European Review for Medical and Pharmacological Sciences 2021; 25: 7044-7050

A systematic review of risk factors for postinduction hypotension in surgical patients undergoing general anesthesia

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Abstract. – OBJECTIVE: Clinical evidence has proved that postinduction hypotension (PIH) is very prevalent in surgical patients undergoing general anesthesia, and commonly develops within 20 min after the induction of general anesthesia. However, the risk factors for PIH are not clear till now, therefore, a systematic review of current evidence was conducted.

MATERIALS AND METHODS: PubMed, Embase, Cochrane library, and Web of Science were searched for articles published in English up to June 2021. The following search items were used: postinduction, postintubation, propofol induction, anesthesia induction, general anesthesia induction, hypotension, risk factor, general anesthesia, surgery. The articles were screened using the inclusion and exclusion criteria, and the data from included studies were extracted and analyzed.

RESULTS: Twelve studies were included. Seven studies reported the association between age and PIH, and six showed age was a risk factor. Five or three studies reported the association between mean arterial pressure (MAP) and PIH or between systolic blood pressure (SBP) and PIH, but the results were conflicting. Results from two studies regarding gender and PIH were conflicting. Two studies reported that weight was negatively correlated with PIH. Low baseline blood volume, emergency operation, long-term intake of the angiotensin converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) were risk factors for PIH. One study showed that ASA III-V, propofol induction, and increasing fentanyl dosage were risk factors for PIH.

CONCLUSIONS: Aging, ASA III-V, emergency operation, low baseline blood volume, long-term intake of ACEI/ARB, propofol induction, and increasing fentanyl dosage are potential risk factors for PIH, while body weight gain is a protective factor. Based on the current evidence, it is difficult to determine whether baseline blood pressure or gender is associated with the development of PIH.

Key Words:
Risk factors, Postinduction hypotension, General anesthesia, Surgical patients.

Introduction

Intraoperative hypotension is an inadvertent event during surgery and anesthesia. It can cause adverse outcomes including myocardial or renal ischemia, and lead to increasing postoperative morbidity and mortality[1-3]. Intraoperative hypotension is very prevalent from the induction of general anesthesia to the incision of surgery, which is called postinduction hypotension (PIH). PIH commonly occurs within 20 min after the induction of general anesthesia, which results from the inhibition of heart function and vasodilatation by general anesthetic agents. During this period, the surgical stimulus is absent, the anesthesiologists are often distracted by adjusting the ventilator, recording anesthesia events, and placing the patients[4], so that PIH can be easily neglected, and the management can be delayed, which might result in adverse outcomes.

An early study showed that age ≥ 50 years, ASA III-V, baseline mean arterial pressure (MAP) < 70 mmHg, administration of propofol, and high dosage of fentanyl for the induction were associated with the development of PIH[5]. For the past decade, it has been largely investigated the risk factors for PIH and, despite the existing variations of population, patients age, ASA classification, comorbidities, medications, general anesthetic agents, and sample sizes in different studies, no comprehensive systematic review of the associated risk factors for PIH has been published till now. This study will further provide instructions for the reduction and prevention of PIH. Thus, we conduct-

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ed a systematic review to quantify the associations between the potential risk factors and PIH.

Materials and Methods

The systematic review was registered with INPLASY (identification number INPLASY202150098) and followed the 2009 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidelines[6].

Literature Search

A systematic literature search was performed up to June 2021 in the PubMed, Embase, Cochrane library, and Web of Science. The key items included postinduction, postintubation, propofol induction, anesthesia induction, general anesthesia induction, hypotension, risk factor, general anesthesia and surgery. The reference lists of the included studies were checked for potentially eligible articles. The citations were restricted to clinical studies and published in English. The participants were adult patients undergoing surgeries under general anesthesia.

Inclusion and Exclusion criteria

The inclusion criteria were: 1) studies examining the association between the risk factors (exposures) and PIH (outcome) under general anesthesia in the operating theater, 2) studies published in peer-review English journals, 3) data on risk factors from multivariate logistic regression analysis and enough data available to do the analyses [i.e., pre-calculated odds ratio (OR)]. The exclusion criteria were: 1) reviews, meta-analysis, abstracts or conference proceedings, overlapping datasets (i.e., analyses of the same patients or samples), 2) studies examining the association between risk factors and PIH under spinal anaesthesia, 3) studies with pediatric patients.

