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Original Article

Impact of Intraoperative Degrees of Hypotensive Anaesthesia Using Dexmedetomidine on Perioperative Renal Injuries in Patients Undergoing Endoscopic Sinus Surgery

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ABSTRACT

Article information

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Background and objective: Although controlled intraoperative hypotension is essential in functional endoscopic sinus surgery [FESS], it could lead to vital organ hypoperfusion. Herein, we evaluated the effects of maintaining mean blood pressure [BP] around 60 mmHg on renal function compared to its maintenance around 70 mmHg.

Patients and Methods: We included 134 patients undergoing FESS procedure in this randomized prospective trial. Patients were divided into two groups; mean BP was kept around 70 mmHg in group A participants, while the same parameter was kept around 60 mmHg in group B patients. Preoperative and intraoperative kidney function were evaluated by the resistive index.

Results: Most preoperative parameters were statistically comparable between the two groups. Group B patients had better surgical field quality. The incidence of acute kidney injury [AKI] was 9% and 20.9% in Groups A and B, respectively [$p = 0.052$]. However, the intraoperative resistive index showed a marked increase in Group B [0.81 vs. 0.75 in Group A]. High baseline creatinine and a high intraoperative resistive index were independent predictors for AKI. High postoperative serum creatinine was also a significant risk factor.

Conclusion: A high preoperative creatinine and intraoperative resistive index are strong risk factors for AKI.

Keywords: Intraoperative hypotension; Renal injury; Predictors; Resistive index.

INTRODUCTION

Nowadays, functional endoscopic sinus surgery [FESS] has become more popular among Otorhinolaryngologists. Not only does it offer a minimally invasive solution approach for chronic sinusitis patients, but it also yields excellent outcomes [1]. Intentional controlled hypotension is of great benefit during such procedures [2]. Controlled intraoperative hypotension is achieved by maintaining the mean blood pressure [BP] at 60–70 mmHg or decreasing it by 30% of its baseline value [3].

Controlled hypotension could precipitate serious perioperative consequences, including acute kidney injury [AKI], hypoperfusion or ischemia to other vital organs, and acidosis [4]. That's why identification of the risk factors for that problem is crucial for its prevention [5].

Although multiple reports have documented that intraoperatively controlled hypotension has no significant negative impact on kidney functions [6], a strong association has been reported between the incidence of intraoperative hypotension and perioperative AKI [7].

In the current literature, there is an apparent paucity of clinical trials defining the safe limit of intraoperative controlled hypotension. That was a good reason for us to do this study, which aimed to compare the effects of keeping mean blood pressure around 70 mmHg versus keeping it around 60 mmHg on renal function [as measured by serum creatinine and doppler-guided resistive index].

PATIENTS AND METHODS

Initially, the study protocol was approved by the Institutional Review Board [IRB] of Mansoura University, code R.19.10.643, and all patients agreed to the terms of our research after we explained the benefits and possible drawbacks of each intervention. This work has been carried out following The Code of Ethics of the World Medical Association [Declaration of Helsinki] for studies involving humans [8]. This prospective, single blinded trial was conducted at the anesthesiology and Otorhinolaryngology Departments of Mansoura University Hospitals. We designed this study for adult patients aged less than 60 years and prepared for FESS under general anesthesia during the period between December 2020 and March 2022.

Before the surgery, all 134 patients were reviewed by the anesthesia team, along with reviewing their investigations. The patients with a physical status of I or II according to the American Society of Anesthesiologists [9] [ASA] classification were included in this study Additionally, we excluded patients with either of the following criteria; age > 60 years, grade I or II left ventricular diastolic dysfunction, left ventricular hypertrophy, left ventricular ejection fraction less than 55%, cardiomyopathy, pericardial pathology, diabetes mellitus, preoperative serum creatinine > 1.30 mg/dL for men and > 1.00 mg/dL for women, or history of chronic alpha-2 receptor agonist intake.

The allocated participants were randomly enrolled into two groups [1:1 allocation ratio] using the "sealed envelope method" for randomization in line with the CONSORT statement; 67 patients were enrolled into group A, which received controlled hypotension down to around 70 mmHg mean BP, while the remaining patients were enrolled into group B, which received controlled hypotension down to around 60 mmHg mean BP. All patients signed informed consent.

