

# Angiotensin axis blockade, acute kidney injury, and perioperative morbidity in patients undergoing colorectal surgery

## A retrospective cohort study

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### Abstract

Patients undergoing surgery and taking angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB) are susceptible to complications related to intraoperative hypotension. Perioperative continuation of such medications in patients undergoing colorectal surgery may be associated with more harm than benefit, as these patients are often exposed to other risk factors which may contribute to intraoperative hypotension. Our objectives were to assess the incidence and severity of postinduction hypotension as well as the rates of acute kidney injury (AKI), 30-day all-cause mortality, 30-day readmission, and hospital length of stay in adult patients undergoing colorectal surgery who take ACEi/ARB.

We performed a retrospective chart review of patients undergoing colorectal surgery of  $\geq 4$  hour duration at a tertiary care academic medical center between January 2011 and November 2016. The preoperative and intraoperative characteristics as well as postoperative outcomes were compared between patients taking ACEi/ARB and patients not taking these medications.

Of the 1020 patients meeting inclusion criteria, 174 (17%) were taking either ACEi or ARB before surgery. Patients taking these medications were more likely to receive both postinduction and intraoperative phenylephrine and ephedrine. The incidences of postoperative AKI ( $P = .35$ ), 30-day all-cause mortality ( $P = .36$ ), 30-day hospital readmission ( $P = .45$ ), and hospital length of stay ( $P = .25$ ), were not significantly different between the 2 groups.

Our results support the current recommendation that ACEi/ARB use is probably safe within the colorectal surgery population during the perioperative period. Intraoperative hypotension should be expected and treated with vasopressors.

**Abbreviations:** ACEi = angiotensin converting enzyme inhibitors, AKI = acute kidney injury, ARB = angiotensin receptor blockers, ERAS = enhanced recovery after surgery, ICD = international classification of diseases, KDIGO = Kidney Disease: Improving Global Outcomes.

**Keywords:** acute kidney injury, angiotensin axis blockade, intraoperative hypotension, perioperative medication continuation

## 1. Introduction

Angiotensin converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB) are some of the most commonly prescribed antihypertensive drugs, due in part to their recom-

mendation as first-line agents by recent prescribing guidelines.<sup>[1,2]</sup> Up to 1 in 3 surgical patients older than 45 years is now taking one of these medications.<sup>[3]</sup> Despite their widespread use, there is still no consensus whether these medications should be continued in the perioperative period.<sup>[3,4]</sup> Continuation of these medications with associated postinduction hypotension and the possibility of acute kidney injury (AKI) is a significant concern. A mean arterial pressure of less than 55 mm Hg for more than 20 minutes was recently shown to be associated with a high likelihood of surgery-related AKI.<sup>[5]</sup> Similarly, a graded response with a risk increase proportional to the degree and duration of intraoperative hypotension has been reported.<sup>[6]</sup> While previous studies have established correlations between the perioperative continuation of ACEi/ARB and adverse outcomes, including hypotension, the general consensus is that the benefits of continuing these medications outweigh their risks in the general surgical population.<sup>[7]</sup>

Certain surgical patients, however, have unique risk profiles limiting the applicability of recommendations made for the general surgical population. Patients undergoing orthopedic and cardiovascular surgery, for example, experience higher rates of hypotension, AKI, and hospital length of stay with the continued use of ACEi/ARB during the perioperative period.<sup>[8,9]</sup> With the increasing use of enhanced recovery after surgery (ERAS)<sup>[10]</sup> protocols in colorectal surgery patients, at-risk surgical patients

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need to be identified early to optimize postsurgical outcomes and avoid complications, particularly AKI.<sup>[11,12]</sup> Factors which may make this surgical population particularly susceptible to postoperative complications with the use of ACEi/ARB include the use of mechanical bowel preparation, fluid-sparing protocols, and/or neuraxial anesthesia techniques, all of which may precipitate hypotension and lead to end-organ dysfunction.<sup>[13]</sup>

We hypothesized that patients taking ACEi/ARB and undergoing colorectal surgery would experience increased rates of postoperative morbidity and mortality compared with a matched patient cohort who were not taking these medications. Our primary objective was to study the incidence of AKI, as defined by the Kidney Disease: Improving Global Outcomes (KDIGO) criteria,<sup>[14]</sup> within the first 48 hours following surgery in these patients. Our secondary objectives were to compare the rates of intraoperative hypotension, vasopressor use and fluid requirements between groups, as well as longer-term outcomes such as hospital length of stay, 30-day all-cause mortality, and 30-day hospital readmission rates.