Outcome Measures and Data Extraction

The main outcomes of interest were the risk factors for PIH. The literature search, data selection, and extraction were conducted by at least two authors independently according to the predefined inclusion and exclusion criteria, any discrepancies resolved by consensus with a senior researcher. The extracted variables included the first author, publication year, country, study design, sample size, age of patients, risk factors for PIH, and PIH criteria. The measurement of association was the precalculated OR with 95% confidence interval (CI) (preferably unadjusted from multivariate logistic regression analysis), when necessary, OR was transformed from the provided coefficient B.

Data Analysis

The Newcastle-Ottawa Scale (NOS) was used to assess the quality of observational studies. The studies were scored 9 points at maximum on the related items including a selection of cohort or cases, comparability of groups, ascertainment of exposure and outcomes, and adequacy of follow-up, studies with a score of 7 or more were considered high quality. Information on the major outcomes of interest, including the risk factors of PIH, was recorded.

Results

Literature Search and Retrieval

Overall, 2734 articles were identified in the database search, 35 articles from other sources. 265 articles were duplicates, and then 2472 articles were excluded after an initial screening of titles and abstracts, then, 32 full texts were checked, and eventually 12 studies met the inclusion criteria and underwent data extraction. The screening procedure was presented in Figure 1.

Study Characteristics

All the included articles were observational studies and evaluated by NOS. These studies were conducted in 8 countries, published from 2005 to 2021, and the sample size ranged from 45 to 3904. Eight studies used MAP value (absolute value and/or drop percentage) and 4 studies used systolic blood pressure (SBP) value (absolute value or drop percentage) to define PIH. The characteristics and quality of the included articles were presented in Table I.

Outcomes and Findings

The outcomes and findings of the included studies were displayed in Table II, and 12 studies described the risk factors for PIH.

Seven studies reported the association between age and PIH, one study showed that age ≥50 years was associated with PIH, the others showed a positive correlation between age (increments in years) and PIH, except for one study that reported a negative correlation.

Five studies reported the association between baseline MAP and PIH, one study showed that baseline MAP < 70 mmHg was a significant risk

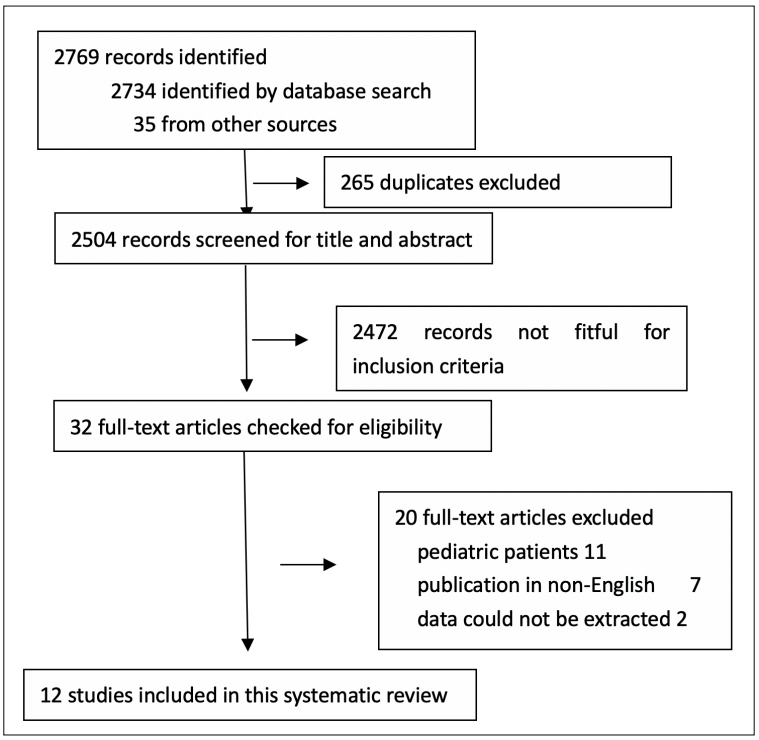

Figure 1. Flowchart of the screening procedure.

factor, 3 reported a positive correlation between baseline MAP (increments in mmHg) and PIH, while one reported a negative correlation. Three studies reported the association between baseline SBP and PIH, one study showed that baseline SBP more than 130 mmHg was significantly as-

Table I. Characteristics of the included studies.

