Original Article

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Risk Factors for Postinduction Hypotension among Elderly Patients Undergoing Elective Non-Cardiac Surgery under General Anesthesia

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Abstract:

Objective: We aimed to determine risk factors for hypotension occurring after induction among elderly patients (aged 65 years and older). We hypothesized that the dosage of intravenous anesthesia drugs as well as the type of inhalation agent have an effect on hypotension during post-induction periods. We aimed to test this hypothesis to determine risk factors for hypotension after induction among elderly patients who underwent non-cardiac surgery.

Material and Methods: This retrospective cohort study analyzed data from 580 patients between December 2017 and July 2018 at a tertiary university hospital in the south of Thailand. Hypotension is defined as a more than 30.0% decrease in mean arterial pressure from baseline after induction and within 20 minutes of the use of a vasopressor agent to treat hypotension. The intraoperative parameters were blood pressure and heart rate immediately after arrival at the operating room, immediately after intubation, and 5, 10, 15, and 20 minutes after intubation.

Results: The median age was 72.5 (68, 78) years. The association of post-induction hypotension was raised with a diuretic drug as preoperative medication (p-value=0.025), and the degree of hypertension immediately after arrival at the operating room (p-value<0.001). Increasing fentanyl dosage during induction was associated with hypotension (p-value<0.010). There was no statistically significant difference in the increase of the propofol dosage.

Conclusion: The degree of hypertension immediately after arrival at the operating room coupled with higher fentanyl dosage were significant risk factors for postinduction hypotension in elderly patients.

Keywords: elderly, hypotension, post-induction, risk factors

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Introduction

There is evidence that hemodynamic instability during general anesthesia is associated with adverse outcomes in both, cardiac and non-cardiac surgery.[1-3] General anesthesia induces hypotension, which commonly occurs in routine practice. An interval of general anesthesia can cause hypotension to occur. This includes the interval during the post-induction period starting from induction of general anesthesia until the beginning of surgery.[4-6] General anesthesia induces a decrease in blood pressure (BP) via a variety of mechanisms such as the vasodilatation effect, which results in a drop in systemic vascular resistance, or hypovolemia.[7]

The definition of hypotension is highly diverse. There is no accepted, single definition of intraoperative hypotension (IOH). The incidence of IOH varies from 5 to 99.0%.[8] Südfeld et al.[6] defined post induction hypotension as: systolic blood pressure (SBP) <90 millimeter of mercury (mmHg), or at least one incidence of norepinephrine infusion at a rate of >6 microgram (mcg) per minute (20-minute post-induction). Jor et al.[9] defined hypotension as decreasing mean arterial pressure (MAP) of more than 30.0%, compared to the baseline, which showed 36.5% had hypotension after induction of general anesthesia within the first 10 minutes after intubation.

With an increase in age comes the prediction that at some point a person may have to undergo some form of surgery. Perioperative morbidity most often occurs among the elderly;[10] hence, increase in age is a predictor of intraoperative hypotension during the post-induction period.[5,6,9,11]

Nevertheless, there is insufficient information to predict which elderly patients are at risk for hypotension during the post-induction period. Reich et al.[5] demonstrated that propofol induction and increases in fentanyl dosage are associated with hypotension within the first 10 minutes after induction. Previous studies revealed that increasing the dosage of propofol is associated with hypotension after induction, especially in patients over 70 years of age.[11] We hypothesized that the dosage of intravenous anesthesia drugs as well as the type of inhalation agent have an effect on hypotension during post-induction periods.

We aimed to test this hypothesis to determine risk factors for hypotension after induction among elderly patients who underwent non-cardiac surgery. The results of this study may predict hypotension after general anesthesia, and assist in the optimization of intraoperative BP.

Material and Methods

This retrospective cohort study was performed over a period of 8 months (from December 2017 to July 2018) at a tertiary university hospital in the south of Thailand. The proposal was approved by the Institute Ethics Committee, Faculty of Medicine, Prince of Songkla University (REC 61-260-8-1) and written informed consent was waived by the Institutional Review Board.