The resistive index of renal vessels [RI] was assessed in all cases before the operation and intraoperatively 1 hour after the targeted MAP was reached by an experienced radiologist via a Doppler ultrasound device [Toshiba XARIO 200 TUS-X200, American Medical Systems Inc.]. An interlobar or arcuate artery was then selected, and pulse-wave Doppler measurements were obtained. The Doppler spectrum was optimal when at least three similar consecutive waveforms were visualized. The resistive index was calculated as [peak systolic velocity − end-diastolic velocity]/ peak systolic velocity. Three measurements were taken in each kidney [top, middle, and lower] for the arcuate or interlobar arteries, giving six readings. The mean of these readings was calculated as the basal and intraoperative resistive indices. An RRI value 0.60±0.01 [mean±SD] is usually taken as normal, with 0.70 considered the upper normal threshold by most authors.

All patients were ordered to stop their chronic medications the night before surgery, apart from angiotensin-converting enzyme inhibitors, which were allowed until the morning of the procedure. All patients received oral diazepam [5–10 mg] the night before the surgery to induce sedation. On transfer to the operating room, basic hemodynamic monitoring was established, and we monitored BP via a 20-gauge cannula inserted into the radial artery [invasive BP measurement]. We induced and maintained general anesthesia according to the protocol of our institution. Induction was done with IV propofol [1.5–2 mg/kg] and fentanyl [3–5 mcg/kg], and IV cisatracurium [0.1 mg/kg] was given to facilitate endotracheal intubation. Anesthetic maintenance was achieved with isoflurane in a mixture of O_2 and air, in addition to cisatracurium [2 mcg/kg/min]. We adjusted the mechanical ventilation to keep arterial CO2 levels between 35 and 45 mmHg. Continuous monitoring of hemodynamic parameters was done throughout the operation.

Before starting surgery, the nasal mucous membrane of all patients was subjected to a mixture of lidocaine 2% [4 ml] and epinephrine 1:1000 [1 ml] dripped over cotton pads and applied for 15 minutes. Controlled hypotension was achieved by IV dexmedetomidine [given as an IV bolus of 1 mcg/kg over ten minutes, followed by an infusion of 0.7-1 mcg/kg/hour till the end of the surgical procedure]. The rate of infusion was adjusted to keep the mean BP around the previously mentioned values according to group allocation. Any drop in the heart rate below 50 bpm was managed with IV atropine 0.5 mg, while a drop in MAP below the required target was managed by decreasing dexmedetomidine infusion rate, and if still not adequate, incremental IV ephedrine 3 mg was used.

All operations were performed by one surgeon who was blinded to group allocation to ensure consistency in estimating the surgical field. All patients received lactated ringer's solution at approximately 3–5 ml/kg/h peri-operatively, and normothermia was maintained during the whole procedure.

The quality of the surgical field was classified according to the grading system for endoscopic surgical field quality previously published by **Boezaart *et al.*** [10]. Mean, systolic, and diastolic BP, measured via the intra-arterial catheter, were recorded at the time of induction and then every 5 minutes during the procedure till the end of anesthesia. Their means were calculated and recorded for each patient, and then the average for each group was calculated. After the surgery, all patients were transferred to the recovery room, where they remained for one hour before being discharged if they met the discharge criteria [11]. After transfer to the internal ward, close monitoring and frequent assessment were done for all patients, including measurement of urine output. Laboratory parameters [serum creatinine and BUN] were ordered 48 hours after the operation.

The presence of AKI and its stage were established based on serum creatinine levels and urine output [when the postoperative serum creatinine increased by 0.3 mg/dL or more within 48 hours or urine output was less than 0.5 mL/kg/h for six hours] as published by the KDIGO classification [12]. Our total participants were also divided in another way according to the incidence of AKI [AKI and non-AKI groups] to establish the risk factor for that complication.

Our primary outcome was the incidence of post-operative AKI, and the secondary outcomes were predictors of AKI in FESS patients and surgical field assessment.

