



**CLINICAL RESEARCH**

## Renal injury after open versus laparoscopic non-cardiac surgery: a retrospective cohort analysis

Hani Essber<sup>a</sup>, Barak Cohen<sup>a,b</sup>, Amanda S. Artis<sup>a,c</sup>, Steve M. Leung<sup>a</sup>, Kamal Maheshwari<sup>a,d</sup>, Mohammad Zafeer Khan<sup>a</sup>, Daniel I. Sessler<sup>a</sup>, Alparslan Turan<sup>a,d</sup>, Kurt Ruetzler<sup>ID a,d,\*</sup>



<sup>a</sup> Cleveland Clinic, Anesthesiology Institute, Department of Outcomes Research, Cleveland, OH

<sup>b</sup> Division of Anesthesia, Intensive Care, and Pain Management, Tel-Aviv Medical Center, Tel-Aviv University, Tel-Aviv Medical Center, Division of Anesthesia, Intensive Care, and Pain Management, Tel-Aviv, Israel

<sup>c</sup> Cleveland Clinic, Department of Quantitative Health Sciences, Cleveland, OH

<sup>d</sup> Cleveland Clinic, Anesthesiology Institute, Department of General Anesthesia, Cleveland, OH

Received 4 January 2020; accepted 11 July 2020

Available online 25 December 2020

### KEYWORDS

Acute kidney injury;  
Laparoscopy;  
Anesthesia

### Abstract

**Background:** Laparoscopic surgical approaches enhance recovery, reduce postoperative pain, and shorten hospital length-of-stay. Nevertheless, increased intra-abdominal pressure is associated with decreased renal blood flow, renal hypoxia and acute kidney injury. When combined with Trendelenburg positioning, renal function may further deteriorate. We tested the primary hypothesis that the combination of laparoscopic surgical approach and Trendelenburg position is associated with larger reductions in estimated Glomerular Filtration Rate (eGFR) within the initial 48 postoperative hours compared to open surgery without Trendelenburg positioning. Secondary, we tested, if laparoscopic procedures are associated with greater incidence of postoperative acute kidney injury.

**Methods:** Adults who had laparoscopic colorectal surgery in Trendelenburg position at the Cleveland Clinic Main Campus from 2009 to 2016 were propensity-matched to patients who had comparable open procedures. Patients with pre-existing renal impairment were excluded.

**Results:** Among 7,357 eligible patients, 1,846 laparoscopic cases with Trendelenburg were matched to 1,846 open cases. No association was found between laparoscopic approach and postoperative eGFR. A significant protective effect of the laparoscopic procedure on the odds of having AKI was found. Patients who had laparoscopic surgeries were an estimated 0.70 (95% CI 0.55, 0.90,  $p_{Holm-adj} = 0.006$ ) times as likely to have AKI as open surgical patients.

**Conclusion:** Despite compelling potential mechanisms, laparoscopic approach with Trendelenburg position in adult colorectal surgeries did not worsen postoperative eGFR, and actually reduced postoperative acute kidney injury. Given the other advantages of laparoscopic surgery, the approach should not be avoided for concerns about renal injury.

© 2021 Sociedade Brasileira de Anestesiologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

\* Corresponding author.

E-mails: RUETZLK@ccf.org, kr@or.org (K. Ruetzler).

## Introduction

Laparoscopy causes less tissue trauma than open surgery, thereby reducing neuroendocrine and inflammatory responses as well as postoperative pain. Laparoscopic procedures are also usually less expensive than open surgery since patients are discharged earlier.<sup>1,2</sup> Laparoscopy is generally considered safe, with complications mostly resulting from traumatic trocar induction. However, intra-abdominal insufflation of carbon dioxide or oxygen is needed to provide adequate visualization of the surgical field and the consequent increase in intra-abdominal pressure can impair cardiovascular, respiratory, and renal systems.

Peritoneal insufflation applies pressure to renal parenchyma and blood vessels, stimulates antidiuretic hormone (vasopressin) secretion, increases activity of the renin-angiotensin-aldosterone axis, promotes release of catecholamines and endothelin, increases vascular resistance, compresses the abdominal vena cava, and reduces cardiac output.<sup>3,4</sup> The kidneys may be especially sensitive to intra-abdominal pressure,<sup>5</sup> and both animal and human studies suggest that even short durations of slightly increased intra-abdominal pressure can impair renal function.<sup>6–8</sup> As might thus be expected, renal impairment is associated with the degree of pneumoperitoneal pressure and the duration of surgery.<sup>3,9</sup>

Surgical positioning may also contribute to Acute Kidney Injury (AKI). Trendelenburg positioning increases intracranial and intraocular pressures by promoting venous return to the heart, but simultaneously decreases renal perfusion. Trendelenburg position nearly doubles central venous pressure which potentially worsens congestive heart failure or even promotes myocardial infarction.<sup>10–12</sup> Trendelenburg position is widely used in laparoscopic colorectal procedures to improve surgical exposure, and is often both steep and prolonged. Patients having colorectal laparoscopic procedures might therefore be at special risk for AKI consequent to both pneumoperitoneum and Trendelenburg positioning.

We therefore compared the risk of postoperative AKI between laparoscopic and open colorectal surgery. Specifically, we tested the primary hypothesis that the combination of laparoscopic surgical approach and Trendelenburg position is associated with larger reductions in estimated Glomerular Filtration Rate (eGFR) within the initial 48 postoperative hours compared to open surgery without Trendelenburg positioning. Secondarily, we tested the hypothesis that laparoscopic surgical approach and Trendelenburg position is associated with a greater incidence of postoperative AKI during the initial 7 postoperative days.