## 2. Materials and methods

This retrospective cohort study included patients undergoing colorectal surgery at a tertiary care academic medical center from January 2011 to November 2016. The study was approved by the Institutional Review Board (Penn State IRB Protocol#5952—November 2016). Inclusion criteria were as follows: patients >18 years old undergoing colorectal surgery, having a scheduled visit to the anesthesia preoperative clinic before surgery, and surgical length of greater than 4 hours' duration. A surgical length of 4 hours or greater was chosen as an inclusion criterion by the investigators before patient enrollment for 2 reasons: (1) short operative procedures are often not accompanied by fluid shifts and hemodynamic changes of significant length or magnitude to significantly affect longer-term postoperative outcomes, and (2) patients undergoing shorter operative procedures are often discharged home soon after surgery, precluding the collection of data for 48 hours following surgery.

Patients undergoing multiple operative procedures within the given study period were excluded from analysis to avoid confounding effects. Preoperative antihypertensive medications were captured electronically from the patients' medication list, reconciled at the preoperative clinic visit before the index surgery. The anesthesiologist at this visit recommended either taking or stopping these medications on the morning of surgery depending on the patient's vital signs and medical comorbidities. Patients were included in the ACEi/ARB cohort if they confirmed long-term use of these medications at the anesthesia preoperative clinic visit immediately before surgery. Conversely, they were included in the non-ACEi/ARB cohort if they were not taking these antihypertensive medications before surgery.

All required intraoperative and postoperative variables were collected from the patients' electronic medical records by an electronic chart search. Postoperative kidney injury was defined using the most recent guidelines, the KDIGO criteria.<sup>[14]</sup> Baseline patient information (demographics, concurrent antihypertensive use, and epidural catheter placement before surgery) as well as intraoperative (hemodynamic variables, vasopressor use, intravenous fluids, colloids, and blood products) and postoperative data (urine output, laboratory values, volume of fluids administered) were collected. Demographic and comorbidity data was collected based on prior description of factors known to

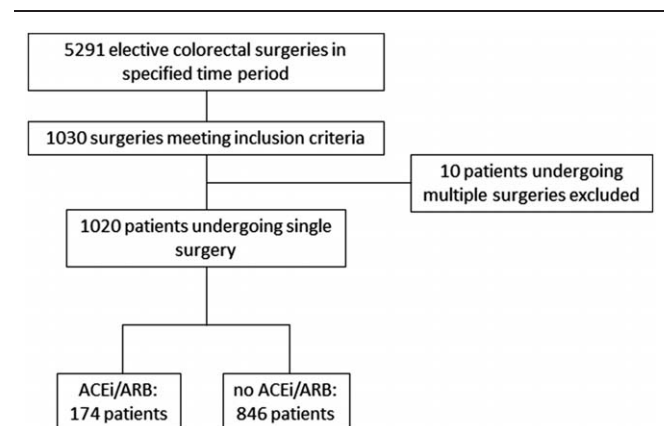
predispose patients to acute renal failure following colon and rectal surgery.<sup>[15]</sup> These included, but were not limited to age, pre-existing chronic kidney or liver disease, congestive heart failure, and peripheral vascular disease. Additional risk factors for AKI, including exposure to nephrotoxic medications (nonsteroidal anti-inflammatory drugs, intravenous contrast, and the antibiotics vancomycin, gentamicin, and cyclosporine) during the perioperative period were also compiled from the electronic medical record. Intraoperative and postoperative hypotension were defined as a systolic blood pressure  $\leq 80$  mm Hg. Data was also collected regarding fluids administered and urine output in 6-hour intervals for a total of 48 hours following the start of surgery to facilitate diagnosis of AKI by KDIGO criteria.

