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Review Article

Intraoperative hypotension and postoperative acute kidney injury: A systematic review

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ABSTRACT

Background: There is no consensus regarding safe intraoperative blood pressure thresholds that protect against postoperative acute kidney injury (AKI). This review aims to examine the existing literature to delineate safe intraoperative hypotension (IOH) parameters to prevent postoperative AKI.

Methods: PubMed, Cochrane Central, and Web of Science were systematically searched for articles published between 2015 and 2022 relating the effects of IOH on postoperative AKI.

Results: Our search yielded 19 articles. IOH risk thresholds ranged from <50 to <75 mmHg for mean arterial pressure (MAP) and from <70 to <100 mmHg for systolic blood pressure (SBP). MAP below 65 mmHg for over 5 min was the most cited threshold (N = 13) consistently associated with increased postoperative AKI. Greater magnitude and duration of MAP and SBP below the thresholds were generally associated with a dose-dependent increase in postoperative AKI incidence.

Conclusions: While a consistent definition for IOH remains elusive, the evidence suggests that MAP below 65 mmHg for over 5 min is strongly associated with postoperative AKI, with the risk increasing with the magnitude and duration of IOH.

1. Introduction

Intraoperative hypotension (IOH) is as a frequent complication of a wide variety of surgical procedures.[1,2] Among 130 studies examined in one systematic review,[3] there were 140 varying definitions of intraoperative hypotension. Interpretations have veered between fixed thresholds predicated on systolic or mean arterial blood pressure values and decreases relative to an individual's baseline measurements.[1,3] Definitions often encompass specific interventions implemented by anesthesiologists such as administering fluids or a vasopressor, further convoluting matters. This definitional ambiguity has led to marked fluctuations in reported IOH prevalence rates in multicenter and single institutional studies and resultant IOH-associated morbidity and mortality.[4–6]

IOH needs to be clearly defined due to its significant association with unfavorable postoperative consequences including prolonged hospital stays, myocardial injury, acute kidney injury, and the necessity for mechanical ventilation, all of which are known causes of preventable morbidity, mortality, and associated costs of care to both patients and hospital systems.[2,7] Among the well-documented complications of IOH, Acute Kidney Injury (AKI) stands out as a significant concern.[8,9] AKI is frequently overlooked and inadequately treated, leading to short- and long-term kidney disease, cardiovascular issues, and higher mortality rates.[10–16] Research has proposed that better control of IOH among non-cardiac surgery patients could lead to an annual cost reduction of $1.6 million per year in hospitals with an annual volume of 10,000 patients, attributable to decreased incidence in postoperative AKI.[7] A single

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episode of postoperative AKI imposes an average hospital cost increase of $9000 even after adjusting for other complications.[11,17]

Unfortunately, following established clinical guidelines for AKI prevention has remained challenging due to a lack of clear definitions for risk factors such as IOH.[18,19] The underlying pathophysiology of postoperative AKI is often intertwined with patients' preexisting health conditions, the specific surgical procedure undertaken, and the management of intraoperative events, particularly as it pertains to IOH.[15,18,20–22] Surgeons are trained to recognize many surgery-specific intraoperative risk factors such as organ ischemia, infected or necrotic tissue, and hemorrhagic potential which may precipitate IOH. By collaborating with the anesthesia team, surgeons can actively identify patients at risk for substantial IOH and seek to minimize the patient's subsequent exposure to low blood pressures or other modifiable risk factors (e.g., nephrotoxic medications).[19] Nonetheless, no consensus exists regarding the safe boundaries of severity and duration of an intraoperative hypotensive episode which may lead to postoperative AKI.[20] Studies examining the association between intraoperative hemodynamic management and postoperative AKI lack unifying criteria for diagnosis and management of both hypotension and AKI. While recent studies[23–27] have reported decreased incidence of postoperative AKI when using intraoperative goal-directed hemodynamic therapy, most do not report the differences in magnitude or duration of the hypotensive episode that must be avoided to achieve clinical benefit.

To our knowledge there have been no studies that have viewed the significance of association between IOH and postoperative AKI with attention to surgery type, particularly as it pertains to cardiac versus non-cardiac surgeries. This is a critical distinction as cardiac surgeries often maintain intraoperative blood pressure by extracorporeal membrane oxygenation which places very different demands on the kidneys compared to other surgeries. Thus, it is crucial to stratify risk factors for AKI by surgery type. The aim of this systematic review is to critically evaluate existing literature regarding associations between intraoperative hypotension and postoperative AKI and delineate the vital sign parameters that represent safe intraoperative blood pressure whilst also accounting for the type of surgery.

2. Materials and METHODS

This systematic review was performed in accordance with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,[28] whose checklist is shown in Supplement A. The review was registered in Open Science Framework (https://osf.io/8k3j9).