## Methods

Our analysis was conducted with IRB approval and waived individual consent. Data were obtained from the Cleveland Clinic Perioperative Health Documentation System.

Analysis was restricted to index surgeries for adults (18–85 years old) who had scheduled colorectal surgery at the Cleveland Clinic Main Campus, Ohio, United States. The Cleveland Clinic is a large tertiary academic health-care institution providing all kinds of surgeries. Only major therapeutic and diagnostic surgeries with general or com-

bined regional and general anaesthesia were considered. We excluded patients who had surgery lasting fewer than 90 minutes, laparoscopic surgery not in Trendelenburg position, and open surgery in Trendelenburg position. We also excluded patients who had preoperative renal insufficiency (defined as creatinine > 1.6 mg.dL<sup>-1</sup>), missing outcome data, fewer than 3 days of hospitalization, preoperative sepsis, or emergency surgeries.

The exposure of interest was the combination of laparoscopic surgery performed in Trendelenburg position ("laparoscopic") versus open approach without Trendelenburg positioning ("open"). Our primary outcome was postoperative eGFR and our secondary outcome was the incidence of Acute Kidney Injury (AKI). Postoperative eGFR was defined using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.

AKI was defined using the AKIN criteria which is based on serum creatinine level at baseline (the last measurement within 30 days prior to surgery) and maximal serum level during the first 7 postoperative days or discharge, whichever occurred first. As per Walsh et al., we extended the normal 48-h window originally used to capture renal events to seven postoperative days to better characterize the postoperative period.<sup>13</sup> And as usual in perioperative studies, we did not consider urine output which is rarely available.

Laparoscopic patients were matched to open patients using propensity matching. We first estimated the propensity score (probability of having laparoscopic surgery) for each patient using multivariable logistic regression given the baseline confounders listed in Table 1 (except colorectal surgical type, which was exactly matched in the next step). We then used a 1:1 greedy matching algorithm to match patients on colorectal procedure type and propensity score. We set the maximum allowable propensity score difference to 0.2 standard deviation of the logit of the propensity score (0.2 × SD [logit (propensity score)] = 1.11).

Balance between laparoscopic and open on *a priori* selected pre-surgical confounder variables before and after matching was assessed using the standardized difference (i.e., the difference in means or proportions divided by the pooled SD). A pre-specified conservative criterion of an Absolute Standardized Difference (ASD) greater than 0.1 was used to indicate imbalance. Confounding variables with ASD > 0.1 after matching were included in all regression models comparing matched laparoscopic to open cases on our outcomes to adjust for any residual confounding which remained after matching.

Data summaries for intraoperative measures are listed in Table 2. These variables were excluded from the propensity score analysis and all subsequent regression models since some are characteristics of either the laparoscopic or open surgical procedure and are thus mediators rather than confounders. Furthermore, intraoperative variables cannot be considered true confounders given they do not precede the exposure of interest.

## Statistical analysis

The primary aim of our study was to evaluate whether surgical approach (laparoscopic vs. open) is independently associated with postoperative eGFR. Multivariable Lin-