We used the PASS software program to calculate the required sample size. A pilot study was conducted at the same hospital, with 10 patients in each of the two groups. The first group had controlled hypotension until reaching a mean blood pressure [MBP] around 70 mmHg, while the second group had controlled hypotension to around 60 mmHg. AKI was detected in 0% and 20% of these two groups, respectively. Thus, 62 patients needed to be enrolled in each of our study groups to achieve an 80% study power and a 5% significance level. For a 5% expected dropout rate, the number was increased to 67 patients in each group.

We used the SPSS [Statistical Package for Social Sciences] version 22 for Windows® [IBM SPSS Inc., Chicago, IL, USA] for data collection, tabulation, and analysis. Categorical data were expressed as numbers [and frequencies] and compared between the two groups using the Fisher exact or Chi-square tests. For numerical data, they were expressed as mean [with standard deviation] or median [with range]. When comparing two groups, the former was compared using the student t test, while the latter was compared using the Mann Whitney test. Regression analysis was used to determine the risk factors for AKI. Any p-value less than 0.05 was considered significant in the statistical analysis.

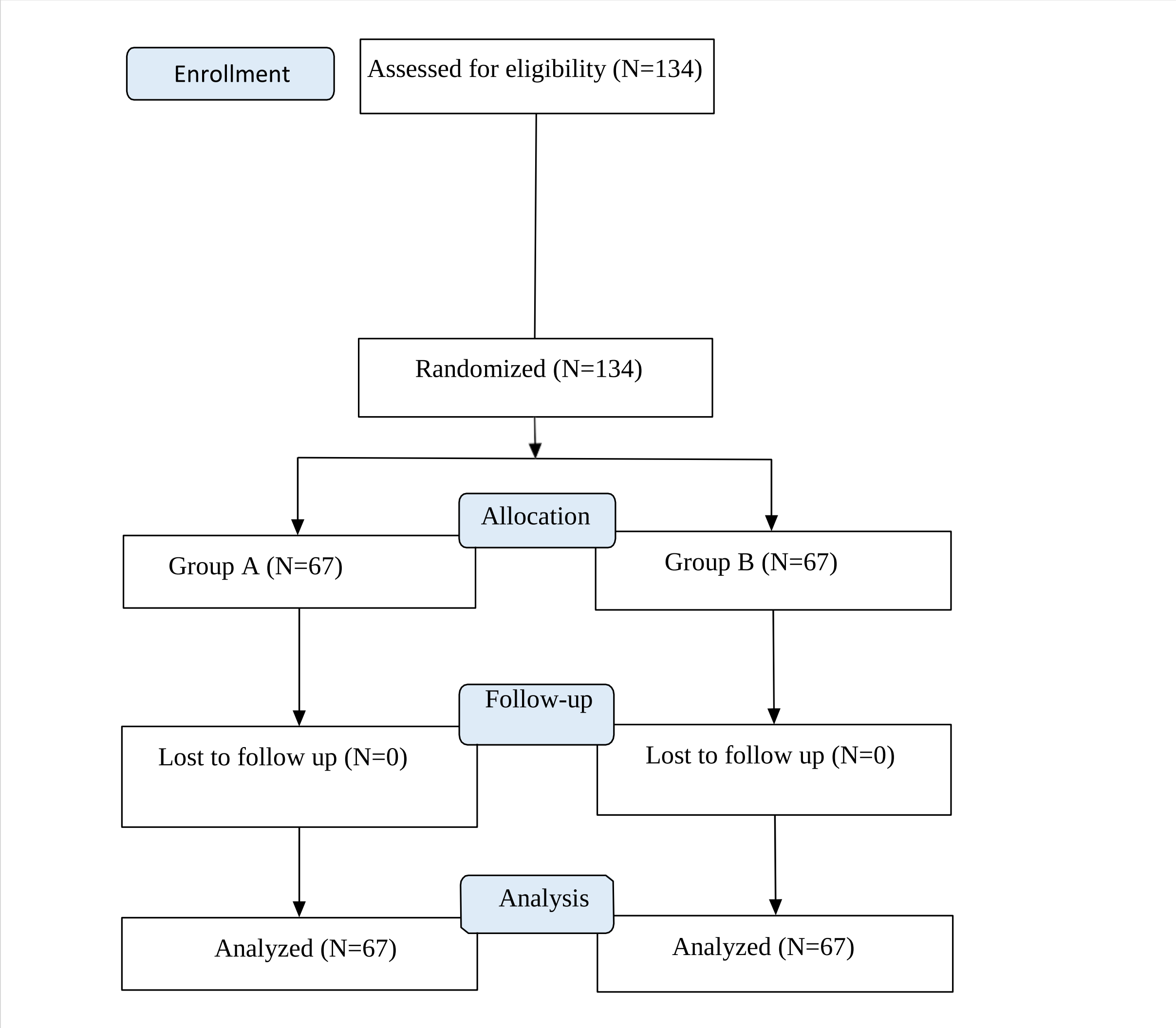

Figure [1]: Consort flow chart for patient eligibility

RESULTS

There were no excluded patients after the start of the study flow [figure 1]. Our patients' demographic criteria were statistically comparable between Groups A and B. Preoperative laboratory parameters and Baseline hemodynamic parameters were also comparable between the two groups [table 1].

Also, the duration of the surgical procedure, duration of controlled hypotension, and average intraoperative heart rate expressed no significant difference between our two groups. The average mean BP was significantly higher in Group A [73.07 vs. 61.032 mmHg in Group B – $p < 0.001$]. There was a significant improvement in the quality of the operative field in Group B [in association with more hypotension] [$p < 0.001$] [table 2].