2.1. Search Strategy

A comprehensive search was performed for all full-text research articles published in English in PubMed, Cochrane Central, and Web of Science between January 1, 2015 and December 17, 2022. The search terms had four central components: AKI, hypotension, perioperative, and prediction/treatment/monitoring. The first component, AKI, contained AKI-associated terms and subject headings with words including, but not limited to, “Acute Kidney Injury”, “Acute Kidney Failure”, “Acute Renal Failure”, and “Acute Kidney Insufficiency”. The second component, hypotension, contained hypotension-associated terms and subject headings with words including “hypotension” or “low blood pressure”. The third component, perioperative, contained perioperative-associated terms and subject headings with words including, but not limited to, “intraoperative”, “perioperative”, “operative”, and “surgical”. The last component, prediction/treatment/monitoring, was comprised of terms and subject headings with words including, but not limited to, “treatment”, “management”, “monitoring”, “forecasting”, and “prediction”. Where possible, these terms were expanded using the Medical Subject Headings ([“Mesh]”) controlled vocabulary. A full list of the search terms for each database is available in Supplement B.

2.2. Article selection

Five investigators (YP, AB, YL, RH, and MR) reviewed the selected studies during the title and abstract screening. Six investigators (YP, AB, YL, RH, AD, JC) reviewed full-text studies during the second stage of our selection process. This included review of the inclusion and exclusion criteria (see below) as well as article quality criteria including ethical standards, methodology strengths, weaknesses, and generalizability. Finally, two investigators (YP, AB) conducted the study extraction process. Title/abstract screening, full-text review, and final extraction were based on the consensus opinion of two independent reviewers. Conflicts were resolved by a third reviewer. Article management and calculations of Inter-rater reliability and Cohen's kappa were performed using Covidence systematic review software (Covidence, Melbourne, AUS).

Inclusion criteria: Titles and abstracts were screened to include research assessing the incidence of postoperative AKI following intraoperative hypotension. We looked for studies with explicitly defined hypotension and kidney injury characteristics, such as the ones listed in Table 1 below.

Exclusion criteria: We excluded studies which did not have clearly defined hypotension or acute kidney injury parameters. We additionally excluded any review articles and case studies or case series articles reporting on management of acute trauma or outcomes in fewer than 10 patients. Incomplete projects or proposals were also excluded.

3. RESULTS

3.1. Article characteristics

The flow diagram detailing our article selection process is shown in Fig. 1. A total of 327 records were identified using the search terms defined above across the PubMed, Cochrane, and Web of Science databases. After removing 72 duplicates, we reviewed 255 articles for title and abstract relevance, of which we excluded a further 199 publications as irrelevant. Cohen's kappa at this step ranged from 0.35 to 0.60 between different pairs of reviewers. Of the remaining 53 articles, 12 were excluded due to wrong outcomes (e.g., no definitions for intraoperative hypotension or postoperative AKI); 9 due to no results available (e.g., proposals, ongoing clinical trials, or partial publications); 7 due to wrong study design (e.g., review articles or case studies with <10 patients); 4 due to wrong setting/population (e.g., pediatric patients or cases of acute

Table 1
IOH and Postoperative AKI inclusion criteria.

Measure	Definition	Timeline
Intraoperative Hypotension		
Absolute	mmHg reduction in intraoperative MAP or SBP	Cumulative (i.e., for the duration of the operative procedure) vs. Episodic (i.e., individual BP measurements or a pre-defined intervals during the surgery
Relative	Percent reduction in intraoperative MAP or SBP relative to baseline immediately prior to anesthesia induction	
Postoperative AKI		
RIFLE[29]	Increase in serum creatinine (SCr) ≥1.5 times baseline, or urine output of <0.5 mL/kg/h	≥6h
KDIGO[19]	Increase in SCr of ≥0.3 mg/dL within 48h or ≥50% within 7 days, or Urine output of <0.5 mL/kg/h	>6h
AKIN[30]	Increase in SCr of ≥0.3 mg/dL or ≥50% within 48h, or urine output of <0.5 mL/kg/h	>6h
Other		

AKIN = Acute Kidney Injury Network; KDIGO = Kidney Disease: Improving Global Outcomes; MAP = Mean Arterial Pressure; RIFLE = Risk of Renal Dysfunction, Injury to kidney, Failure or Loss of kidney function, and End-stage kidney disease; SBP = Systolic Blood Pressure; SCr = Serum Creatinine.