**Table 1** Summary statistics of baseline and intraoperative characteristics.

Variable	All patients			Matched patients		
	Laparoscopic (n = 1976)	Open (n = 5531)	ASD	Laparoscopic (n = 1846)	Open (n = 1846)	ASD
<b>Baseline variables</b>						
Age, years <sup>b</sup>	51 ± 17	52 ± 16	0.03	51 ± 17	52 ± 16	0.02
BMI, kg. m <sup>-2</sup> <sup>a,b</sup>	27.1 ± 6.2	26.8 ± 6.4	0.04	27.0 ± 6.2	27.0 ± 6.4	0.01
Risk Stratification Index (RSI) <sup>b</sup>	-4.9 ± 0.76	-4.9 ± 0.72	0.03	-4.9 ± 0.76	-4.9 ± 0.73	0.02
Preoperative eGFR, mL. min <sup>-1</sup> /1.73 m <sup>2</sup> <sup>b</sup>	92.6 ± 22.3	91.7 ± 23.8	0.04	92.7 ± 21.6	92.4 ± 22.2	0.01
Preoperative hemoglobin <sup>a,b</sup>	12.9 ± 2.0	12.6 ± 2.0	0.17	12.9 ± 2.0	12.9 ± 1.9	0.02
Number of antihypertensive agents <sup>c</sup>	0 [0,1]	0 [0,1]	0.00	0 [0,1]	0 [0,1]	0.04
Female sex	1048 (53.0)	2834 (51.2)	0.04	982 (53.2)	968 (52.4)	0.02
Aspirin	154 (7.8)	398 (7.2)	0.02	144 (7.8)	136 (7.4)	0.02
Calcium-antagonists	103 (5.2)	312 (5.6)	0.02	93 (5.0)	96 (5.2)	0.01
Beta-blocker	210 (10.6)	639 (11.6)	0.03	197 (10.7)	186 (10.1)	0.02
Diuretics	213 (10.8)	510 (9.2)	0.05	196 (10.6)	181 (9.8)	0.03
ACE-Inhibitors	170 (8.6)	416 (7.5)	0.04	159 (8.6)	150 (8.1)	0.02
AT II-antagonists	83 (4.2)	169 (3.1)	0.06	68 (3.7)	70 (3.8)	0.01
Statins	239 (12.1)	529 (9.6)	0.08	224 (12.1)	210 (11.4)	0.02
Proton-pump inhibitor	318 (16.1)	981 (17.7)	0.04	295 (16.0)	268 (14.5)	0.04
NSAIDs	132 (6.7)	421 (7.6)	0.04	126 (6.8)	129 (7.0)	0.01
Immunosuppressants (cyclosporine, tacrolimus)	67 (3.4)	181 (3.3)	0.01	59 (3.2)	54 (2.9)	0.02
Steroids	465 (23.5)	941 (17.0)	0.16	416 (22.5)	361 (19.6)	0.07
History of MI	82 (4.1)	233 (4.2)	0.00	76 (4.1)	81 (4.4)	0.01
History of CHF	135 (6.8)	422 (7.6)	0.03	131 (7.1)	131 (7.1)	0.00
History of PVD	67 (3.4)	181 (3.3)	0.01	62 (3.4)	57 (3.1)	0.02
History of stroke	64 (3.2)	198 (3.6)	0.02	62 (3.4)	57 (3.1)	0.02
Pulmonary circulation disease	18 (0.91)	82 (1.5)	0.05	18 (0.98)	18 (0.98)	0.00
Liver disease	40 (2.0)	132 (2.4)	0.02	37 (2.0)	44 (2.4)	0.03
Hypothyroidism	193 (9.8)	558 (10.1)	0.01	183 (9.9)	186 (10.1)	0.01
Hypertension	652 (33.0)	1810 (32.7)	0.01	610 (33.0)	593 (32.1)	0.02
Diabetes	194 (9.8)	627 (11.3)	0.05	180 (9.8)	190 (10.3)	0.02
Smoker	905 (45.8)	2820 (51.0)	0.10	847 (45.9)	890 (48.2)	0.05
Obesity	279 (14.1)	736 (13.3)	0.02	263 (14.2)	248 (13.4)	0.02
Chronic obstructive pulmonary disease	199 (10.1)	655 (11.8)	0.06	188 (10.2)	195 (10.6)	0.01
Dyslipidemia	449 (22.7)	1030 (18.6)	0.10	417 (22.6)	406 (22.0)	0.01
Angina decubitus	3 (0.15)	4 (0.07)	0.02	3 (0.16)	2 (0.11)	0.01
Coronary artery disease	106 (5.4)	241 (4.4)	0.05	97 (5.3)	91 (4.9)	0.01
Cardiac dysrhythmias	85 (4.3)	319 (5.8)	0.07	81 (4.4)	78 (4.2)	0.01
Race			0.08			0.03
Caucasian	1818 (92.0)	4962 (89.7)		1697 (91.9)	1685 (91.3)	
African American	107 (5.4)	397 (7.2)		101 (5.5)	105 (5.7)	
Other	51 (2.6)	172 (3.1)		48 (2.6)	56 (3.0)	
Surgeon			1.00			0.14
Surgeon 1	25 (1.3)	688 (12.4)		25 (1.4)	25 (1.4)	
Surgeon 2	224 (11.3)	105 (1.9)		146 (7.9)	92 (5.0)	
Surgeon 3	139 (7.0)	272 (4.9)		137 (7.4)	149 (8.1)	
Surgeon 4	122 (6.2)	262 (4.7)		119 (6.4)	145 (7.9)	
Surgeon 5	52 (2.6)	364 (6.6)		52 (2.8)	46 (2.5)	
Surgeon 6	152 (7.7)	553 (10.0)		151 (8.2)	158 (8.6)	
Surgeon 7	226 (11.4)	332 (6.0)		215 (11.6)	223 (12.1)	
Surgeon 8	100 (5.1)	238 (4.3)		99 (5.4)	98 (5.3)	
Surgeon 9	142 (7.2)	301 (5.4)		140 (7.6)	170 (9.2)	
Surgeon 10	0 (0.0)	933 (16.9)		. (. )	. (. )	
Other Surgeon	794 (40.2)	1483 (26.8)		762 (41.3)	740 (40.1)	
Colorectal procedure type			0.61			0.00
Colostomy or colorectal resection	1845 (93.4)	3990 (72.1)		1717 (93.0)	1717 (93.0)	

Table 1 (Continued)

Variable	All patients			Matched patients		
	Laparoscopic (n = 1976)	Open (n = 5531)	ASD	Laparoscopic (n = 1846)	Open (n = 1846)	ASD
Illeostomy, small bowel resection, and other enterostomy	119 (6.0)	929 (16.8)		117 (6.3)	117 (6.3)	
Hernia repair	1 (0.05)	153 (2.8)		1 (0.05)	1 (0.05)	
Exploratory laparotomy	0 (0.0)	61 (1.1)		0 (0.0)	0 (0.0)	
Excision; lysis peritoneal adhesions	3 (0.15)	98 (1.8)		3 (0.16)	3 (0.16)	
Other procedures	8 (0.40)	300 (5.4)		8 (0.43)	8 (0.43)	
ASA physical status			0.11			0.01
1	28 (1.4)	38 (0.69)		25 (1.4)	23 (1.2)	
2	887 (44.9)	2255 (40.8)		821 (44.5)	838 (45.4)	
3	986 (49.9)	2969 (53.7)		930 (50.4)	914 (49.5)	
4	75 (3.8)	269 (4.9)		70 (3.8)	71 (3.8)	
Year of the surgery			0.37			0.09
2009	199 (10.1)	966 (17.5)		197 (10.7)	247 (13.4)	
2010	208 (10.5)	897 (16.2)		206 (11.2)	222 (12.0)	
2011	191 (9.7)	761 (13.8)		185 (10.0)	220 (11.9)	
2012	284 (14.4)	745 (13.5)		265 (14.4)	246 (13.3)	
2013	306 (15.5)	656 (11.9)		283 (15.3)	256 (13.9)	
2014	311 (15.7)	647 (11.7)		284 (15.4)	250 (13.5)	
2015	132 (6.7)	274 (5.0)		125 (6.8)	121 (6.6)	
2016	345 (17.5)	585 (10.6)		301 (16.3)	284 (15.4)	