For binary outcomes, we constructed frequencies and percentages as descriptive statistics, and we applied Fisher exact test to compare the non-ACEi/ARB and ACEi/ARB groups. For ordinal outcomes, we also constructed frequencies and percentages for combined categories as descriptive statistics, and we applied the nonparametric Jonckheere–Terpstra trend test to compare non-ACEi/ARB and ACEi/ARB groups. For continuous outcomes, we constructed medians and quartiles as descriptive statistics, and we applied the Wilcoxon rank-sum test to compare non-ACEi/ARB and ACEi/ARB groups. SAS version 9.4 (SAS Institute, Cary, NC) was used to analyze the results. *P* was regarded as significant at the .05 level.

Given the retrospective nature of our study, we performed two subsequent analyses of our outcome data to account for possible confounding variables. The first adjusted for severity of illness in our comparison groups. We used the American Society of Anesthesiologists (ASA) physical class designation as a surrogate for severity of systemic illness, and thus compared outcomes between study groups stratified by ASA class. The second was a subgroup analysis of all patients in the ACEi/ARB group, comparing primary outcomes between patients concurrently taking beta blockers and those who were not.

## 3. Results

A total of 1020 patients met study inclusion criteria (Fig. 1). Patients taking ACEi/ARB were more likely to be obese, have diabetes, have a higher ASA physical class designation, and have chronic kidney disease based on international classification of



**Figure 1.** CONSORT diagram showing distribution of patients included in our study cohort. ACEi=angiotensin converting enzyme inhibitors, ARB=angiotensin receptor blockers.

**Table 1**

**Comparison of baseline and demographic data and risk profile in patients taking angiotensin converting enzyme inhibitors/angiotensin receptor blockers and those not taking these medications.**

Variable	Non-ACEi/ARB N = 846	ACEi/ARB N = 174	P
Male	456/846 (53.9%)	87/174 (50.0%)	.36
Beta blocker use	26/212 (12.3%)	22/71 (31.0%)	.001
Diabetes	84/846 (9.9%)	53/174 (30.5%)	<.0001
Chronic kidney disease (any stage)	40/846 (4.7%)	15/174 (8.6%)	.04
Hypertension	272/846 (32.1%)	148/174 (85.1%)	<.0001
Malignancy	318/846 (37.6%)	88/174 (50.6%)	.002
Obesity	180/846 (21.3%)	52/174 (29.9%)	.02
Heart failure	17/846 (2.0%)	19/174 (10.9%)	<.0001
Liver disease	16/846 (1.9%)	4/174 (2.3%)	.76
Lung disease	116/846 (13.7%)	32/174 (18.4%)	.12
Alcoholism	9/846 (1.1%)	0/174 (0.0%)	.37
Colectomy	459/846 (54.3%)	93/174 (53.5%)	.87
ASA class = 1, 2	344/846 (40.7%)	42/174 (24.1%)	
= 3	461/846 (54.5%)	122/174 (70.1%)	
= 4, 5	41/846 (4.8%)	10/174 (5.8%)	.0002
*Body mass index (kg/m <sup>2</sup> )	N = 706 28.0 (23.9, 32.9)	N = 161 30.3 (26.6, 35.8)	<.0001
*Baseline systolic blood pressure (mm Hg)	N = 291 126 (117, 137)	N = 81 134 (124, 145)	.0004
*Baseline diastolic blood pressure (mm Hg)	N = 291 77 (70, 85)	N = 81 78 (70, 87)	.76
Nephrotoxic antibiotics (gentamicin, vancomycin, cyclosporine)	41/846 (4.9%)	15/174 (8.6%)	.07
Nonsteroidal anti-inflammatory drugs	224/846 (26.5%)	26/174 (14.9%)	.001
Intravenous contrast administration	9/846 (1.1%)	4/174 (2.3%)	.25

ACEi = angiotensin converting enzyme inhibitors, ARB = angiotensin receptor blockers, ASA = American Society of Anesthesiologists Physical Class.