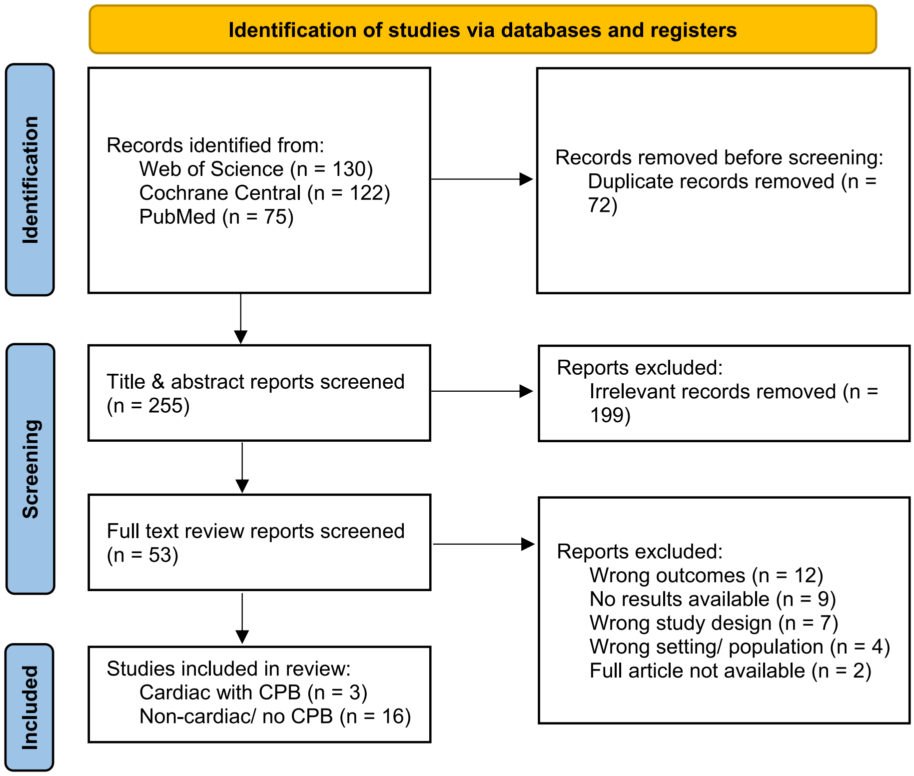

Fig. 1. PRISMA 2020 flow diagram detailing study selection and reasons for study exclusion for all articles considered for this systemic review. CPB = Cardio-Pulmonary Bypass.

trauma), and 2 due to the full article being unavailable. Cohen's kappa at the full text review stage ranged from 0.71 to 1.00 between different pairs of reviewers.

Study characteristics of the remaining 19 articles included in our final analysis are detailed in Table 2. The frequency of surgical specialties among the studies is shown in Fig. 2. The most cited surgery types were General[31–34] and Hepatobiliary[35–38] surgery, with 4 (21%) articles each. An additional 4 articles reported on Cardiac surgery, of which 3 (16%)[39–41] reported on procedures with and 1 (5%)[42] without cardio-pulmonary bypass (CPB). Gastrointestinal[43–45] and Urologic[46–48] surgeries were the next most common, with 3 (16%) articles each. Finally, one (5%)[49] article reported on Gynecologic surgery outcomes and complications.

Fifteen (79%) of the included articles were based on predominantly male patient populations, with Kim et al., 2021; Huepenbecker et al., 2021, Shaw et al., 2022, and Wickham et al., 2022 being the only exceptions. All articles reported on adult patients, with average participant ages ranging from 53.49[38] to 81.30[44] years old. Only 3 articles reported patient ethnicity, among which all 3 were based on predominantly white participants, representing between 69% and 83% of the patient population.[31,47,49]

All studies except three investigations focused on General Surgery presented data from single-center investigations only.[31–33] Guo et al., 2020 and Wickham et al., 2022 (General Surgery) are the only prospective studies in the cohort, with the rest focusing on retrospective analyses. Similarly, Guo et al., 2020 is the only investigation which excluded patients with baseline high grade hypertension.

3.2. IOH definitions

To measure IOH, 11 (58%) studies used invasive (e.g., arterial line, Swan-Ganz catheter) and 4 (21%) used noninvasive (e.g., automated BP cuff, doppler ultrasound) hemodynamic monitoring techniques, with 3 (16%) making use of both. Of note, 4 (21%) studies did not specify their intraoperative hemodynamic monitoring methodology. Twelve (63%) studies considered IOH over the cumulative time the patient spent under their predefined BP criteria, while 4 (21%) counted individual episodes of hypotension during the procedure, with 3 (16%) of studies considering both.

Among all studies, 16 (84%) defined IOH using MAP, of which 15 (94%) measured absolute and 2 (13%) relative drops in MAP. Among the studies looking at absolute MAP reduction, MAP thresholds for defining IOH ranged from 50 to 75 mmHg, with 65 mmHg being the most used in 13 (87%) of studies (Fig. 3a). Among the studies looking at relative MAP drops, thresholds ranged from 20% to 40% reductions from baseline MAP, with 20% being used in both (100%) studies (Fig. 3b). Of the 10 studies reporting time requirements for IOH definition based on MAP, duration thresholds ranged from 1 to 20 min, with 5 and 10 min being the most used in 4 (40%) of studies each (Fig. 3c).

A further 4 (26%) studies defined IOH using SBP, of which 3 (75%) measured absolute and all 4 (100%) measured relative drops in SBP. Among the studies investigating absolute SBP reduction, SBP thresholds ranged from 70 to 100 mmHg, with 90 mmHg being the most used in 2 (67%) of studies (Fig. 3d). Among the studies looking at relative SBP drops, thresholds ranged from 15% to 35%, with all 4 (100%) of studies using 20% (Fig. 3e). SBP duration thresholds ranged from 1 to 50 min across all 4 studies, with 5 min being the most used in 3 (75%) of the articles (Fig. 3f).

3.3. AKI definitions

The frequencies of postoperative AKI criteria used in the identified articles are represented in Fig. 4. AKI was most commonly defined via Kidney Disease: Improving Global Outcomes (KDIGO)[31–34,36,38–41,43–47] Among the other articles, Liao et al., 2020 and Loffel et al., 2020 used AKIN and Huepenbecker et al., 2021 used RIFLE criteria. Two articles used other, surgery-specific criteria, with Marschall et al., 2020 defining AKI as a rise in SCr of $\geq$ 25% or $\geq$ 0.5 mg/dL within 48 h after cardiac

Table 2
Article characteristics.