Data are given as n (column %) unless otherwise indicated.

Variables with ASD > 0.1 after matching were considered imbalanced and thus included in subsequent multivariable regression models to control for residual confounding.

<sup>a</sup> Data not available for all subjects before matching. Missing values: Body Mass Index = 77, Preoperative Hemoglobin = 73, Time weighted average MAP = 1.

<sup>b</sup> Data are given as mean ± SD.

<sup>c</sup> Data are given as median [Q1, Q3].

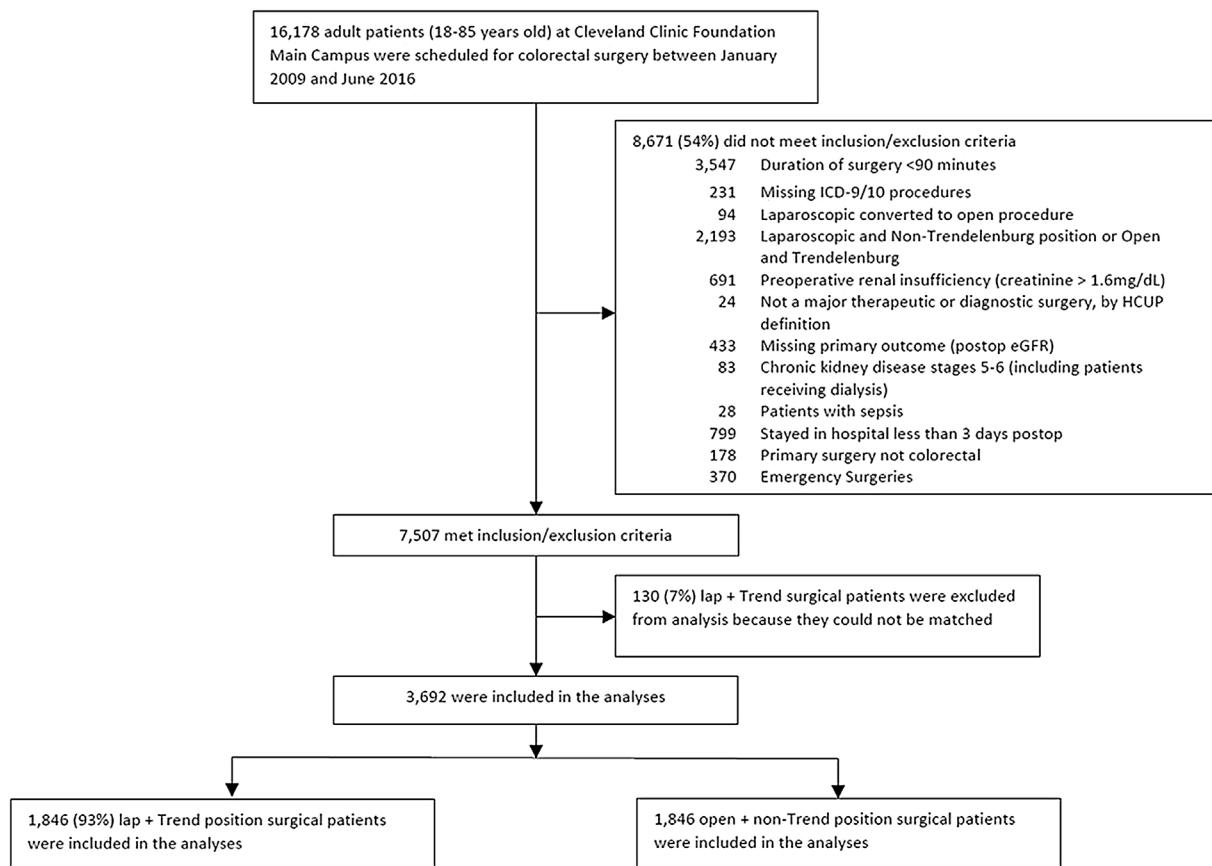
Table 2 Summary Statistics of Intraoperative Characteristics.