Inclusion criteria were:

1. Age 65 years and older undergoing elective non-cardiac surgery involving general anesthesia using endotracheal intubation and balanced technique.
2. American Society of Anesthesiologists (ASA) physical status I-IV.

Exclusion criteria were:

1. Combined general anesthesia with spinal or epidural anesthesia.
2. Two or more attempts with endotracheal intubation.
3. Patients who were intubated before surgery.
4. Vasopressor, or inotropic infusion before inducing general anesthesia.
5. Change in position of BP measurement during induction.
6. Deliberate hypotension within 20 minutes after intubation.
7. Incomplete data in medical records, including, systolic/diastolic BP and heart rate (HR) within 20 minutes after intubation.

Our sample size was calculated based on a study by Reich et al.[5] with the minimum study size being determined using 2 populations (n for 2 p) in the R Foundation for Statistical Computing. A total of 579 patients were calculated as adequate to detect differences with 80.0% power and a two-tailed α error of 5.0%.

Hypotension in this study is defined as more than a 30.0% decrease in MAP from baseline after induction and within 20 minutes, or the use of vasopressor agents to treat low BP. This definition is based on a study by Bijker et al.[12] that demonstrated decreases in MAP of more than 30.0% from baseline are associated with the occurrence of ischemic stroke.

All data was collected from medical records, the electronic hospital information system and anesthetic records. We preoperatively recorded gender, age, weight, height, ASA classification, and comorbidity diseases (hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, cerebrovascular disease, end stage renal disease requiring hemodialysis and current medications (beta-blockers, calcium-channel blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, diuretics, insulin, oral antidiabetics and thyroid therapy)

Intraoperative parameters were: SBP, diastolic blood pressure (DBP), MAP, HR immediately after arrival at the operating room(T0), immediately after intubation (TEI), 5 minutes after intubation (T5), 10 minutes after intubation (T10), 15 minutes after intubation (T15) and 20 minutes after intubation (T20). BP was recorded every three to five minutes; either directly from an arterial catheter or using noninvasive methods.

Descriptive statistical results are displayed by the median and interquartile range (IQR), or mean with standard deviation (S.D.) for continuous data and frequency, and with percentages for categorical data. Differences between non-hypotension and post-induction hypotension were evaluated with Ranksum tests, or t-tests, for continuous variables and Fisher's exact tests, or chi-square tests, for categorical data.

Factors associated with post-induction hypotension were determined using a multivariate logistical regression model. Measurements using Generalized Estimating Equations were utilized to evaluate blood pressure levels at various times. R software, version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria), was used for data management and analysis. Statistical significance was assumed if the p-value was less than 0.050.

Results

Patient selection is shown in the flow chart (Figure 1). A total of 580 subjects were included for end analysis.

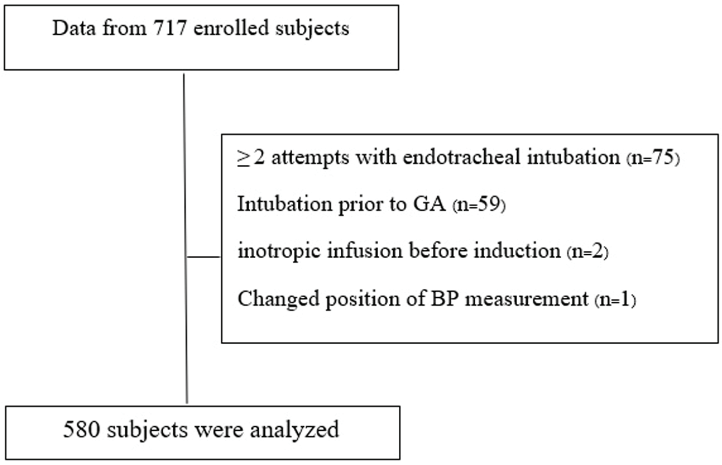
Preoperative characteristics of patients to compare hypotension and non-hypotension groups are shown in Table 1. One hundred and ninety-six (33.8%) patients had arterial catheter insertion. Three hundred and seventy-six (64.8%) patients had hypotension at least one time within 20 minutes after intubation. However, four (0.7%) patients had persistent hypotension from intubation to the first 20 minutes after intubation.