Study ID	Study Type	Study Setting	Surgery Type	Cohort Size (N)	Outcome Measure	AKI Definition	IOH Definition	Odds Ratio (CI, p-value)[a]
Chen 2022	Retrospective observational	Single center	Cardiac with CPB	5127	AKI incidence within 7 days post-op	KDIGO	Absolute MAP threshold per minute	<55 mmHg: 1.05 (99% CI 1.02–1.09; p < 0.001) <65 mmHg: 1.02 (99% CI 1.01–1.04; p < 0.001) <75 mmHg: 1.02 (99% CI 1.01–1.02; p < 0.001)
Ju 2022	Retrospective observational	Single center	Cardiac with CPB	394	AKI incidence within 7 days post-op	KDIGO	Absolute MAP threshold over 10 min	<50 mmHg: 1.118 (95% CI 1.009–1.237) <55 mmHg: 1.064 (95% CI 1.006–1.125) <60 mmHg: 1.046 (95% CI 1.005–1.088) <65 mmHg: 1.037 (95% CI 1.007–1.067)
Ngu 2020	Retrospective observational	Single center	Cardiac with CPB	6523	Decision to initiate renal replacement therapy within primary admission period	KDIGO	Absolute MAP threshold over 10 min	<55 mmHg: 1.09 (95% CI 1.02–1.16, p = 0.007) <65 mmHg: 1.13 (95% CI 1.06–1.20, p = 0.0001)
Marschall 2020	Retrospective observational	Single center	Cardiac without CPB	60	Incidence of postoperative AKI within primary admission period	Other	Relative SBP threshold over 15 min	≥20% drop: 1.72 (p = 0.003)
Shaw 2022	Retrospective observational	Multi-center	General	112,912	AKI incidence within 7 days post-op	KDIGO	Absolute MAP threshold over 10 min	<55 mm Hg: HR 1.1 (95% CI 1.38–1.22; p < 0.004)
Wickham 2022	Prospective observational	Multi-center	General	4750	AKI incidence within 7 days post-op	KDIGO	Absolute MAP or SBP threshold over 5 min	<65 mmHg: **1.05** (0.77–1.46, p = 0.73)
Mathis 2020	Retrospective observational	Multi-center	General	138,021	AKI incidence within 7 days post-op	KDIGO	Absolute or relative MAP threshold over 10 min	Medium risk patients: <50 mmHg: 1.77 (95% CI 1.20–2.61, p = 0.004) High risk patients: <55 mmHg: 1.38 (95% CI 1.08–1.76) <60 mmHg: 1.22 (95% CI 1.04–1.43) <65 mmHg: 1.18 (95% CI 1.03–1.36)
Kobayashi 2021	Retrospective observational + Prospective experimental	Single center	General	6296	AKI incidence within 7 days post-op	KDIGO	Absolute or relative SBP threshold over 1, 5, and 20 min	Absolute: <70 for ≥ 20 min OR 1.60 (95% CI 1.06–2.38) <75 for ≥ 20 min OR 1.41 (95% CI 1.00–2.00) Relative: >35% for ≥ 20 min OR 1.49 (95% CI 1.07–2.09) >30% for ≥ 20 min OR 1.58 (95% CI 1.03–2.52)
Guo 2020	Prospective Experimental	Single center	Gastro-Intestinal	162	AKI incidence within 7 days post-op	KDIGO	Relative MAP threshold by number of episodes or duration	≥3 episodes of >20% drop: 1.28 (95% CI 1.04–1.57, p = 0.02) Duration of >20% drop: 1.03 (95% CI0.99-1.07, p = 0.145)
Shen 2022	Retrospective observational	Single center	Gastro-Intestinal	573	AKI incidence within 7 days post-op	KDIGO	Absolute MAP threshold over 5 min	≤65 mmHg: 3.51 (95% CI 1.55–7.93, p = 0.03)
Kim 2021	Retrospective observational	Single center	Gastro-Intestinal	3834	AKI incidence within 2 days post-op	KDIGO	Absolute MAP threshold over 20 min	Intraoperative hypotension was NOT found to be associated with AKI
Huepenbecker 2021	Retrospective observational	Single center	Gynecologic	1334	AKI incidence within 30 days post-op	RIFLE	Absolute MAP threshold over 1 and 5 min	<65 mmHg for >1 min (p < 0.001) and >5 min (p < 0.001)
Liao 2020	Retrospective observational	Single center	Hepatobiliary	796	AKI incidence within 7 days post-op	AKIN	Absolute MAP threshold over 10 min	<65 mmHg: 2.565 (p = 0.009)
Joosten 2021	Retrospective observational	Single center	Hepatobiliary	242	AKI incidence within 7 days post-op	KDIGO	Absolute MAP threshold over quartiles of	<65 mmHg: 1st quartile: 1.05 (95% CI 1.02–1.09, p < 0.001) 2-3rd quartiles: 9.7 (95%

(*continued on next page*)

Table 2 (*continued*)