Variable	All patients			Matched patients		
	Laparoscopic (n = 1976)	Open (n = 5531)	ASD	Laparoscopic (n = 1846)	Open (n = 1846)	ASD
Duration of surgery (min)	259 (90,722)	199 (90,942)	0.56	258 (90,722)	208 (90,942)	0.47
Epinephrine (mg)	0.0 (0.0,0.1)	0.0 (0.0,11.3)	0.06	0.0 (0.0,0.1)	0.0 (0.0,1.0)	0.06
Ephedrine (mg)	0 (0.85)	0 (0.90)	0.07	0 (0.85)	0 (0.90)	0.07
Norepinephrine (mg)	0.0 (0.0,1.4)	0.0 (0.0,4.9)	0.06	0.00 (0.0,1.4)	0.00 (0.0,1.4)	0.04
Phenylephrine (mg)	0.1 (0.0,27.2)	0.1 (0.0,29.7)	0.01	0.1 (0.0,27.2)	0.1 (0.0,26.0)	0.02
Urine output	300 (0, 3,850)	250 (0,4460)	0.28	300 (0, 3,850)	225 (0, 4,460)	0.36
Estimated blood loss	100 (0, 4,300)	150 (0, 16,100)	0.30	100 (0, 4,300)	100 (0, 8,500)	0.15
RBC transfusion (cc)	0 (0.2814)	0 (0.10608)	0.26	0 (0.2814)	00 (0.10608)	0.19
FFP transfusion (cc)	0 (0.658)	0 (0.3188)	0.14	0 (0.658)	0 (0.2995)	0.11
Platelet transfusion (cc)	0 (0.522)	0 (0.1210)	0.10	0 (0.522)	0 (0.1210)	0.08
Amount of crystalloids	2900 (400,9225)	2600 (0,16000)	0.27	2900 (400,9225)	2500 (100,15000)	0.30
Amount of colloids	0 (0.3500)	0 (0.3750)	0.27	0 (0.3500)	0 (0.2750)	0.17
Time weighted average MAP <sup>a</sup>	87 (67,128)	83 (58,131)	0.44	87 (67,128)	83 (61,125)	0.39
Regional analgesia (yes)	74 (3.7)	709 (12.8)	0.33	70 (3.8)	276 (15.0)	0.39

Data are given as median (min, max).

Intraoperative characteristics were not considered in propensity score nor any regression modeling.

<sup>a</sup> Data not available for all subjects. Time weighted average MAP = 1.



**Figure 1** Types and numbers of exclusions of the available colorectal surgical cases (January 2009 – June 2016) at Cleveland Clinic Foundation Main Campus.

ear Regression (MLR) was used to assess the relationship between postoperative eGFR and surgical approach in the matched sample, adjusting for covariates with ASD > 0.1 after matching. Residuals were examined to ensure there were no gross deviations from regression model assumptions.

We also assessed whether laparoscopy was associated with our secondary outcome of AKI stage, adjusting for imbalanced covariates. Holm-Bonferroni step-down procedure for multiple testing adjustment was utilized to adjust the *p*-values from our secondary analyses.

A multivariable logistic regression model on the matched data adjusted for unbalanced confounders after matching was used to estimate an adjusted Odds Ratio (OR) comparing the odds of AKI in the laparoscopic surgical procedure to those in the open group.

SAS software version 9.4 (SAS Institute, Cary, NC, USA) was used for all statistical analyses.

## Results

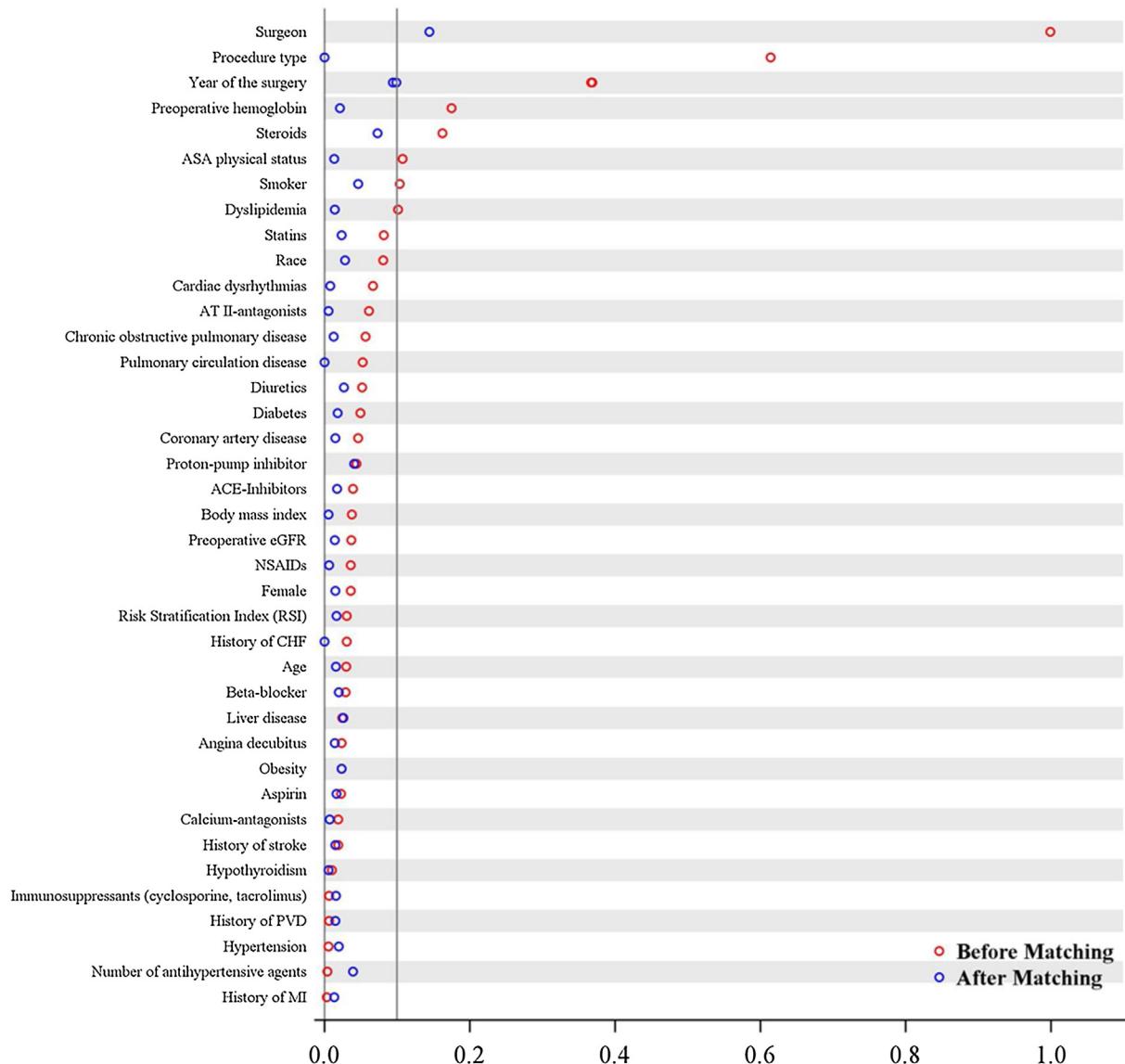
There were 16,178 adults scheduled for colorectal surgery between January 2009 and June 2016 at the Cleveland Clinic Main Campus, of whom 7,507 qualified for analysis (Fig. 1). Among those, 7,357 (98%) had complete data for the primary covariate-adjusted analysis comparing laparoscopic vs. open surgical procedures. Thus, only 2% of eligible