There were 39 (6.7%), 132 (22.8%), 193 (33.3%), 230 (39.7%) and 211 (36.4%) subjects who had hypotension at TEI, T5, T10, T15 and T20, respectively (Table 2). Five hundred and seventy-four patients (98.9%) received propofol as an intravenous induction drug, and five hundred and seventy-eight (99.6%) patients received fentanyl as analgesia. The mean of propofol induction was 2.3 milligram per kilogram (mg/kg) and the mean of fentanyl induction was 1.7 mcg/kg. After the induction period, 53.3% of patients received desflurane as an inhalation agent. The hypotension group had a higher age median of 73 (68, 79) years, while the median in the non-hypotension group was 71 (68, 76) years.

Table 1 Demographic and clinical characteristics, comparing hypotension and non-hypotension groups

Characteristics	Total Number (%)	Non-hypotension Number (%)	Hypotension Number (%)	p-value
	580 (100.0)	204 (35.2)	376 (64.8)	
Sex				0.304
Male	294 (50.7)	97 (47.5)	197 (52.4)	
Female	286 (49.3)	107 (52.5)	179 (47.6)	
Age in years, median (IQR)	72.5 (68.0, 78.0)	71.0 (68.0, 76.0)	73.0 (68.0, 79.0)	0.026
65-74 years	348	134 (38.5)	214 (61.5)	
75-84 years	191	61 (31.9)	130 (68.1)	
≥85 years	41	9 (22.0)	32 (78.0)	
Weight (kg) median (IQR)	59.0 (50.2, 66.7)	59.6 (51.0, 67.0)	58.8 (50.0, 66.0)	0.166
Height (cm) median (IQR)	158.0 (150.0, 165.0)	157.5 (150.0, 164.0)	158.0 (150.0, 165.0)	0.786
BMI, median (IQR)	23.4 (20.7, 26.5)	23.8 (21.2, 26.6)	23.2 (20.6, 26.2)	0.169
ASA classification				0.389
II	308 (53.1)	116 (56.9)	192 (51.1)	
III	267 (46.0)	87 (42.6)	180 (47.9)	
IV	5 (0.9)	1 (0.5)	4 (1.1)	
Comorbidity disease	526 (90.7)	182 (89.2)	344 (91.5)	0.453
Hypertension	373 (64.3)	129 (63.2)	244 (64.9)	0.759
Dyslipidemia	237 (40.9)	88 (43.1)	149 (39.6)	0.464
Cancer	228 (39.3)	89 (43.6)	139 (37.0)	0.139
Diabetes mellitus	119 (20.5)	44 (21.6)	75 (19.9)	0.723
Chronic heart disease	113 (19.5)	38 (18.6)	75 (19.9)	0.785
Ischemic heart disease	51 (8.8)	18 (8.8)	33 (8.8)	1.000
End stage renal disease	13 (0.02)	0 (0.0)	13 (3.5)	0.006
Preoperative medications	388 (66.9)	130 (63.7)	258 (68.6)	0.270
Beta blockers	126 (21.7)	36 (17.6)	90 (23.9)	0.099
Calcium channel blockers	216 (37.2)	80 (39.2)	136 (36.2)	0.526
ACE inhibitors	70 (12.1)	21 (10.3)	49 (13.0)	0.405
ARBs	75 (12.9)	24 (11.8)	51 (13.6)	0.626
Diuretic	75 (12.9)	20 (9.8)	55 (14.6)	0.128
Oral antidiabetic	84 (14.5)	36 (17.6)	48 (12.8)	0.141
Pre-induction period, median (IQR)				
Systolic (mmHg)	160 (140.0, 170.2)	150 (135.0, 165.0)	160 (145.0, 180.0)	<0.001
Diastolic (mmHg)	80 (70.0, 90.0)	75 (70.0, 80.0)	80 (70.0, 90.0)	<0.001
Mean arterial pressure (mmHg)	105.5 (97.0, 115.0)	100 (92.0, 108.0)	110 (98.8, 117.0)	<0.001
Heart rate (bpm)	75 (65.0, 85.0)	75 (69.5, 85.0)	70 (65.0, 85.0)	0.100
Hematocrit baseline (%) mean (S.D.)	36.3 (5.2)	36.8 (4.9)	36 (5.3)	0.083
Propofol (mg) median (IQR)	120 (100.0, 160.0)	130 (100.0, 170.0)	120 (100.0, 160.0)	0.200
Fentanyl (mcg) median (IQR)	100 (75.0, 100.0)	100 (75.0, 100.0)	100 (75.0, 100.0)	0.554
Desflurane	309 (53.3)	102 (50.0)	207 (55.1)	0.281
Sevoflurane	271 (46.7)	102 (50.0)	169 (44.9)	0.311
Nitrous oxide used	4 (0.7)	1 (0.5)	3 (0.8)	1.000