\*Median (interquartile range).

diseases (ICD)-9 or 10 diagnosis code (Table 1). In general, there were no significant differences between the types of surgery undergone by patients taking ACEi/ARB and their normotensive counterparts (Table 2). Patients taking ACEi/ARB were more likely to require intravenous ephedrine or phenylephrine within 30 minutes following anesthetic induction, and to receive increased total doses of both of these vasopressors during surgery (Table 3). The majority of patients did not require norepinephrine, epinephrine, or vasopressin during the intraoperative period, and the doses of these vasopressors did not differ between comparison groups. The recorded number of episodes classified as “hypotensive” did not differ, despite increased requirements for ephedrine or phenylephrine in patients taking ACEi/ARB (Table 3).

Our observed rates of AKI by creatinine criteria alone were 9.8% in the ACEi/ARB group and 5.9% in the control group ( $P = .07$ , Table 4). The rates of postoperative AKI as determined by urine output alone were much higher: 59.8% in the ACEi/ARB

group and 55.6% in the control group ( $P = .35$ , Table 4). Both groups displayed similar rates of hospital length of stay, 30-day all-cause mortality, and 30-day hospital readmission rates. Our negative results were confirmed when patients were risk-stratified by ASA physical class (data not shown). Surgery-related complications, including conversion rates from laparoscopic to open approach, were similar between groups (Table 2). Subgroup analysis comparing patients taking beta blockers and patients not taking these medications similarly did not demonstrate any difference in our primary outcome variables (data not shown).

The volume of intravenous crystalloids administered 12 to 24 hours postoperatively was inversely related to the volume of urine output during this same period, although there was no significant difference in volume of intravenous fluid administered or measured urine output between the groups. The median intraoperative volume of crystalloid administered in the non-ACEi/ARB group and ACEi/ARB group was similar (2.7 L [5.9 mL/kg/hour] vs. 2.7 L [5.8 mL/kg/hour]). Median values were assessed rather than means because the Wilcoxon rank-sum test was used to compare the 2 groups. The median volume of crystalloid administered within the first 24 hours following surgery was 1.9 L in both groups (translating to 1 mL/kg/hour in the non-ACEi/ARB group and 0.9 mL/kg/hour in the ACEi/ARB group). Most intravenous crystalloids were administered within the first 18 hours after surgery, and postoperative urine output rate decreased to its nadir between 12 to 24 hours after surgery.

#### 4. Discussion

In this retrospective study, we demonstrated that patients taking ACEi/ARB and undergoing colorectal surgery were more likely to need intraoperative vasopressors, but that they did not

**Table 2**

**Surgical details of the surgical cohort.**

Variable	Non-ACEi/ARB N = 839	ACEi/ARB N = 172	P
Laparoscopic Procedures	274/839 (32.7%)	60/172 (34.9%)	.59
Open procedures	386/839 (46.0%)	75/172 (43.6%)	.61
Laparoscopic Converted to open	45/839 (5.4%)	10/172 (5.8%)	.85
Segmental resection	225/839 (26.8%)	59/172 (34.3%)	.05
Total abdominal colectomy	98/839 (11.7%)	20/172 (11.6%)	.99
Ileocelectomy	78/839 (9.3%)	9/172 (5.2%)	.10
Abdominal perineal resection	42/839 (5.0%)	8/172 (4.6%)	.99

ACEi = angiotensin converting enzyme inhibitors, ARB = angiotensin receptor blockers.