patients (150) were excluded from consideration in the propensity score matching due to missing covariate values. Specifically, BMI was missing in 77 patients and preoperative hemoglobin was missing in 73.

We successfully matched 1,846 laparoscopic surgical patients (93% of the total) with 1,846 open patients for a total analysis set of 3,692 surgical patients. As indicated by the Absolute standardized difference in Table 1 and the absolute standardized difference plot in Fig. 2, we were able to successfully balance all but one variable, surgeon (standardized difference = 0.14), after matching exactly on colorectal surgical type and propensity score. Therefore, we adjusted for surgeon in all subsequent regression models comparing laparoscopic vs. open surgical procedures to control for residual confounding.

There was no association between laparoscopic approach and postoperative eGFR (Table 3). The covariate-adjusted estimate of the difference in postoperative eGFR between the laparoscopic surgical procedure and the reference open procedure was 1.1 (95% CI -0.42, 2.67) mL·min<sup>-1</sup>/1.73 m<sup>2</sup>, *p* = 0.15. Examination of the residuals revealed no gross deviations from multiple regression model assumptions.

We also considered the association between surgical approach and absolute change in creatinine level from baseline (postoperative – preoperative creatinine). The difference in means for change in creatinine was not statistically different from 0: -0.01 (95% CI -0.03, 0.01), *p*



**Figure 2** Absolute standardized difference plot showing balance between laparoscopic and open before (red) and after (blue) matching. The vertical line at absolute standardized difference = 0.1 is the pre-specified cutoff indicating balanced (left) and imbalanced (right) variables.

= 0.16). Similarly, we considered the association between surgical approach and the fold change (postoperative creatinine/preoperative creatinine). The difference in fold change in creatinine was not statistically different from 0: -0.12 (95% CI -0.03, 0.01),  $p = 0.19$ .

Initially, we planned to analyze AKI via multivariable ordinal logistic regression. However, the proportional odds assumption for this outcome suggested it may have been violated ( $\chi^2_{20} = 34$ ,  $p = 0.026$ ). Thus, we used multivariable logistic regression, modeling the odds of any AKI (Stages I, II or III) vs. no AKI adjusting for surgeon, to assess the relationship between AKI and surgical procedure. A significant protective effect of the laparoscopic procedure on the odds of having AKI was found. Patients who had laparoscopic surgeries were an estimated 0.70 (95% CI 0.55, 0.90,  $p_{Holm-adj} = 0.006$ ) times as likely to have AKI as open surgical patients. A

similar result was observed in the proportional odds logistic model (OR (95% CI) = 0.70 [0.54, 0.90],  $p_{Holm-adj} = 0.006$ ).

AKI Stage I (5.0% vs. 6.8%) and Stage II (0.8% vs. 1.4%) were less common in patients who had laparoscopic surgery, whereas Stage III (0.3% vs. 0.2%) was similar.

## Discussion

Postoperative Acute Kidney Injury (AKI), defined by a sudden loss of renal function, affects 7% to 13% of patients having non-cardiac surgery.<sup>14,15</sup> Postoperative AKI is associated with significant morbidity, increased mortality, prolonged hospital and ICU stays, and high health care costs.<sup>16</sup> Even small increases in creatinine after surgery are associated with a three-fold increased risk of developing end-stage renal disease<sup>17</sup> and a marked increase in mortality.<sup>18</sup> It

**Table 3** Summary of raw and surgeon-adjusted associations between surgical procedure and postoperative kidney outcomes in the propensity matched analysis set.