kg=kilogram, cm=centimeter, BMI=body mass index, IQR=interquartile range, ARBs=angiotensin receptor blockers, ACEIs=angiotensin converting enzyme inhibitors, mmHg=millimeter of mercury, bpm=beat per minute, S.D.=standard deviation



GA=general anesthesia, BP=blood pressure

Figure 1 Flow chart of patient enrollment

Table 2 Hypotension events at any time points within 20 minutes after induction period according to age groups

Age group	Time points				
	TEI	T5	T10	T15	T20
65-74 years	24	70	111	136	118
75-84 years	13	50	62	77	72
≥85 years	2	12	20	17	21
Total (times)	39	132	193	230	211

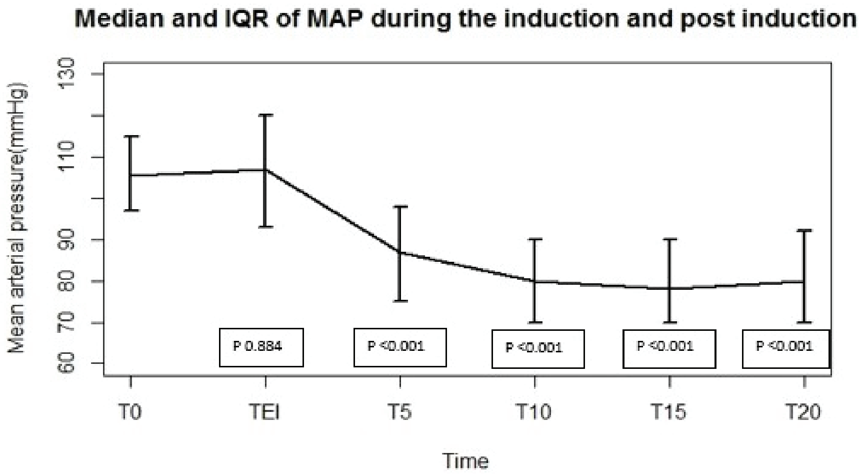
TEI=time after intubation, T5=5 minutes after intubation, T10=10 minutes after intubation, T15=15 minutes after intubation, T20=20 minutes after intubation

There was no statistically significant association between ASA classification, long term medication and the occurrence of post-induction hypotension. The median of SBP, DBP and MAP were higher in the hypotension group. All patients who had end stage renal disease with hemodialysis (n=13) had hypotension at least at one time point after induction.

