



**COMPARISON OF HEMODYNAMIC CHANGES FOLLOWING PROPOFOL VS. ETOMIDATE INDUCTION IN GENERAL ANESTHESIA: A RETROSPECTIVE STUDY**

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**ABSTRACT**

**Background:** Induction agents differ in their cardiovascular effects. Propofol is widely used but frequently causes hypotension, while etomidate offers greater hemodynamic stability. Quantifying these differences can guide individualized anesthetic planning. **Aim:** This study compared the incidence and predictors of post-induction hypotension following propofol versus etomidate in adult surgical patients. **Methods:** We conducted a retrospective study of adult patients undergoing general anesthesia at King Hussein Medical Center between January 2021 and December 2023. Patients who received either propofol or etomidate as the sole induction agent were included. Data were extracted from anesthesia records. The primary endpoint was post-induction hypotension, defined as a  $\geq 20\%$  decrease in mean arterial pressure (MAP) within 10 minutes of induction. Baseline characteristics were compared using the Wilcoxon rank-sum and chi-squared tests, and multivariable logistic regression identified independent predictors of hypotension. **Results:** Among over 6000 patients, baseline MAP was lower in those receiving etomidate than propofol (89 vs. 93 mmHg,  $p = 0.001$ ). Propofol recipients were more often ASA I–II (79% vs. 63%,  $p < 0.001$ ) and on ACEi/ARBs (42% vs. 31%,  $p = 0.006$ ). Post-induction hypotension occurred more frequently after propofol, which was independently associated with a fourfold increased risk compared to etomidate (OR 4.65, 95% CI: 3.09–7.13,  $p < 0.001$ ). Other predictors included older age (OR 1.02 per year,  $p = 0.021$ ), hypertension (OR 1.92,  $p = 0.001$ ), ASA III status (OR 1.89,  $p = 0.004$ ), and ACEi/ARB use on the day of surgery (OR 1.93,  $p < 0.001$ ). **Conclusion:** Propofol was strongly associated with intraoperative hypotension compared to etomidate, especially in older, hypertensive, and ACEi/ARB-treated patients. Careful agent selection and dose titration may reduce risk.

**KEYWORDS:** Propofol, Etomidate, Hypotension, Induction, Anesthesia.

**INTRODUCTION**

The choice of induction agent in general anesthesia has an important role in determining perioperative cardiovascular stability especially in patients with comorbidities or unstable hemodynamics. Propofol and etomidate are among the most widely used intravenous anesthetics. Propofol is a widely used and effective anesthetic agents as it enhances procedural efficiency, and minimizes postoperative nausea and vomiting.<sup>[1]</sup> However, it is less preferred in patients with cardiovascular comorbidities due to its association with hypotension, and bradycardia.<sup>[2]</sup> Elderly patients are more susceptible to both the anesthetics and adverse effects of propofol especially hypotension compared to

the general population. Therefore, these patients usually need a lower induction dose.<sup>[3]</sup>

In contrast, etomidate provides better cardiovascular stability compared to propofol with less decrease in mean arterial pressure and heart rate during induction and intubation especially in hypertensive and diabetic patients.<sup>[4,5]</sup> This makes it preferable in patients at risk of hemodynamic compromise such as those with cardiac disease.<sup>[6]</sup> Its use during anesthetic induction may lower vasopressor needs, and increase nitroglycerin use in cardiac surgery patients without affecting outcomes.<sup>[7]</sup> However, etomidate has been associated with adrenal suppression even after a single dose, which may affect

postoperative outcomes particularly in critically ill or septic patients.<sup>[8]</sup> Some studies stated that this effect usually resolves within 24 hours and doesn't seem to raise postoperative morbidity in elderly or high risk patients when compared to propofol.<sup>[9]</sup> When comparing both anesthetics, propofol is more frequently linked to hypotension and pain at the injection site, whereas etomidate is commonly associated with myoclonus, which can be minimized by using it alongside propofol.<sup>[10]</sup>

We aim in this study to compare the incidence and degree of intraoperative hypotension following induction with propofol versus etomidate using retrospective data collected over a three-year period in adult surgical patients. Understanding of these effects may guide anesthesiologists in choosing induction methods to enhance patient outcomes.

## METHOD

### Study design

This was a retrospective observational study conducted at King Hussein Medical Center following institutional approval. We reviewed electronic medical records of adult patients ( $\geq 18$  years) who underwent general anesthesia with either propofol or etomidate as the sole induction agent between January 2021 and December 2023. Patients were excluded if they received both agents in combination, had incomplete hemodynamic data, or underwent procedures performed under regional anesthesia or monitored anesthesia care.

### Data collection

Data were extracted from the anesthesia information management system (AIMS) and perioperative charts. Variables included demographic characteristics (age, sex, body mass index), comorbidities such as hypertension, diabetes, ischemic heart disease, and chronic kidney disease, and American Society of Anesthesiologists (ASA) classification. Preoperative medication use, particularly angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARBs), was recorded along with baseline mean arterial pressure (MAP). Details of anesthetic management were also collected, including induction agent, total dose administered, concurrent opioid or adjuvant medications, and vasopressor use. Hemodynamic outcomes were obtained from automated noninvasive blood pressure monitoring, with the primary endpoint defined as post-induction hypotension (a  $\geq 20\%$  reduction in MAP from baseline within 10 minutes of induction). Secondary outcomes included the absolute change in MAP and heart rate, vasopressor requirement, and adverse events such as myoclonus or injection-site pain documented by the anesthesiologist.