Fluid balance did not differ between the two groups after surgery. Also, baseline and follow-up creatinine levels, along with their percent change, were statistically comparable between the two groups. Although the baseline resistive index did not differ between our two groups, the same parameter showed a significant drop in Group A [0.75 vs. 0.81 in Group B – $p = 0.017$]. Nonetheless, the percent of change was statistically comparable between our two groups [table 3].

The incidence of perioperative AKI increased in group B [20.9%] compared to Group A [9%] [$p = 0.052$] [table 4].

To elucidate the risk factors for AKI in our patients, our patients were divided into two groups: AKI and non-AKI ones. The AKI group showed a significant increase in preoperative and postoperative creatinine along with its percent change. Additionally, the intraoperative resistive index was significantly higher in association with AKI [table 5].

Only baseline creatinine and intraoperative resistive index maintained their significance as predictors for AKI in the multivariate analysis [table 6].

Table [1]: Demographic characteristics and preoperative assessment of the studied groups

		Group A [n= 67]	Group B [n= 67]	95% CI	P
Age [years]		36.51± 10.06	35.18 ± 10.4	-2.18, 4.8	0.521
Gender	Male	38.8% [26]	52.2% [35]	-	0.171
	Female	61.2% [41]	47.8% [32]		
Weight [kg]		76.13 ± 7.2	74.6 ± 7.596	-1.01, 4.03	0.240
BMI [kg/m2]		26.85 ± 1.888	26.30 ± 2.739	-0.28, 1.3	0.205
ASA	I	88.1% [59]	83.6% [56]	-	0.459
	II	11.9% [8]	16.4% [11]		
Preoperative hematocrit [%]		35.56 ± 1.849	35.08 ± 1.678	-0.11, 1.10	0.110
Baseline BUN [mg/dl]		18.32 ± 5.5	18.69 ± 6.8	-2.42, 1.83	0.785
Baseline heart rate [bpm]		91.96 ± 11.94	89.01 ± 14.07	-1.52, 7.4	0.195
Baseline SBP [mmHg]		118.21 ± 12.2	117.09 ± 8.3	-2.4, 4.6	0.537
Baseline DBP [mmHg]		78.51 ± 10.6	77.69 ± 11.19	-2.9, 4.5	0.664
Baseline MBP [mmHg]		91.7 ± 10.6	90.6 ± 10.02	-2.3, 4.7	0.504

Data is expressed as mean and standard deviation or as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05. ASA American Society of Anesthesiologists, BMI body mass index, BUN blood urea nitrogen, SBP systolic blood pressure, DBP diastolic blood pressure, MBP mean blood pressure.