Study ID	Study Type	Study Setting	Surgery Type	Cohort Size (N)	Outcome Measure	AKI Definition	IOH Definition	Odds Ratio (CI, p-value)[a]
							duration under threshold	CI 4.1–22.7, p < 0.0001) 4th quartile: 34.6 (95% CI 11.5–108.6, p < 0.0001)
Bredt 2022	Retrospective observational	Single center	Hepatobiliary	145	AKI incidence within 7 days post-op	Other	Absolute MAP threshold over 5 min or any time	<65 mmHg for ≥ 5 min or any exposure to < 55 mmHg: 1.935 (p < 0.001)
Xin 2021	Retrospective and prospective observational	Single center	Hepatobiliary	272	AKI incidence within 30 days post-op	KDIGO	Absolute and relative SBP threshold over 5 min	<90 mmHg or >20% decrease: 1.09 (95% CI 1.016–1.169, p = 0.016) per minute
Hua 2021	Retrospective observational	Single center	Urologic	143	AKI incidence within 7 days post-op	KDIGO	Absolute MAP threshold over 20 min	<65 mmHg: 1.30 (95% CI 1.04–1.64; p = 0.024)
Mano 2022	Retrospective observational	Single center	Urologic	3240	AKI incidence within 7 days post-op	KDIGO	Absolute MAP threshold over 5 min	<55 mmHg: **1.14** (95% CI 0.98–1.32, p = 0.085)
Loffel 2020	Retrospective observational	Single center	Urologic	416	Incidence of postoperative AKI within primary admission period	AKIN	Absolute MAP threshold per minute	<60 mmHg: 1.012 (95% CI 1.001–1.023, p = 0.02) <65 mmHg: 1.01 (95% CI 1.005–1.015, p < 0.001)

AKI = Acute Kidney Injury; AKIN = Acute Kidney Injury Network; KDIGO = Kidney Disease: Improving Global Outcomes; MAP = Mean Arterial Pressure; RIFLE = Risk of Renal Dysfunction, Injury to kidney, Failure or Loss of kidney function, and End-stage kidney disease; SBP = Systolic Blood Pressure.

[a] only significant results reported unless study had no significant results in which case all results were reported.

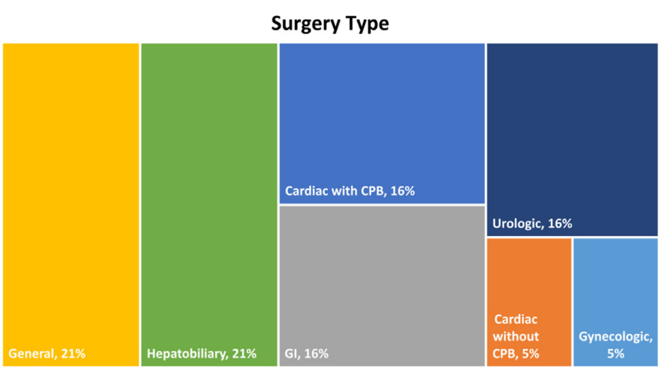

Fig. 2. Frequency of surgical specialties among all articles.

resynchronization therapy (non-CPB), and Bredt et al., 2022 as a rise in SCr of >50% from baseline or by > 26.4 mmol/L (>0.3 mg/dL in <48 h) after liver transplantation surgery. Among the 15 studies reporting explicit thresholds for defining postoperative AKI timing, the most used timeframe was through the 7th postoperative day, used in 8 (53%) of studies.[31,36,37,39,41,43,46,47] A further 3(20%)[32,35,44] of studies measured AKI through the 2nd postoperative day, 2(13%) [38,49]through the end of the first postoperative month, and 2(13%)[40,48] through the end of the hospitalization period.

3.4. Association of IOH and postoperative AKI

Statistically significant associations of IOH and postoperative AKI are reported in Table 2. Twelve (80%)[31,33,35–37,39–41,44,46,48,49] of the fifteen studies which analyzed reductions in absolute intraoperative MAP reported statistically significant associations with postoperative AKI. Among the 9 studies[31,33,35–37,44,46,48,49] reporting on surgeries without CPB use, odds ratios (ORs) for developing postoperative AKI after IOH with MAP <65 were estimated to range from 1.01[48] to 3.51[44] (or 9.7 for patients in the highest quartile for IOH duration according to Joosten et al., 2021), <60 from 1.01[48] to 1.22[33], <55 from 1.10[31] to 1.38[33], and