First author	Year	Country	Design	Sample size	Age (year)	PIH criteria	NOS score
Reich et al[5]	2005	USA	Observational	3904	adult	MAP decrease > 40% and MAP < 70 mmHg, or MAP < 60 mmHg	8
Morley et al[7]	2010	UK	Observational	130	38±10	MAP decrease > 40% and MAP < 70 mmHg, or MAP < 60 mmHg	7
Zhang et al[8]	2016	USA	Observational	90	52±17	MAP decrease > 30%, or MAP < 60 mmHg	7
Südfeld et al[9]	2017	Germany	Observational	2037	60 (median)	SBP < 90 mmHg	8
Choi et al[10]	2020	Korea	Observational	77	55.9±14.3	MAP decrease > 30% or MAP < 65 mmHg	7
Jor et al[11]	2018	Czech	Observational	661	55 (median)	MAP decrease > 30%	7
Okamura et al[12]	2019	Japan	Observational	82	61 (median)	MAP decrease > 30% or MAP < 60 mmHg	7
Kaydu et al[13]	2018	Turkey	Observational	80	41.6±16.0	MAP decrease > 20%	7
Tarao et al[14]	2021	Japan	Observational	200	69.5±12.3	MAP < 50 mmHg	8
Morimoto et al[15]	2015	Japan	Observational	72	61.7±11.7	SBP < 80 mmHg	7
Juri et al[16]	2018	Japan	Observational	45	adult	SBP < 90 mmHg or < 80%	7
Lin et al[17]	2011	Taipei China	Observational	1017	46.5±16.8	SBP < 90 mmHg or SBP decrease > 30%	8

Table II. The risk factors for PIH.

Risk factors	OR (95% CI)	References
Age		
Age ≥ 50 yr	2.25 (1.75-2.89)	Reich et al[5]
Age (increment in year)	1.03 (1.02-1.04)	Südfeld et al[9]
	1.35 (1.16-1.58)	Choi et al[10]
	1.02 (1.01-1.04)	Jor et al[11]
	1.08 (1.02-1.15)	Okamura et al[12]
	0.94 (0.89-0.99)	Kaydu et al[13]
	1.03 (1.01-1.04)	Lin et al[17]
Baseline MAP		
< 70 mmHg	5.00 (2.78-9.02)	Reich et al[5]
MAP (increment in mmHg)	1.55 (1.42-1.68)	Morley et al[7]
	1.05 (1.01-1.11)	Zhang et al[8]
	0.91 (0.85-0.98)	Okamura et al[12]
	1.05 (1.00-1.09)	Kaydu et al[13]
Baseline SBP		
130-139 mmHg	2.67 (1.51-4.79)	Jor et al[11]
140-159 mmHg	2.13 (1.30-3.57)	Jor et al[11]
160-179 mmHg	4.09 (2.31-7.37)	Jor et al[11]
> 180 mmHg	6.24 (2.98-13.52)	Jor et al[11]
SBP (increment in mmHg)	0.97 (0.97-0.98)	Südfeld et al[9]
	1.08 (1.07-1.10)	Lin et al[17]
Gender		
Female	3.17 (1.89-9.88)	Tarao et al[14]
Male	1.44 (1.00-2.07)	Lin et al[17]
Weight		
Weight (increment in kg)	0.85 (0.79-0.91)	Morley et a[17]
	0.90 (0.82-0.98)	Juri et al[16]
ASA III-V	1.55 (1.22-1.99)	Reich et al[5]
Emergency surgery	1.75 (1.20-2.56)	Südfeld et al[9]
	2.35 (1.08-5.15)	Lin et al[17]
Baseline blood volume status		
SVV (%)	1.16 (1.00-1.34)	Juri et al[16]
IVC-CI	1.17 (1.09-1.26)	Zhang et al[8]
ACEI/ARB		
ACEI/ARB	29.3 (2.41-357.0)	Okamura et al[12]
ARB	3.61 (1.58-9.15)	Tarao et al[14]
General anesthetics		
Propofol induction	3.94 (2.42-6.43)	Reich et al[5]
Increasing fentanyl dosage	1.32 (1.13-1.56)	Reich et al[5]

sociated with PIH, while the results from the other two were conflicting regarding the association between SBP (increments in mmHg) and PIH.

Two studies described the association between sex and PIH, but the results were conflicting, male patient was a risk factor in one study, and female in the other.

Two studies reported that weight (increments in kg) was negatively associated with PIH. Only one study reported that ASA III-V was a significant risk factor for PIH. Two studies showed that emergency surgery was significantly associated with the development of PIH. Two studies reported that low baseline blood volume was a significant risk factor, in which one measured stroke volume variation (SVV) and the other measured inferior vena cava-cardiac index (IVC-CI) to detect low blood volume before anesthesia. Two studies showed that long-term intake of the angiotensin converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) was a significant risk factor for PIH.