**Table 3**  
**Comparison of perioperative data in patients taking angiotensin converting enzyme inhibitors/angiotensin receptor blockers and those not taking these medications.**

Variable	Non-ACEi/ARB N=846	ACEi/ARB N=174	P
*Duration of anesthesia (min)			.52
	312 (272, 377)	312 (273, 360)	
Presence of epidural catheter	117/846 (13.8%)	28/174 (16.1%)	.47
*Estimated blood loss (ml)	N=699	N=145	.29
	180 (100, 350)	150 (100, 300)	
Systolic blood pressures <80 mm Hg within 30 min following induction			
=0	694/846 (82.0%)	136/174 (78.2%)	.20
=1	78/846 (9.2%)	14/174 (8.0%)	
=2	30/846 (3.6%)	11/174 (6.3%)	
≥3	44/846 (5.2%)	13/174 (7.5%)	
*Nadir systolic blood pressure (mm Hg)	N=842	N=173	.89
	83 (75, 91)	82 (75, 92)	
*Nadir diastolic blood pressure (mm Hg)	N=842	N=173	.95
	45 (38, 51)	46 (37, 51)	
Number of recorded systolic blood pressures <80 mm Hg intraoperatively			
=0	509/846 (60.2%)	100/174 (57.5%)	.76
=1	127/846 (15.0%)	25/174 (14.4%)	
=2	68/846 (8.0%)	14/174 (8.0%)	
≥3	142/846 (16.8%)	35/174 (20.1%)	
Ephedrine within 30 min postinduction (mg)			
=0	757/846 (89.5%)	142/174 (81.6%)	.02
=5	48/846 (5.6%)	14/174 (8.0%)	
=10	25/846 (3.0%)	12/174 (6.9%)	
>10	16/846 (1.9%)	6/174 (3.5%)	
Phenylephrine within 30 min postinduction (mg)			
=0	695/846 (82.1%)	121/174 (69.5%)	.0003
=0.1–0.2	0/846 (0.0%)	0/174 (0.0%)	
>0.2	151/846 (17.9%)	53/174 (30.5%)	
Total epinephrine administered intraoperatively (mg)=0	841/846 (99.4%)	173/174 (99.4%)	.99
Total norepinephrine administered intraoperatively (mg)=0	820/846 (96.9%)	160/174 (91.9%)	.005
Total ephedrine administered intraoperatively (mg)			
=0	549/846 (64.9%)	82/173 (47.4%)	<.0001
=5–15	204/846 (24.1%)	54/173 (31.2%)	
=20–30	73/846 (8.6%)	27/173 (15.6%)	
>30	20/846 (2.4%)	10/173 (5.8%)	
Total phenylephrine administered intraoperatively (mg)			
=0.0–0.05	460/846 (54.4%)	77/174 (44.2%)	.02
=0.1–0.25	0/846 (0.0%)	0/174 (0.0%)	
=0.3–0.50	0/846 (0.0%)	0/174 (0.0%)	
>0.5	386/846 (45.6%)	97/174 (55.8%)	
*Crystalloids administered intraoperatively (mL)	2713 (1800, 4000)	2700 (2000, 3500)	.62
Albumin administered intraoperatively (mL)			
=0	621/846 (73.4%)	114/173 (65.9%)	.02
=100–500	137/846 (16.2%)	28/173 (16.2%)	
>500	88/846 (10.4%)	31/173 (17.9%)	
Fresh frozen plasma administered intraoperatively (mL)=0	819/846 (96.8%)	169/174 (97.1%)	.99
Packed red blood cells administered intraoperatively (mL)=0	775/846 (91.6%)	155/174 (89.1%)	.30
Platelets administered intraoperatively (mL)=0	834/846 (98.6%)	170/174 (97.7%)	.50
*Urine output rate intraoperatively (mL/kg/hour)	0.7 (0.4, 1.2)	0.7 (0.5, 1.1)	.78
AKI based on intraoperative urine output rate <0.5 mL/kg/hour for ≥6 hours	64/819 (7.8%)	13/169 (7.7%)	.99

ACEi=angiotensin converting enzyme inhibitors, AKI=acute kidney injury, ARB=angiotensin receptor blockers.