Figure 2 reveals the MAP median at every moment measured, at T0 it was 105 millimeters of mercury (mmHg), then immediately after intubation, it slightly increased to 0.14 mmHg, it then decreased from T0 to 18, 24, 25, and 23 mmHg at T5, T10, T15 and T20, respectively. The lowest MAP median was at 15 minutes after intubation. The T15 time point presented the highest incidence of postinduction hypotension, occurring in 39.7% of subjects.

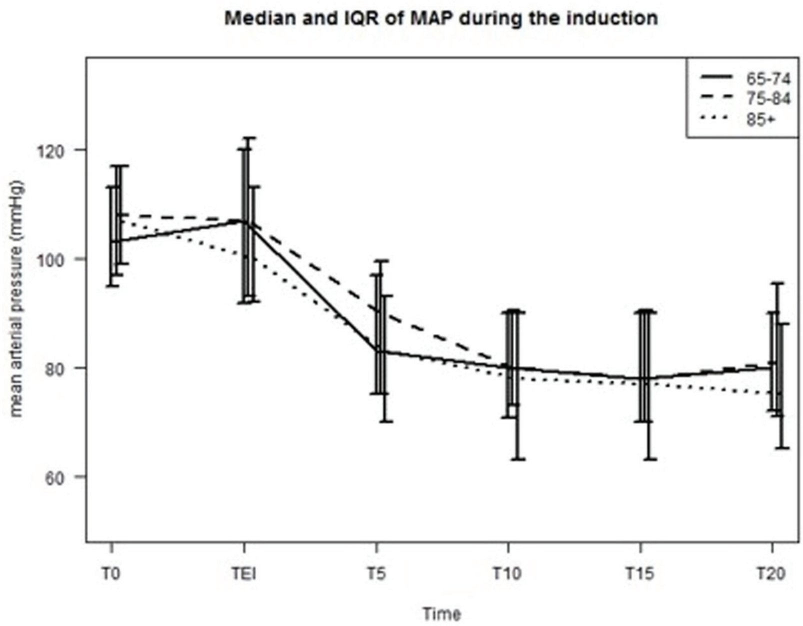
Figure 3 reveals MAP from immediately arriving at the operating room (T0) up to 20 minutes after endotracheal intubation, according to age groups as well as aggregate plot median and IQR. There was no statistically significant difference between age groups.

Figure 4 presents intubation time for patients who received amounts of propofol less than or equal to 2.3 mg/kg, and fentanyl of more than 1.7 mcg/kg, and had significant hypotension (p-value=0.048).



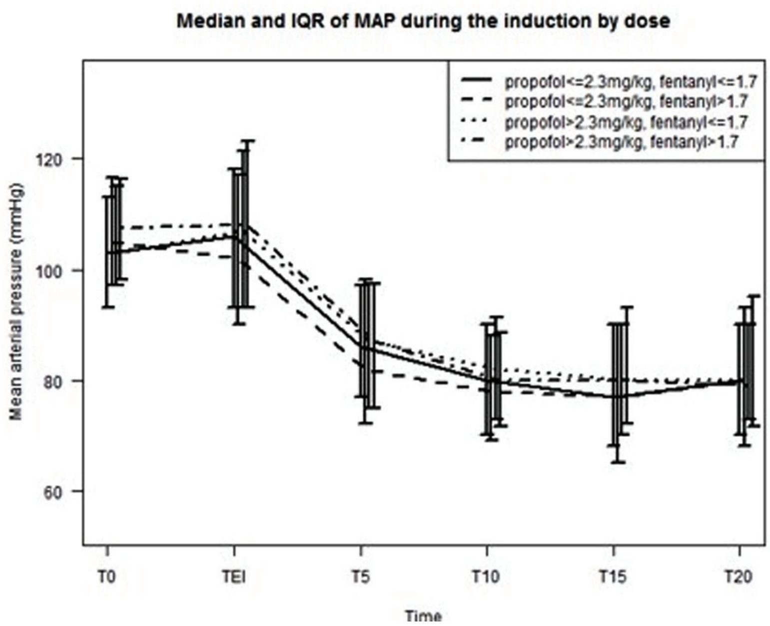
IQR=interquartile range, MAP=mean arterial pressure, mmHg=millimeter of mercury
T0=time after arrival at the operating room, TEI=time after intubation, T5=5 minutes after intubation, T10=10 minutes after intubation, T15=15 minutes after intubation, T20=20 minutes after intubation