Outcome	Raw estimates		Regression estimate (95% CI) <sup>a</sup>	p-value
	Laparoscopic n = 1846	Open n = 1846		
Primary Postoperative eGFR, mL. min <sup>-1</sup> /1.73 m <sup>2</sup>	90 ± 25 92 [76, 106]	89 ± 23 92 [74, 106]	1.1 (-0.4, 2.7)	0.155
Secondary AKI (Any AKI vs. None)	113 (6)	155 (8)	0.7 (0.6, 0.9)	0.006 <sup>b</sup>
AKIN stages <sup>c</sup>			0.7 (0.5, 0.9)	0.006 <sup>b</sup>
Stage 1	93 (5)	126 (7)		
Stage 2	14 (0.8)	25 (1)		
Stage 3	6 (0.3)	4 (0.2)		

Primary outcome: The raw group estimates of postoperative eGFR are mean ± SD and the regression estimate (95% CI) is the surgeon-adjusted multivariable linear regression estimated difference (laparoscopic – open) in eGFR group means. Median (Q1, Q3) of postoperative eGFR by procedure are also presented.

#### Secondary outcomes:

AKI (Any AKI vs. None): The raw group estimates for any acute kidney injury (AKI) are incidences of any AKI by procedure type, presented as n (%) and the regression estimate (95% CI) is the multivariable logistic regression Odds Ratio (OR) for the odds of any AKI for the laparoscopic procedures vs. the open procedures. AKIN (Stage 3, Stage 2, Stage 1, Stage 0): The raw group estimates for AKI by stage are incidences of AKI stage by procedure type, presented as n (%) and the regression estimate (95% CI) is the multivariable ordinal logistic regression OR for the odds of AKI for the laparoscopic procedures vs. the open procedures. The Chi-Square p-value for testing the proportional odds assumption suggests that this assumption was violated ( $p = 0.026 < 0.05$ ), yet the results are presented as a sensitivity analysis. All p-values presented are from their respective regression analysis. The p-values for the secondary analysis were adjusted for multiple testing via Holm step-down procedure.

<sup>a</sup> Surgeon-adjusted regression estimate (95% CI).

<sup>b</sup> Holm-adjusted p-value.

<sup>c</sup> Sensitivity analysis using AKIN Stages (0, 1, 2, 3) instead of binary AKI (Any AKI – Stages 1, 2, 3 vs. No AKI – Stage 0).

is thus of considerable interest to consider whether peritoneal insufflation combined with Trendelenburg positioning impairs renal function.<sup>3</sup>

Although there were convincing reasons to expect an association between the surgical approach and renal injury, none was observed in our analysis. Laparoscopic surgical approach was not associated with a reduction of postoperative eGFR. Consequently, the choice of surgical approach (open vs. laparoscopic) should not be influenced by the attempt to prevent renal injury. Well known benefits of laparoscopic surgical approach including reduced blood loss, decreased postoperative pain, and shorter in-hospital recovery should be considered instead.

Our secondary analyses showed that patients who had open surgery were more likely to develop AKI within the initial 48 postoperative hours in our cohort. However, about 80% of all postoperative AKI cases were Stage 1 of the AKIN criteria, considered to be “risk” rather than injury. The importance of Stage 1 AKI remains unclear. Several studies, based on limited numbers of young and relatively healthy patients, did not identify long-lasting impairment.<sup>19–22</sup> But there are other analyses that suggest increased mortality even with Stage 1 AKI.<sup>23–25</sup> We did only detect a minor difference in AKI Stage 2 (0.8% vs. 1.4%) and no meaningful difference in AKI Stage 3 (0.3% vs. 0.2%) between the groups which is unsurprising considering the low baseline incidence of these serious outcomes.

Laparoscopic procedures usually require restricted intravenous fluid administration which may have promoted

hemoconcentration and slight increases in creatine that are perhaps of little physiological consequence. Consistent with this theory, our laparoscopic patients received 11 mL/minute of intravenous fluids during laparoscopic surgery compared to 13 mL/minute in the open group.

Intraoperative hypotension, perioperative anemia, and preoperative use of aspirin are potential causes of postoperative kidney injury.<sup>13,26,27</sup> But none of these factors seems to be likely to explain our results as blood pressures did not differ meaningfully (time weighted average mean arterial pressure 87 vs. 83 mmHg). Nor did perioperative anemia requiring blood transfusions and aspirin use differ substantially in patients with each surgical approach.

It is possible that surgeons selected open surgery for patients whom they expected might need more extensive and complicated operations, which in turn would be associated with more blood loss and vasopressor use. However, there were negligible differences in blood loss and vasopressor requirements. Our analysis surely suffered from some degree of residual confounding. But we reduced the risk of selection bias by carefully matching patients on a long list of baseline characteristics. After matching, patients having each type of surgery were well balanced on most variables.

In summary, laparoscopic surgical approach combined with steep Trendelenburg positioning does not appear to cause substantial renal impairment as measured by estimated glomerular filtration rate. Given the other advantages of laparoscopic surgery, the approach should not be avoided for concerns about renal injury.

## Funding

Financial support was provided solely from institutional and departmental sources. None of the authors has a personal financial interest related to this analysis.

## Conflicts of interest

The authors declare no conflicts of interest.