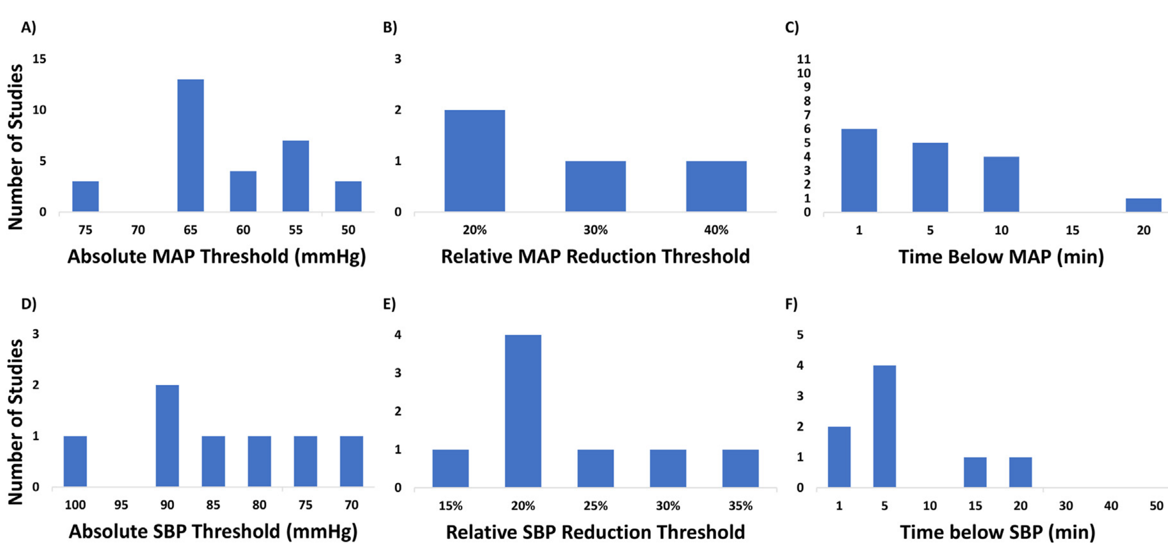

Fig. 3. Number of studies defining IOH by A) absolute MAP threshold, B) relative MAP threshold, C) duration below MAP threshold, D) absolute SBP threshold, E) relative SBP threshold, and E) duration below SBP threshold.

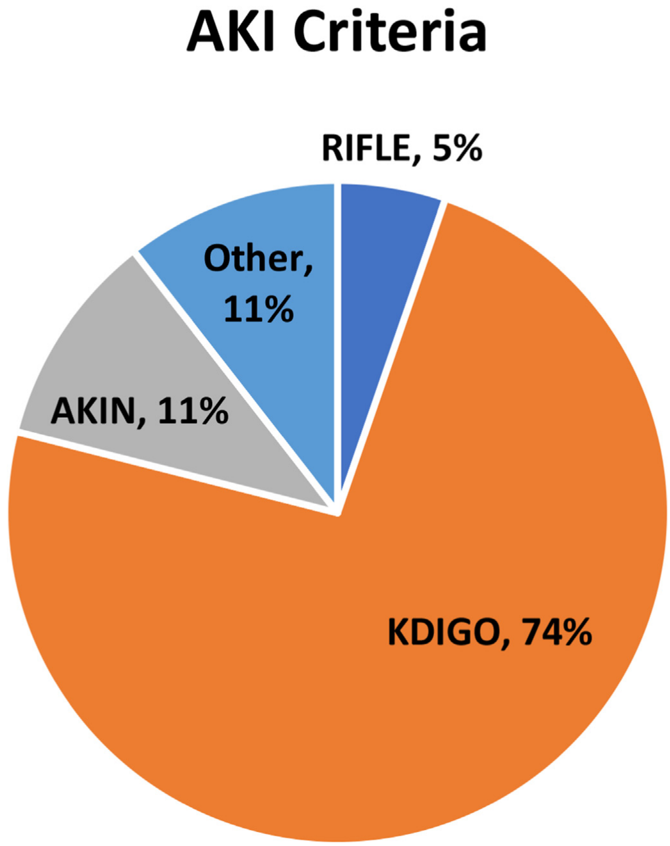

Fig. 4. Frequency of postoperative AKI criteria among all articles included in the review.

<50 at 1.77[33]. These trends were consistent with those for cardiac surgeries with CPB use, where statistically significant ORs for developing AKI after MAP <75 mmHg were estimated at 1.02[39], <65 between 1.02[39] and 1.13[40], <60 at 1.05[41], <55 from 1.05[39] to 1.09[40], and <50 at 1.12.[41] Notably, of the 3 studies using absolute MAP which failed to reject the null hypothesis, Wickham et al., 2022 and Mano et al., 2022 still reported increased, but nonsignificant association with OR of 1.05 ($p = 0.73$) and 1.14 ($p = 0.085$), respectively, while Kim et al., 2021 noted that their results might differ from the rest of the literature owing to not calculating time below absolute MAP threshold using time-weighted averages. Finally, both studies which analyzed reductions in relative intraoperative MAP demonstrated statistically significant associations with postoperative AKI, with Guo et al., 2020 reporting OR = 1.28 for ≥ 3 episodes of >20% intraoperative MAP reduction, and Mathis et al., 2020 reporting OR of 1.24 and up to 1.48 for patients with high and low preoperative risk experiencing >10 min of >40% intraoperative MAP reduction.

Of the 4 studies which measured postoperative AKI against intraoperative reductions in SBP, Kobayashi and Yamaoka 202134 reported increased ORs of 1.08, 1.16, and 1.12 for absolute SBP below 80, 75, and 70 mmHg, respectively, while Xin et al., 2021 reported a significantly increased OR of 1.09 per minute of SBP <90 mmHg or >20% decrease from baseline at 1.09. Kobayashi et al., 2021 provided further evidence for the association with relative SBP decrease with statistically significant ORs of 1.29, 1.25, 1.58, and 1.49 for SBP reductions of >20%, >25%, >30%, and >35%, respectively, while Marschall et al., 2022 demonstrated OR of 1.72 for >20% SBP reduction. Finally, while Wickham et al., 2022 failed to reject the null hypothesis, the study still reported increased, but nonsignificant OR of 1.11 ($p = 0.07$) for >20% reduction in SBP.