\*Median (interquartile range).

experience a significantly increased rate of postoperative AKI. Furthermore, postoperative morbidity, assessed by comparing 30-day all-cause mortality, hospital length of stay, and 30-day hospital readmission, was not statistically significant in patients taking ACEi/ARB up to and including the day of surgery. These findings were confirmed in analyses stratified by severity of illness.

Several meta-analyses have been performed to analyze the safety and feasibility of continuing ACEi/ARB in the perioperative period,<sup>[3,16,17]</sup> but none have specifically addressed the colorectal surgery population. In the most recent of these meta-analyses, ACEi/ARB use on the morning of noncardiac surgery caused more intraoperative hypotension compared to patients foregoing their morning antihypertensive dose. However, there

**Table 4**  
**Postoperative outcomes of patients taking angiotensin converting enzyme inhibitors/angiotensin receptor blockers and patients not taking these medications.**

Variable	Non-ACEi/ARB N=846	ACEi/ARB N=174	P
AKI based on postoperative serum creatinine increase by $\geq 0.3$ mg/dL	50/846 (5.9%)	17/174 (9.8%)	.07
AKI based on postoperative urine output rate $< 0.5$ mL/kg/hour for $\geq 6$ hours	455/819 (55.6%)	101/169 (59.8%)	.35
Postoperative AKI by urine output criteria or serum creatinine level	464/819 (56.7%)	103/169 (61.0%)	.35
Postoperative AKI by urine output criteria and serum creatinine level	40/819 (4.9%)	14/169 (8.3%)	.09
*Hospital length of stay (days)	6.5 (4.5, 10.1)	7.0 (5.3, 10.2)	.25
30-day all-cause mortality	8/846 (0.9%)	0/174 (0.0%)	.36
30-day readmission rate	109/827 (13.2%)	18/166 (10.8%)	.45

ACEi=angiotensin converting enzyme inhibitors, AKI=acute kidney injury, ARB=angiotensin receptor blockers.

\* Median (interquartile range).

were no differences in the rate of adverse outcomes between groups.<sup>[3]</sup>

Patients undergoing colorectal surgery may be particularly susceptible to hypovolemic hypotension due to the frequent use of preoperative mechanical bowel preparation (which could cause lower gastrointestinal fluid losses of between 500 mL and 1000 mL)<sup>[18]</sup> and preoperative dehydration, (the incidence of which has been reported to be as high as 27%).<sup>[19]</sup> Perioperative fluid-restricting strategies have become the standard of care in order to reduce postoperative complications such as ileus and anastomotic leak in this patient population, but they may also exacerbate hypotension and its associated consequences.<sup>[20–22]</sup> Indeed, a recent study reported that, while ERAS protocols conferred several outcome benefits in elective colorectal resections, the rate of postoperative AKI increased following implementation of this protocol.<sup>[23]</sup>

Standard care for patients undergoing colorectal surgery at our institution involves the use of components of the ERAS protocol. However, the implementation of these components is at the discretion of the operating surgeon and the consultant anesthesiologist. General anesthesia is administered by a member of a core group of colorectal anesthesiologists, who often use neuraxial (epidural) or regional (transversus abdominis plane block) techniques and nonopioid analgesic adjuncts (acetaminophen, gabapentin, nonsteroidal anti-inflammatory drugs) to minimize perioperative opioid use; observe goal-directed fluid administration protocols including a continuous infusion of 3 to 5 mL/kg/hour crystalloid infusion during surgery with continuous monitoring of urine output via Foley catheter and invasive (FloTrac System: Edwards Lifesciences Corp, Irvine, CA) or noninvasive (ClearSight System: Edwards Lifesciences Corp) monitoring of pulse pressure variation for assessment of fluid-responsiveness; and/or routine administration of antiemetic therapy when appropriate.

