduced incidence of postoperative AKI. These findings suggest that dexmedetomidine may exert renoprotective effects in patients with limited preoperative renal reserve during the early postoperative period, yet it failed to confer long-term benefits for renal function improvement in this patient population. Future RCTs focusing specifically on high-risk populations are warranted to validate these observations.

Data Sharing Statement

The data are available from the corresponding author Hao Kong on reasonable request.

Ethical Approval Statement

The study protocol was approved by the Ethics Committee of Peking University First Hospital (No.: 2025-1513) on October 24, 2025.

Patient Consent Statement

The Ethics Committee waived the requirement for written informed consent, given the retrospective nature of our study.

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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.

References

1. An JY, Ball MW, Gorin MA, et al. Partial vs radical nephrectomy for T1-T2 renal masses in the elderly: comparison of complications, renal function, and oncologic outcomes. *Urology*. 2017;100:151–157. doi:10.1016/j.urology.2016.10.047

2. Trevisani F, Belladelli F, Floris M, et al. Acute kidney injury (AKI) and end stage kidney disease (ESKD) in CKD patients undergoing partial or radical nephrectomy for renal cancer: are we ready to unravel the uncertainty and create new hope? *World J Urol*. 2025;43(1):634. doi:10.1007/s00345-025-06030-4
3. Zhu K, Song H, Zhang Z, et al. Acute kidney injury in solitary kidney patients after partial nephrectomy: incidence, risk factors and prediction. *Transl Androl Urol*. 2020;9(3):1232–1243. doi:10.21037/tau.2020.03.45
4. Kong H, Li M, Deng CM, Wu YJ, He ST, Mu DL. A comprehensive overview of clinical research on dexmedetomidine in the past 2 decades: a bibliometric analysis. *Front Pharmacol*. 2023;14:1043956. doi:10.3389/fphar.2023.1043956
5. Chotinaruemol K, Leurcharusmee P, Chattipakorn SC, Chattipakorn N, Apaijai N. Dexmedetomidine mitigation of renal ischaemia-reperfusion injury: comprehensive insights from cellular mechanisms to clinical application. *Br J Anaesth*. 2025;134(5):1350–1372. doi:10.1016/j.bja.2025.02.006
6. Zhao C, Liu S, Zhang H, Gao M. Does dexmedetomidine reduce the risk of acute kidney injury after cardiac surgery? A meta-analysis of randomized controlled trials. *Braz J Anesthesiol*. 2024;74(3):744446. doi:10.1016/j.bjane.2023.07.003
7. Zhuang K, Yang HT, Long YQ, Liu H, Ji FH, Peng K. Dexmedetomidine and acute kidney injury after non-cardiac surgery: a meta-analysis with trial sequential analysis. *Anaesth Crit Care Pain Med*. 2024;43(3):101359. doi:10.1016/j.accpm.2024.101359
8. Kwon HM, Kang SJ, Han SB, et al. Effect of dexmedetomidine on the incidence of postoperative acute kidney injury in living donor liver transplantation recipients: a randomized controlled trial. *Int J Surg*. 2024;110(7):4161–4169. doi:10.1097/JS9.0000000000001331
9. Shan XS, Dai HR, Zhao D, et al. Dexmedetomidine reduces acute kidney injury after endovascular aortic repair of Stanford type B aortic dissection: a randomized, double-blind, placebo-controlled pilot study. *J Clin Anesth*. 2021;75:110498. doi:10.1016/j.jclinane.2021.110498
10. Kong H, Yin QL, Li M, et al. Effect of perioperative dexmedetomidine on acute kidney injury after partial nephrectomy: a single-centre, randomised, double-blind, placebo-controlled trial. *Br J Anaesth*. 2025;135(5):1212–1222. doi:10.1016/j.bja.2025.08.010
11. Levey AS, Stevens LA, Schmid CH, et al. CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604–612. doi:10.7326/0003-4819-150-9-200905050-00006
12. Weerink MAS, Struys MMRF, Hannivoort LN, Barends CRM, Absalom AR, Colin P. Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine. *Clin Pharmacokinet*. 2017;56(8):893–913. doi:10.1007/s40262-017-0507-7
13. Kutikov A, Uzzo RG. The R.E.N.A.L. nephrometry score: a comprehensive standardized system for quantitating renal tumor size, location and depth. *J Urol*. 2009;182(3):844–853. doi:10.1016/j.juro.2009.05.035
14. Kellum JA, Lameire N, KDIGO AKI Guideline Work Group. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). *Crit Care*. 2013;17(1):204. doi:10.1186/cc11454
15. VanderWeele TJ, Ding P. Sensitivity analysis in observational research: introducing the E-value. *Ann Intern Med*. 2017;167(4):268–274. doi:10.7326/M16-2607
16. Wong R, Guerra-Londono JJ, Muthukumar A, Cortes-Mejia N, Bejarano-Ramirez DF, Cata JP. Intraoperative dexmedetomidine administration and acute kidney injury in patients undergoing unilateral partial nephrectomy: a retrospective study. *Ren Fail*. 2024;46(2):2409334. doi:10.1080/0886022X.2024.2409334
17. Kong H, Zhang YX, Ye PC, et al. Intraoperative intravenous mannitol administration failed to provide added value on renal functional preservation after partial nephrectomy in patients with chronic kidney disease: a matched cohort study. *J Endourol*. 2022;36(5):626–633. doi:10.1089/end.2021.0620
18. Zabell J, Isharwal S, Dong W, et al. Acute kidney injury after partial nephrectomy of solitary kidneys: impact on long-term stability of renal function. *J Urol*. 2018;200(6):1295–1301. doi:10.1016/j.juro.2018.07.042
19. Attawettayanon W, Yasuda Y, Zhang JH, et al. Functional recovery after partial nephrectomy in a solitary kidney. *Urol Oncol*. 2024;42(2):32.e17–32.e27. doi:10.1016/j.urolonc.2023.12.004
20. Kälble S, Engelmann SU, Haas M, et al. Acute kidney injury causes chronic kidney disease progression after partial nephrectomy: a retrospective study identifying patients at risk. *Urol Int*. 2025:1–11. doi:10.1159/000547649.
21. Flammia RS, Anceschi U, Tuderti G, et al. Development and internal validation of a nomogram predicting 3-year chronic kidney disease upstaging following robot-assisted partial nephrectomy. *Int Urol Nephrol*. 2024;56(3):913–921. doi:10.1007/s11255-023-03832-6
22. Shan X, Zhang J, Wei X, et al. Dexmedetomidine attenuates renal ischemia-reperfusion injury through activating PI3K/Akt-eNOS signaling via α2 adrenoreceptors in renal microvascular endothelial cells. *FASEB J*. 2022;36(11):e22608. doi:10.1096/fj.202101626RR
23. Ding W, Xie L, Wang L, et al. Dexmedetomidine alleviates renal ischemia reperfusion injury via suppressing SLC2A1-mediated glycolysis. *Biochem Pharmacol*. 2025;241:117166. doi:10.1016/j.bcp.2025.117166
24. Tao WH, Shan XS, Zhang JX, et al. Dexmedetomidine attenuates ferroptosis-mediated renal ischemia/reperfusion injury and inflammation by inhibiting ACSL4 via α2-AR. *Front Pharmacol*. 2022;13:782466. doi:10.3389/fphar.2022.782466
25. Gao X, Wu Y. Perioperative acute kidney injury: the renoprotective effect and mechanism of dexmedetomidine. *Biochem Biophys Res Commun*. 2024;695:149402. doi:10.1016/j.bbrc.2023.149402
26. Song L, Feng S, Yu H, Shi S. Dexmedetomidine protects against kidney fibrosis in diabetic mice by targeting miR-101-3p-Mediated EndMT. *Dose Response*. 2022;20(1):15593258221083486. doi:10.1177/15593258221083486
27. Jiang L, Zhang T, Zhang Y, Yu D, Zhang Y. Dexmedetomidine postconditioning provides renal protection in patients undergoing laparoscopic partial nephrectomy: a randomized controlled trial. *Front Pharmacol*. 2022;13:988254. doi:10.3389/fphar.2022.988254
28. Li CJ, Wang BJ, Mu DL, et al. Randomized clinical trial of intraoperative dexmedetomidine to prevent delirium in the elderly undergoing major non-cardiac surgery. *Br J Surg*. 2020;107(2):e123–e132. doi:10.1002/bjs.11354
29. Shih PY, Wu TT, Chan KC, et al. Intraoperative dexmedetomidine enhances postoperative microcirculation and reduces acute kidney injury in cardiac surgery: a double-blind randomized trial. *Drug Des Devel Ther*. 2025;19:8451–8462. doi:10.2147/DDDT.S541433
30. Feng Y, Bao R, Zhang L, Gong Z, Chen W. Effects of intravenous dexmedetomidine on hemodynamic stability, inflammatory factors, and brain injury biomarkers in patients with Moyamoya disease undergoing revascularization surgery. *Am J Transl Res*. 2026;18(1):409–420. doi:10.62347/XUXW7265
31. Yang W, Li H, Cheng Z, et al. Dex modulates the balance of water-electrolyte metabolism by depressing the expression of AVP in PVN. *Front Pharmacol*. 2022;13:919032. doi:10.3389/fphar.2022.919032
32. Gu J, Sun P, Zhao H, et al. Dexmedetomidine provides renoprotection against ischemia-reperfusion injury in mice. *Crit Care*. 2011;15(3):R153. doi:10.1186/cc10283