4. Discussion

This systematic review aimed to provide an overview of the most recent research on the association of intraoperative hypotension and postoperative acute kidney injury. We used stringent selection criteria to identify and analyze a total of 19 well-designed original research articles on the topic. The findings serve to characterize the most common surgical fields reporting on postoperative AKI, the methodologies and definitions they use for measuring and reducing intraoperative hypotension and subsequent kidney injury, and areas for improvement.

Findings from this review are important because prior research on the association of IOH and postoperative AKI has been based on largely inconsistent definitions, precluding the identification of specific BP thresholds for prevention and/or treatment. The predictive value of intraoperative hypotension for postoperative outcomes is significantly influenced by how hypotension is described or modeled.[5] In current literature examining the associations between intraoperative hypotension and postoperative AKI, definitions for both hypotension and AKI are highly variable, which limits generalizability and interpretability across study populations and institutions.

4.1. Article characteristics

Our research identified a paucity of studies on the association of IOH and postoperative AKI in some surgical fields. While the identified articles encompassed a variety of General, Hepatobiliary, Cardiac, Gastrointestinal, Urologic, and Gynecologic surgeries, a notable lack of fields such as General Thoracic and Vascular Surgery, Orthopedics, Neurosurgery, Plastic and Reconstructive Surgery, and Otolaryngology was observed. Omissions in the latter fields suggest a possible role for further analysis and perioperative risk stratification based on blood pressure measurement to improve postoperative renal outcomes.

We additionally identified a lack of prospective research trials in the field, with only 2 recent articles on General Surgery[32,43] of the 19 total articles included in the review reporting on experimental results. While observational studies have a role in informing specific clinical guidelines using already available data, to improve clinical practice in a way that is definitive and generalizable, investigators must also establish the causality of the relationship between IOH and postoperative AKI. We therefore recommend that future research should focus on prospective experimental designs to definitively improve perioperative risk reduction strategies.

Finally, we also noted an overall underrepresentation of female and of non-white research participants. To improve the generalizability of their findings and subsequent clinical recommendations, we recommend that future research efforts stratify and enrich their participant populations based on patient demographics which are more representative of the general surgical patient population.

4.2. IOH and AKI definitions

Across all studies included in this review, IOH was most commonly defined in absolute terms by a MAP <65 mmHg for an episode of >5 min. AKI was most commonly defined by KDIGO criteria as an increase in SCr of ≥0.3 mg/dL within 48h or ≥50% within 7 days, or Urine output of <0.5 mL/kg/h for >6h within the first postoperative week. While our research included examples of alternative definitions of IOH (e.g., <90 mmHg SBP or >20% reduction in MAP or SBP) and AKI (e.g., RIFLE and AKIN criteria), we recommend that future investigators use the above criteria as standard due to their ubiquity to allow for direct comparability of outcomes.

4.3. Association of IOH and postoperative AKI

IOH was associated with up to a 10-fold[36] increase in risk for postoperative AKI compared with patients who did not experience intraoperative hypotension. Mathis et al., 2022 furthermore demonstrated that the increase in AKI risk was generally proportional to the magnitude and duration of blood pressure below the predefined thresholds, with statistically significant ORs steadily increasing from 1.22 for <60 mmHg MAP to 1.38 for <55 mmHg, and 1.77 for <50 mmHg for general surgeries without CPB use. These trends were generally reaffirmed by studies using alternative IOH and/or AKI criteria, suggesting that both MAP- or SBP-based definitions of intraoperative hypotension can consistently estimate AKI risk. Notably, of the 4 studies which failed to confirm the association, 3 lacked statistical significance but still reported increased odds ratios, suggesting that the association of IOH and AKI was almost universally positive.

While the proportionality of the association between IOH and postoperative AKI was lost for cardiac surgeries with CPB use, all 3 studies[39–41] reporting on such surgeries confirmed the overall increased odds of postoperative AKI following episodes of IOH. This implies that IOH may be a critical determinant of postoperative AKI irrespective of surgical context, while the magnitude and duration of blood pressure below the predefined thresholds may be procedure- or patient-specific. While it is known to impact postoperative complications, the temperature at which cardiopulmonary bypass was run was not specifically mentioned in any of the other studies which reported use of the technology. Ngu et al., 2022 and Chen et al., 2022 reported that anemia was independently associated with AKI risk in the setting of intraoperative hypotension, suggesting that renal oxygen delivery may contribute to risk for AKI. Oxygen delivery during cardiopulmonary bypass is determined by many factors including pump flow, hemoglobin concentration, oxygen saturation, and arterial oxygen tension, and MAP is often maintained at a lower level than would be typical for non-cardiac surgery. Underlying endothelial dysfunction is additionally common among cardiac surgery patients and likely contributes to postoperative renal dysfunction. The complex interplay of these variables may reasonably explain the lost proportionality of the IOH-AKI association in the CPB studies included in our analysis.