While our study showed that postinduction and intraoperative vasopressor use differed between normotensive patients and those chronically taking ACEi/ARB, the rate of intraoperative hypotension did not. The discrepancy may be related to anesthesiologist bias toward more aggressive use of vasopressors in patients known to be taking ACEi/ARB. Alternatively, it may be due to our numeric definition of “hypotension.” Most studies define hypotension as a systolic blood pressures between 80 to 100 mm Hg, or a decrease of  $\geq 20\%$  from baseline systolic blood pressure.<sup>[24]</sup> This definition could actually signify profound hypotension in chronically hypertensive patients having altered renal autoregulatory flow (and a so-called “rightward shift” of the renal autoregulation curve).<sup>[25]</sup> Given our retrospective study

design, we opted for a more stringent definition of hypotension to avoid a false positive categorization of hypotensive patients. It is possible that our cohort would have demonstrated higher rates of postinduction hypotension if we used a more liberal numeric cutoff, or if we defined hypotension in relation to a patient’s baseline blood pressure.

One of the main strengths of our study is our dual analysis of intraoperative and postoperative fluid administration and urine output when diagnosing AKI. The changing definition of AKI over the past 2 decades is a source of confusion, limiting the utility of previously published research in the management of surgery-associated AKI.<sup>[26]</sup> Our observed rate of AKI by KDIGO creatinine criteria alone was consistent with that reported in the medical literature,<sup>[6]</sup> as was our observed rate of AKI by KDIGO urine output criteria.<sup>[27]</sup> Most perioperative AKI studies we encountered based this diagnosis solely on serum creatinine level, and postoperative urine output is seldom considered due to the purported confounding effects of stress hormones (e.g., aldosterone and antidiuretic hormone) on urine output. In contrast, two large, recent retrospective analyses supported the utility of postoperative oliguria in independently predicting postoperative AKI after noncardiac surgery.<sup>[28,29]</sup> Furthermore, Mizota et al<sup>[30]</sup> demonstrated that, in living donors for liver transplantation, patients who had isolated urine output-based AKI had longer intensive care unit and hospital stays compared with patients having solely serum creatinine-based AKI. Thus, while the significance of postoperative oliguria is still widely questioned, its prevalence in our study and others underlines the importance of further research into its postoperative implications.

Our results should be taken within the context of the study’s limitations. First, given the retrospective nature of our analysis, there may be a significant degree of residual confounding. Factors such as the dose and type of angiotensin axis blocking medication, as well as the time of the last dose taken before surgery, are variables that we could not control for but which could influence the degree of observed hypotension and its associated complications. Nevertheless, since the majority of patients seen in our preoperative clinic are advised to withhold their antihypertensive medication on the morning of surgery and the half-life of most commonly administered ACEi/ARB is at least 9 to 12 hours, it is reasonable to assume that at least 50% of the active drug is present on anesthetic induction if the antihypertensive medication was not taken on the morning of surgery. Furthermore, we could not control for cotherapy with other antihypertensives due to our study design, although cotherapy with beta blockers did not appear to affect the primary outcome of interest.

A further study limitation is that we elected to report our single-center experience with the perioperative use of ACEi/ARB over a 5-year period, although the relatively low incidence of AKI by serum creatinine alone made it inadequately powered to detect small differences in the incidence of postoperative AKI by serum creatinine alone. Conversely, given the high incidence of postoperative oliguria, our study was more than adequately powered to detect AKI by urine output criteria alone. We would recommend that future consensus statements regarding the definition of surgery-associated AKI should clarify whether postoperative oliguria is to be considered in the diagnosis of surgery-associated AKI. This will enable the design of effective research studies that are statistically powered to detect a difference in the outcome of interest.

## 5. Conclusion

Our results support the current recommendation that ACEi/ARB use is probably safe in the perioperative period. Despite the fluid restrictions and dehydration often encountered in patients undergoing colorectal surgery, these medications were not associated with an increased risk of AKI, hospital length of stay, 30-day all-cause mortality, or hospital readmission rates. Intraoperative hypotension should, however, be expected in these patients and treated with intravenous vasopressors. Further studies are warranted to evaluate the effects of ACEi/ARB in the context of intravenous vasopressor use on perioperative outcomes.

## Author contributions

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