One study reported the association between general anesthetics and PIH, propofol administration and increasing fentanyl dosage for the induction of general anesthesia were risk factors for PIH.

Discussion

This study is the first systematic review to describe the risk factors for PIH, and the results

showed that several factors, including age, low baseline blood volume, emergency operation, propofol induction, and increasing fentanyl dosage were significantly associated with the development of PIH.

Age was a significant risk factor for PIH. Only one study showed that age≥ 50 years old could cause a significantly increased risk of PIH[5] but results from other studies made it clear that age was positively correlated with the development of PIH, which meant the older the patient was, the more likelihood of PIH would be. But till now, it is too early to show at what stage of age the risk of PIH will be significantly increased. Bodyweight was negatively correlated with PIH, which meant the higher body weight was, the less likelihood of the development of PIH would be. Just like age, it is unclear about the threshold of body weight for reducing the risk of PIH nowadays.

In the clinic, it seems that low blood pressure can more easily lead to PIH, but the results from this review showed that, MAP and SBP were positively correlated with the development of PIH in some studies, and the results in others were conflicting. It suggested that blood pressure, either high or low, was not critical in the development of PIH. Poorly controlled hypertension before surgery can more easily lead to intraoperative hypotension[18]. Baseline low blood volume was a risk factor for PIH, many factors contributed to low blood volume before anesthesia, such as physical status, comorbidities, bowel preparation, and fasting. Nowadays, paranesthesia ultrasonography[19] or microinvasive techniques[20] was used to detect low blood volume status. In the included studies in this review, SVV and IVC-CI were measured to represent blood volume status, since general anesthetics can cause vasodilatation, blood volume status monitoring is of great significance for predicting and preventing the development of PIH.

An emergency operation was a risk factor for PIH. The reason might be potential comorbidities and long-term medications often exist in emergency surgical patients. ACEI/ARB should be discontinued on the day of surgery according to the clinical practice because continued use of ACEI/ARB on the day of surgery can cause severe hypotension after the induction of general anesthesia[21]. In the included two studies, the authors in one study did not mention whether the increased risk of PIH by ACEI/ARB resulted from the long-term medication or not discontinued on the day of surgery, but the other made it clear that PIH was from long-term oral intake of ARB.

Recent studies[22,23] showed that propofol could more easily cause hypotension when administered for induction of general anesthesia. This review showed that propofol induction and increasing fentanyl dosage were risk factors for PIH, as propofol has a stronger potent vasodilative effect than etomidate or thiopental, and opioids with higher dosage can cause significant vasodilatation as well. Thus, to reduce the incidence of PIH, we might use less propofol and opioids or choose other alternatives for the induction, especially in patients with ASA III-V, who are in a state of physical weakness. In addition to the dosage of propofol or fentanyl, the speed of injection is critical as well for the development of PIH, but no study reported these potential risk factors till now.

The implication of our findings is that the results may advance preventive strategies. Nowadays, we cannot predict which surgical patient will develop PIH after induction of general anesthesia. If we know any of these risk factors, we can focus our preventive strategies or modulations on these measures. Although the contribution of each measure is small, simultaneous modulation of multiple risk factors together could confer a significant risk reduction.

This study has some limitations. First, the criteria of PIH were not uniform in the included studies, so that the results could not be quantitatively synthesized. Nonetheless, the results were compatible between groups in each study. Second, in the included studies, surgical types, preoperative preparation, induction strategies of general anesthesia were different, which might cause the varied incidence of PIH and risk factors.

Conclusions

This systematic review identified 12 studies with risk factors associated with the development of PIH. The results showed that aging, ASA III-V, emergency operation, low baseline blood volume, long-term intake of ACEI/ARB, propofol induction, increasing fentanyl dosage are risk factors for PIH, while body weight gain is a protective factor. Based on the current evidence, it is difficult to determine whether baseline blood pressure or gender is associated with the development of PIH. Future efforts should be directed towards the application of uniform PIH criteria in each type of surgery and evaluation of the incidence of PIH and its risk factors using multi-center studies at high-volume medical centers.

Acknowledgements
This work was supported by grants from the National Science Foundation Project of Chongqing (cstc2017jcyjBX0043 and cstc2019jcyj-msxmX0608).

Contributions
BC and HL had full access to the data and take responsibility for the accuracy and reporting, HL participated in the design of the review and revised the manuscript, BC collected data and drafted the manuscript, QP and RA participated in data collection and extraction. All authors read and approved the final version.

Conflict of Interest
The Authors declare that they have no conflict of interests.

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