In noncardiac surgery, the weight of evidence suggests that minimizing duration of MAP below 65 mmHg can significantly reduce the incidence of postoperative AKI. Although Wickham et al., 2022 showed that noncardiac surgery patients may be able to tolerate some duration of MAP below 65 mmHg without a significantly increased AKI risk, Loffel et al., 2020 demonstrated that each minute spent under that threshold was associated with an increased OR of 1.01 (1.005–1.015, $p < 0.001$). Similarly, while Chen et al., 2022 demonstrated that cardiac surgery patients on CPB may be able to tolerate individual episodes of MAP dips below 65 mmHg without increased AKI risk, Ju et al., 2022 and Ngu et al., 2022 demonstrated a significant association of IOH <65 mmHg with AKI with episodes lasting beyond 10 min.

Importantly, these conclusions are consistent with grey literature data. While such sources were not included in the stringent criteria of our systematic review of evidence-based literature, academic theses and dissertations provide a useful context for our findings that is free of publication bias. A survey of the top 20 closest-matching grey literature results using the same search criteria in ProQuest's Dissertations & Theses Global database[50] yields four relevant articles, all of which support the conclusion for significant association of intraoperative MAP below 65 mmHg and postoperative AKI.[51–54] This conclusion is likewise consistent with a consensus statement that reported intraoperative MAP below 60–70 mmHg being associated with AKI.[55] Importantly, this statement does not suggest that shorter durations of MAP below this threshold are free of risk across all populations. In noncardiac surgery, any duration of MAP below 55 mmHg should be avoided entirely,[31,33] a conclusion which is furthermore supported by randomized controlled trials evaluating the efficacy of goal-directed hemodynamic therapy in reducing postoperative organ dysfunction.[25,27]

Finally, it is important to acknowledge that postoperative AKI may be influenced by a variety of factors in addition to IOH. Our analysis demonstrated an abundance of risk factors including patient age, sex, and demographics, which should be taken into consideration when developing a patient's postoperative care plan. In terms of minimizing modifiable risk factors, goal-directed therapy aimed at reducing postoperative AKI should focus on minimizing IOH but also the extent of baseline hypertension, diabetes, alcohol and tobacco intake, among others, and unnecessary perioperative fluid or vasopressor administration which have been documented to make patients more susceptible to post-induction refractory hypotension.[56,57] As perioperative risk prediction models expand in their generalizability and use of intraoperative physiological data, understanding and defining significant prognostic parameters of intraoperative hypotension is critical to accurately represent risk and alert clinicians accordingly.

4.4. Limitations

While this systematic review provides valuable insights into the most recent literature on the association between intraoperative hypotension and postoperative acute kidney injury, it is not without limitations. Chiefly, our review was limited by strict inclusion and exclusion criteria which allowed for better comparability of results but narrowed our review to just 19 original research articles. Among these, most studies reported on single-center investigations with additional heterogeneity owing to the variety of surgical fields represented which may overall limit the validity of direct comparisons between the studies. Moreover, comparing results across studies that use absolute and relative MAP and SBP outcomes as a measure of intraoperative hypotension is challenging since it is ultimately unclear what component of blood pressure is the major contributor to risk of postoperative AKI. Finally, all but one study included in our review retained patients with hypertension in their analyses.[43] Future research should consider using standardized IOH and AKI definitions as suggested above, and stratifying patients based on prior hypertension status to allow for better result interpretability and elimination of possible confounding effects.

5. CONCLUSION

MAP below 65 mmHg for longer than 5 min is the most common definition of intraoperative hypotension associated with postoperative acute kidney injury. While patients may be able to tolerate individual short episodes of IOH with MAP below this threshold, greater magnitude and duration of blood pressure decreases were associated with dose-dependent increases in postoperative AKI incidence and other complications among noncardiac surgery patients. These trends were generally reaffirmed by studies using alternative MAP and/or SBP criteria for IOH. While the dose-dependency was lost in cardiac surgery patients on CPB, the association of IOH and AKI was preserved for MAP below 65 mmHg longer than 10 min. Further research needs to stratify patients according to actionable perioperative characteristics to develop patient- and procedure-specific risk modeling encompassing IOH and additional risk factors to improve postoperative renal outcomes.

CRediT authorship contribution statement

Yordan Penev: Data curation, Investigation, Writing – original draft, Writing – review & editing. **Matthew M. Ruppert:** Data curation, Investigation, Writing – original draft. **Ahmet Bilgili:** Data curation, Investigation, Writing – original draft. **Youlei Li:** Data curation, Investigation, Writing – original draft. **Raiya Habib:** Data curation, Investigation, Writing – original draft. **Abdul-Vehab Dozic:** Data curation, Investigation, Writing – original draft. **Coulter Small:** Writing – original draft. **Esra Adiyeke:** Data curation, Formal analysis, Methodology. **Tezcan Ozrazgat-Baslanti:** Data curation, Formal analysis, Methodology. **Tyler J. Loftus:** Data curation, Formal analysis, Methodology, Supervision. **Chris Giordano:** Data curation, Formal analysis, Methodology, Supervision. **Azra Bihorac:** Data curation, Formal analysis, Methodology, Supervision.

Declaration of competing interest

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Appendix A. Supplementary data

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