Table [2]: Intraoperative parameters of the studied sample

	Group A [n= 67]	Group B [n= 67]	95% CI	P
Duration of surgery [minute]	95.1 ± 17.1	90.07 ± 15.03	-0.40, 10.5	0.070
Duration of controlled hypotension [minute]	77.61 ± 18.45	73.04 ± 16.14	-1.37, 10.4	0.131
Average intraoperative heart rate [bpm]	62.19 ± 6.1	63.15 ± 6.7	-3.16, 1.25	0.395
Average intraoperative MBP [mmHg]	73.07 ± 2.80	61.3 ± 1.457	11.0, 12.5	< 0.001
Boezaart grading of intraoperative field	2.93 ± 0.464	2.52 ± 0.503	0.24, 0.57	< 0.001

Data is expressed as mean and standard deviation or as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05. MBP; mean blood pressure.

Table [3]: Postoperative follow up of the studied groups

	Group A [n= 67]	Group B [n= 67]	95% CI	P
Fluid balance first day after surgery [ml]	1492.53 ± 545.2	1373.57 ± 530.1	- 64.3, 303	0.201
Baseline creatinine [mg/dl]	0.95 ± 0.222	0.987 ± 0.216	-0.10, 0.04	0.362
48-hour window creatinine [mg/dl]	1.06 ± 0.276	1.15 ± 0.310	-0.19, 0.00	0.062
Creatinine change [mg/dl]	0.10 ± 0.134	0.16 ± 0.216	-0.12, 0.00	0.061
Creatinine change percent [%]	11.11 ± 12.109	17.68 ± 25.44	-13.3, 0.23	0.059
Baseline resistive index	0.67 ± 0.050	0.69 ± 0.059	-0.03, 0.01	0.079
Intraoperative resistive index	0.75 ± 0.116	0.81 ± 0.183	-.11, -.012	0.015
Resistive index change	0.07 ± 0.093	0.12 ± 0.177	-0.09, 0.00	0.051
Resistive index changes percent [%]	11.06 ± 13.679	18.24 ± 26.48	-14.3, 0.26	0.052

Data is expressed as mean and standard deviation or as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table [4]: Incidence and stage of AKI in the current study

AKI		Group A [n= 67]	Group B [n= 67]	Odds ratio	P
Incidence		9% [6]	20.9% [14]	2.68	0.052
Stage	1	100.0% [6]	92.8% [13]	-	0.126
	2	0.0% [0]	7.2% [1]		

Data is expressed as percentage and frequency. Odds ratio was calculated for Group B using Group A as a reference. P is significant when < 0.05.

Table [5]: Comparison between AKI and Non-AKI patients

		No AKI [n=114]	AKI [n=20]	P
Age		36±10.4	34±9.00	0.512
Sex	Female [n, %] Male [n, %]	61 [53.5%] 53 [46.5%]	12 [60%] 8 [40%]	0.450
Body mass index		26.6±2.2	26.3±3.03	0.549
Baseline BUN [mg/dl]		18.5±6.1	18.4±6.9	0.937
Duration of surgery [min]		92±16.08	96.0±17.3	0.348
Average intraoperative HR [b/min]		62±6.4	63±6.4	0.379
Average intraoperative MBP [mmHg]		67.5±6.296	65.1±6.150	0.122
Fluid balance first day after surgery		1442.9±546.5	1375.0±503.2	0.587
Baseline creatinine		0.95±0.23	1.07±0.17	0.012
48-hour window creatinine		1.04±0.25	1.55±0.22	<0.001
Creatinine change percent [%]		9.8±12.5	40.5±32.48	<0.001
Baseline resistive index		0.68±.055	0.68±.055	0.819
Intraoperative resistive index		0.75±.11	0.97±.22	<0.0001
Data is expressed as mean ± standard deviation or as percentage and number or as median [range]. P is significant when < 0.05				

Table [6]: Multivariate Logistic regression in which the occurrence of AKI is the dependent variable

	B	S.E.	Wald	Sig.
Age [years]	-.020	0.04	0.21	0.643
Average intraoperative MBP [mmHg]	.013	0.06	0.04	0.840
Duration of controlled hypotension [minutes]	-0.01	0.02	0.18	0.669
% change of preoperative and intraoperative renal resistive index	-.285	0.07	14.0	< 0.001
Baseline creatinine	-7.46	2.76	7.28	0.007

DISCUSSION

In this study, we tried to explore if the degree of intraoperative controlled hypotension could increase the risk of perioperative AKI. We chose the FESS population because controlled hypotension is usually recommended by the operating surgeon to achieve a "less bloody" surgical field [2]. We should also mention that we chose dexmedetomidine because of its additional anesthetic advantages, including analgesia, sedation, and opioid sparing effects [13], without harmful effects on the kidneys [14].