Figure 2 Aggregate plot median and interquartile range of mean arterial pressure during the induction and post-induction



IQR=interquartile range, MAP=mean arterial pressure, mmHg=millimeter of mercury
T0=time after arrival at the operating room, TEI=time after intubation, T5=5 minutes after intubation, T10=10 minutes after intubation, T15=15 minutes after intubation, T20=20 minutes after intubation

Figure 3 Aggregate plot median and interquartile range of mean arterial pressure during the induction and post-induction by age groups



IQR=interquartile range, MAP=mean arterial pressure, mmHg=millimeter of mercury
T0=time after arrival at the operating room, TEI=time after intubation, T5=5 minutes after intubation, T10=10 minutes after intubation, T15=15 minutes after intubation, T20=20 minutes after intubation

Figure 4 Aggregate plot median and interquartile range of mean arterial pressure during the induction and post-induction by dose propofol and fentanyl

Table 3 summarizes the multivariate logistic regression, which highlighted risk factors for hypotension for at least one time point. These included diuretic used as preoperative medication (p-value=0.025), increased BP at pre-induction period (p-value<0.001) and heart rate baseline (p-value=0.018).

Multivariate logistic regression was associated with hypotension from intubation to 20 minutes after intubation. Increasing fentanyl dosage (every 10 mcg) was an associated risk of hypotension post-induction, especially at intubation time; odds-ratio (OR) 1.14, 95% confidence interval (95% CI) 1.05-1.24, p-value<0.010) and 5 minutes after intubation (OR 1.15, 95% CI 1.09-1.23), p-value<0.001). There was no statistically significant difference in the propofol dosage.

Table 3 Risk factors for hypotension at least one time point during 20 minutes after intubation, based on multivariate logistic regression

Factors	crude OR (95% CI)	adj. OR (95% CI)	P (Wald's test)	p-value
Age group				
ref.=65-74				0.251
75-84	1.33 (0.92, 1.94)	1.17 (0.77, 1.76)	0.461	
85+	2.23 (1.03, 4.81)	1.96 (0.84, 4.53)	0.118	
Body mass index	0.98 (0.94, 1.02)	0.97 (0.93, 1.02)	0.213	0.212
Diuretic as currently medication	1.58 (0.92, 2.71)	1.91 (1.07, 3.42)	0.029	0.025
Pre-induction (DBP)	1.04 (1.03, 1.06)	1.04 (1.02, 1.06)	<0.001	<0.001
Pre-induction heart rate	0.99 (0.98, 1.00)	0.98 (0.97, 1.00)	0.019	0.018
Hematocrit baseline	0.97 (0.94, 1.00)	0.97 (0.93, 1.00)	0.084	0.083
Pre-induction (SBP)				<0.001
ref.=<139				
140-159	1.28 (0.80, 2.05)	1.11 (0.67, 1.83)	0.693	
160-179	2.20 (1.37, 3.53)	1.61 (0.96, 2.70)	0.073	
180+	4.94 (2.70, 9.05)	3.33 (1.72, 6.44)	<0.001	

SBP=systolic blood pressure, DBP=diastolic blood pressure, OR=odds ratio, CI=confidence interval