## References

1. Glerup H, Heindorff H, Flyvbjerg A, Jensen SL, Vilstrup H. Elective laparoscopic cholecystectomy nearly abolishes the postoperative hepatic catabolic stress response. *Ann Surg.* 1995;221:214–9.
2. Crawshaw BP, Chien HL, Augestad KM, Delaney CP. Effect of laparoscopic surgery on health care utilization and costs in patients who undergo colectomy. *JAMA Surg.* 2015;150:410–5.
3. Inbar R, Swissa L, Greenberg R, White I, Lahat G, Avital S. Laparoscopic colorectal surgery in patients with impaired renal function: impact on postoperative renal function compared with open surgery. *J Laparoendosc Adv Surg Tech A.* 2014;24:236–40.
4. Wiesenthal JD, Fazio LM, Perks AE, et al. Effect of pneumoperitoneum on renal tissue oxygenation and blood flow in a rat model. *Urology.* 2011;77:1508.e1509–15.
5. Saggi BH, Sugerman HJ. Abdominal compartment syndrome. In: Holzheimer RG, Mannick JA, editors. *Surgical Treatment: Evidence-Based and Problem-Oriented.* Munich: Zuckschwerdt; 2001. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK6965/>.
6. Bishara B, Karram T, Khatib S, et al. Impact of pneumoperitoneum on renal perfusion and excretory function: beneficial effects of nitroglycerine. *Surg Endosc.* 2009;23:568–76.
7. Abassi Z, Bishara B, Karram T, Khatib S, Winaver J, Hoffman A. Adverse effects of pneumoperitoneum on renal function: involvement of the endothelin and nitric oxide systems. *Am J Physiol Regul Integr Comp Physiol.* 2008;294:R842–850.
8. Dunn MD, McDougall EM. Renal physiology. Laparoscopic considerations. *Urol Clin North Am.* 2000;27:609–14.
9. Henny CP, Hofland J. Laparoscopic surgery: pitfalls due to anesthesia, positioning, and pneumoperitoneum. *Surg Endosc.* 2005;19:1163–71.
10. Bruch C, Rothenburger M, Gotzmann M, et al. Chronic kidney disease in patients with chronic heart failure – impact on intracardiac conduction, diastolic function and prognosis. *Int J Cardiol.* 2007;118:375–80.
11. Miyazato J, Horio T, Takiuchi S, et al. Left ventricular diastolic dysfunction in patients with chronic renal failure: impact of diabetes mellitus. *Diabet Med.* 2005;22:730–6.
12. Hirvonen EA, Nuutinen LS, Kauko M. Hemodynamic changes due to Trendelenburg positioning and pneumoperitoneum during laparoscopic hysterectomy. *Acta Anaesthesiol Scand.* 1995;39:949–55.
13. Walsh M, Garg AX, Devereaux PJ, Argalious M, Honar H, Sessler DI. The association between perioperative hemoglobin and acute kidney injury in patients having noncardiac surgery. *Anesth Analg.* 2013;117:924–31.
14. O'Connor ME, Hewson RW, Kirwan CJ, Ackland GL, Pearse RM, Prowle JR. Acute kidney injury and mortality 1 year after major non-cardiac surgery. *Br J Surg.* 2017;104:868–76.
15. O'Connor ME, Kirwan CJ, Pearse RM, Prowle JR. Incidence and associations of acute kidney injury after major abdominal surgery. *Intensive Care Med.* 2016;42:521–30.
16. Huber M, Ozrazgat-Baslanti T, Thottakkara P, et al. Mortality and cost of acute and chronic kidney disease after vascular surgery. *Annals Vascular Surg.* 2016;30, 72-81.e72.
17. Huber M, Ozrazgat-Baslanti T, Thottakkara P, et al. Mortality and cost of acute and chronic kidney disease after vascular surgery. *Annals Vascular Surg.* 2016;30, 72-81.e71-72.
18. Kork F, Balzer F, Spies CD, et al. Minor postoperative increases of creatinine are associated with higher mortality and longer hospital length of stay in surgical patients. *Anesthesiology.* 2015;123:1301–11.
19. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Annals Surg.* 2004;240:205–13.
20. Koivusalo AM, Kellokumpu I, Ristkari S, Lindgren L. Splanchnic and renal deterioration during and after laparoscopic cholecystectomy: a comparison of the carbon dioxide pneumoperitoneum and the abdominal wall lift method. *Anesth Analg.* 1997;85:886–91.
21. Miki Y, Iwase K, Kamiike W, Taniguchi E, Sakaguchi K, Sumimura J, et al. Laparoscopic cholecystectomy and time-course changes in renal function. The effect of the retraction method on renal function. *Surgical Endosc.* 1997;11(8):838–41.
22. Nguyen NT, Perez RV, Fleming N, Rivers R, Wolfe BM. Effect of prolonged pneumoperitoneum on intraoperative urine output during laparoscopic gastric bypass. *J Am Col Surg.* 2002;195:476–83.
23. Abelha FJ, Botelho M, Fernandes V, Barros H. Determinants of postoperative acute kidney injury. *Crit Care.* 2009;13:R79.
24. Khetpal S, Tremper KK, Heung M, et al. Development and validation of an acute kidney injury risk index for patients undergoing general surgery: results from a national data set. *Anesthesiology.* 2009;110:505–15.
25. Pan Y, Wang W, Wang J, Yang L, Ding F, Consortium IAbC. Incidence and Risk Factors of in-hospital mortality from AKI after non-cardiovascular operation: A nationwide Survey in China. *Sci Rep.* 2017;7:13953.
26. Salmasi V, Maheshwari K, Yang D, et al. Relationship between intraoperative hypotension, defined by either reduction from baseline or absolute thresholds, and acute kidney and myocardial injury after noncardiac surgery: a retrospective cohort analysis. *Anesthesiology.* 2017;126:47–65.
27. Garg AX, Kurz A, Sessler DI, et al. Perioperative aspirin and clonidine and risk of acute kidney injury: a randomized clinical trial. *JAMA.* 2014;312:2254–64.