33. Zhou BY, Yang J, Luo RR, et al. Dexmedetomidine alleviates ischemia/reperfusion-associated acute kidney injury by enhancing autophagic activity via the α2-AR/AMPK/mTOR pathway. *Front Biosci*. 2023;28(12):323. doi:10.31083/j.fbl2812323
34. Balkanay OO, Goksedef D, Omeroglu SN, Ipek G. The dose-related effects of dexmedetomidine on renal functions and serum neutrophil gelatinase-associated lipocalin values after coronary artery bypass grafting: a randomized, triple-blind, placebo-controlled study. *Interact Cardiovasc Thorac Surg*. 2015;20(2):209–214. doi:10.1093/icvts/ivu367
35. Li H, Wang L, Shi C, Zhou B, Yao L. Impact of dexmedetomidine dosing and timing on acute kidney injury and renal outcomes after cardiac surgery: a meta-analytic approach. *Ann Pharmacother*. 2025;59(4):319–329. doi:10.1177/10600280241271098
36. Xu Z, Wang D, Zhou Z, et al. Dexmedetomidine attenuates renal and myocardial ischemia/reperfusion injury in a dose-dependent manner by inhibiting inflammatory response. *Ann Clin Lab Sci*. 2019;49(1):31–35.
37. Park JH, Koo BN, Kim MS, Shin D, Kwak YL. Effects of intraoperative dexmedetomidine infusion on renal function in elective living donor kidney transplantation: a randomized controlled trial. *Can J Anaesth*. 2022;69(4):448–459. doi:10.1007/s12630-021-02173-1
38. Qin C, Jiang Y, Lin C, Li A, Liu J. Perioperative dexmedetomidine administration to prevent delirium in adults after non-cardiac surgery: a systematic review and meta-analysis. *J Clin Anesth*. 2021;73:110308. doi:10.1016/j.jclinane.2021.110308