Our study has a unique advantage in handling the previous concept, which is rarely discussed in the literature for this specific population. One can see the comparable findings between our two groups as regards most preoperative findings. That reflects our proper randomization, and that should decrease any bias shifting our findings in favor of one group rather than the other.

The incidence of AKI in our trial was 14.9% [20/114]. Our incidence is slightly higher than some previous studies, which reported an incidence ranging between 6.8% and 13% [15]. However, another report reported an incidence of 39.3% for the same complication [16]. The various characteristics of the population included, the surgeries carried out, and practice variations could all be factors in the variations between studies.

We noticed a significant improvement in the surgical field quality in Group B, which is a reasonable consequence of the more hypo-tension achieved in that group, leading to a clearer surgical field. Our findings revealed a comparable incidence of AKI between our two main groups [9% vs. 20.9% in groups A and B, respectively – p = 0.052]. Despite the statistical irrelevance, the reader may observe the slightly increased incidence of AKI associated with more hypotension.

In agreement with our findings, **Choi and Samman** [6] conducted a systematic review that showed intraoperatively controlled hypotension did not have any significant deleterious impact on perioperative kidney function. Additionally, **Thompson *et al.*** [17] also noted that intra-operative hypotension did not induce significant effects on renal function, as manifested in stabilized blood and urine chemistries. On the other hand, a previous report from the Mayo Clinic confirmed the association between hypotensive anesthesia and postoperative AKI in both cardiac and non-cardiac procedures [5]. **Sun *et al.*** [18] reported a graded relationship between the severity and duration of hypotension and the incidence of AKI. In our study, the duration of hypotension did not show a significant association with AKI

Although the incidence of AKI was comparable between our two groups, the intraoperative renal resistive index showed a significant increase in Group B [the more hypotensive group]. In addition, the increase in the previous parameter was a significant risk factor for AKI. The renal resistive index is a doppler-based parameter that reflects intrarenal arterial compliance and vascular resistance. The increased index indicates worse renal outcomes [19]. Other studies reported that the same parameter was predictive for AKI [12, 19, 20]. As the pathology of AKI comprises renal hypoperfusion and intrarenal vasoconstriction [12], it is expected to find this radiological marker increased in patients who develop AKI.

Our findings showed that preoperative serum creatinine was a strong predictor for AKI. This is in accordance with a recent report that reported similar findings [21]. Also, **Long *et al.*** [22] reported the same findings. This might indicate a subtle kidney dysfunction that is exaggerated by intraoperative hypotension.

We did not detect any significant association between age and AKI development [p = 0.64]. **Sun *et al.*** [18] agreed with our findings regarding age [p = 0.049]. However, **Moguel-González *et al.*** [23] reported that older age was a strong risk factor for the same complication.

In our study, BMI was not significantly associated with AKI [p = 0.54]. Although our finding was previously confirmed in the literature [12], other studies reported a significant association between obesity and perioperative AKI, and they explained it by the generalized oxidative stress in obese patients [24].

Heterogenicity among studies regarding AKI-related risk factors could be attributed to differences in sample size, patient characteristic, type of surgery, the hypotensive agent used, and levels of perioperative care.

All in all, we can summarize our findings in multiple points; [1] there were significant changes in the renal resistive index, and [2] the increased preoperative creatinine and intraoperative resistive index are strong predictors for AKI in FESS patients subjected to controlled hypotensive anesthesia.

Our study addressed a unique anesthetic viewpoint. Nonetheless, it has some drawbacks. Collecting patients from one center, and using one hypotensive medication are the main drawbacks. More studies should be conducted to detect more risk factors for AKI in patients undergoing surgeries requiring controlled hypotension.

Conclusion: Based on the preceding findings, the more hypotensive approach was associated with a significant increase in the renal resistive index. High preoperative creatinine and a high intraoperative resistive index are strong risk factors for that complication. Patients who meet the previous criteria should be closely monitored to avoid the consequences of that dreadful complication.

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