Discussion

In this study, the definition of hypotension was based on the study by Bijker et al.[12], which was a decrease in MAP of more than 30.0% compared to baseline and that significantly increases the risk of postoperative stroke. This study stands in contrast with a previous study by Südfeld et al.[6], which had an incidence of post-induction hypotension of 18.1%. The present study showed a higher incidence than the study by Jor et al.[9] possibly due to the higher median age: 72.5 (68, 78) years, and the post-induction duration, which was 20 minutes, in contrast to 55 (41, 67) years, with the duration of post-induction being 10 minutes. Increasing age is a predictor of intraoperative hypotension during the post-induction period.[5,6,9,11] Reich et al.[5] presented that the incidence of hypotension was more frequent 5-10 minutes after induction, whereas, Jor et al.[9] illustrated the highest occurrence of hypotension was observed within the first 5 and 10 minutes after intubation, while this study showed the time point at T15 having the highest incidence of post-induction hypotension. The reason why our study had a more delayed time point in hypotension than previous studies was because the subjects' ages were that of an elderly group, who had altered pharmacokinetic and pharmacodynamics. (decreased renal and hepatic function, decreased protein binding and altered volume of distribution).[10]

Reich et al.[5] showed that risk factors for hypotension were: ASA III-IV, age >50 years, pre-induction MAP lower than 70mmHg, use of propofol as an induction drug and high dosages of fentanyl (>5 mcg/kg). Jor et al.[9] presented increased age, degree of hypertension at pre-induction period and presence of diabetes as predictors of post-induction hypotension. Südfeld et al.[6] revealed that independent variables for post-induction hypotension were: emergency surgery, increased age and pre-induction SBP. The results from Jor et al.[9] were comparable to the results in this study because similar criteria for hypotension were used. Our results presented no statistically significant difference in increased age, or presence of diabetes. On the other hand, our study showed results in the degree of hypertension at the pre-induction period to be associated with the occurrence of post-induction hypotension. This may be explained by the high BP baseline during pre-induction, and the anesthesiologist may have preferred to decrease BP during induction, or also by the fact that vascular tone variation induces changes in BP in hypertensive patients so that BP may markedly decrease after general anesthesia.[13]

This study presents diuretics used as current medication to be associated with post-induction hypotension. In a previous study, by Anastasian et al.[14], it was shown that patients who took preoperative diuretic drugs required significantly more vasopressor in carotid endarterectomy surgery. However, a previous study by Khan et al.[15] revealed, in a randomized control trial, that administration of furosemide on the day of surgery did not significantly increase intraoperative hypotension when compared with a placebo. Nevertheless, the present results may indicate that it is possible that the clinical indications for diuretic drugs may pose risks to the population that lean towards intraoperative hypotension.

Propofol dosage was not associated with post-induction hypotension because the difference in intravenous volume status for each patient may have disrupted the hypotension results. In a future study, a prospective method should be recorded.

The strength of this study was that there were many elderly patients who underwent general anesthesia. On the other hand, there were several limitations to our study. First, this study did not take into account the duration of hypotension episodes. A previous study revealed that longer durations of hypotension increase the risks of post-operative, acute kidney injury and myocardial injury.[2] Secondly, it is unlikely that surgical stimulation started within the first 20 minutes after intubation, nevertheless, mildly stimulating procedures; such as, positional changes, or urinary catheterization may have occurred. Therefore, if there were any noxious stimuli during this period it may have influenced the incidence of hypotension. Thirdly, the pre-induction period is a time of anxiety, so BP and HR in this period may be higher than normal. Fourthly, the BP was intermittently measured for those who did not have an arterial catheter. Hypotension might have been missed between these interval measurements. Fifthly, the intravenous fluid and minimum alveolar concentration of inhalation agent these were given, were not recorded.

Conclusion

In conclusion, there continue to be several unanswered questions including what the optimal BP during the intraoperative period, and accurate BP may be. Our results provide evidence that the degree of hypertension at pre-induction period is a risk factor that is linked to hypotension in elderly patients after induction. Higher dosages of fentanyl are used in obtaining optimal BP for elderly patients who present with hypertension, or are at risk of developing hypotension. This evidence suggests that fentanyl ought to be used in lower dosages to avoid hypotension. Future research in this field, via a randomized control trial is necessary.

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Conflict of interest

All authors declare there is no conflict of interest.

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