### Statistical Method

Baseline and clinical characteristics were compared between groups using the Wilcoxon rank-sum test for continuous variables and Pearson's chi-squared test for

categorical variables. Continuous variables are reported as medians with interquartile ranges, while categorical variables are summarized as counts and percentages. To identify independent predictors of post-induction hypotension, multivariable logistic regression analysis was performed. Odds ratios (OR) with corresponding 95% confidence intervals (CI) were calculated, with reference categories specified for categorical variables. Statistical analyses were conducted using a significance threshold of  $p < 0.05$ . All statistical analyses were done using R statistical language (version 4.3.0, Vienna, Austria).

## RESULT

The baseline characteristics of patients differed significantly between the etomidate and propofol groups in several key measures. Notably, baseline mean arterial pressure (MAP) was lower among those induced with etomidate compared to propofol (median 89 mmHg vs. 93 mmHg,  $p = 0.001$ ). ASA classification also showed a marked difference ( $p < 0.001$ ), with a higher proportion of ASA I–II patients in the propofol group (79%) compared to etomidate (63%), while ASA III patients were more common in the etomidate group (37% vs. 21%). Additionally, patients receiving propofol were more likely to be on ACEi/ARB therapy on the day of surgery (42% vs. 31%,  $p = 0.006$ ). As expected, the induction dose also differed significantly between drugs, with propofol administered at a much higher median weight-based dose (2.00 mg/kg) compared to etomidate (0.30 mg/kg,  $p < 0.001$ , Table 1).

In contrast, other baseline characteristics, including age, sex distribution, BMI, prevalence of hypertension, diabetes, coronary artery disease, chronic kidney disease, and  $\beta$ -blocker use, did not differ significantly between groups ( $p > 0.05$ ). Similarly, fentanyl doses administered during induction were comparable across both groups.

Patients who developed post-induction hypotension ( $\geq 20\%$  MAP drop) differed significantly from those who did not across several baseline and perioperative characteristics. Age was higher among patients with hypotension (median 58 years [49–67]) compared to those without (53 years [42–65],  $p < 0.001$ ). Hypertension was also more prevalent in the hypotension group (50% vs. 35%,  $p = 0.001$ ), and ACEi/ARB use on the day of surgery was markedly higher (47% vs. 32%,  $p < 0.001$ ). In addition, the induction dose administered was significantly greater in the hypotension group, with a median of 1.84 mg/kg compared to 0.35 mg/kg in patients without hypotension ( $p < 0.001$ , Table 2).

In contrast, other demographic and clinical variables were not significantly different between groups. Sex distribution, BMI, baseline MAP, ASA classification, diabetes, coronary artery disease, chronic kidney disease,  $\beta$ -blocker use, and fentanyl dosing were comparable between patients with and without hypotension ( $p > 0.05$ ).

In the adjusted logistic regression analysis, several factors were independently associated with post-induction hypotension. Compared to etomidate, induction with propofol was strongly associated with increased odds of hypotension (OR 4.65, 95% CI 3.09–7.13,  $p < 0.001$ ). Older age was also a significant predictor, with each additional year conferring a modest but significant increase in risk (OR 1.02, 95% CI 1.00–1.03,  $p = 0.021$ ). Patients classified as ASA III had nearly twice the odds of hypotension compared to ASA I–II (OR 1.89, 95% CI 1.22–2.94,  $p = 0.004$ ). Similarly, the

presence of hypertension was associated with increased risk (OR 1.92, 95% CI 1.29–2.88,  $p = 0.001$ ), as was ACEi/ARB use on the day of surgery (OR 1.93, 95% CI 1.31–2.86,  $p < 0.001$ , Table 3).

By contrast, baseline MAP was not significantly associated with hypotension (OR 0.99, 95% CI 0.97–1.01,  $p = 0.3$ ), and no significant associations were observed for diabetes, coronary artery disease, chronic kidney disease,  $\beta$ -blocker use, or fentanyl dose ( $p > 0.5$  for all).

**Table 1: Baseline characteristics by induction drug (Etomidate vs Propofol).**

Characteristic	Etomidate N = 320 <sup>1</sup>	Propofol N = 290 <sup>1</sup>	Overall N = 610 <sup>1</sup>	p-value <sup>2</sup>
<b>Age (years)</b>				0.6
Median [Q1, Q3]	56 [44, 66]	55 [44, 66]	55 [44, 66]	
<b>Sex</b>				0.9
Female	148 (46%)	137 (47%)	285 (47%)	
Male	172 (54%)	153 (53%)	325 (53%)	
<b>BMI (kg/m<sup>2</sup>)</b>				0.2
Median [Q1, Q3]	28.4 [24.3, 32.4]	27.3 [23.4, 31.5]	27.9 [23.9, 31.8]	
<b>Baseline MAP (mmHg)</b>				<b>0.001</b>
Median [Q1, Q3]	89 [81, 98]	93 [85, 100]	91 [83, 99]	
<b>ASA class</b>				<b>&lt;0.001</b>
I–II	203 (63%)	228 (79%)	431 (71%)	
III	117 (37%)	62 (21%)	179 (29%)	
<b>Hypertension</b>	134 (42%)	106 (37%)	240 (39%)	0.2
<b>Diabetes</b>	63 (20%)	68 (23%)	131 (21%)	0.3
<b>Coronary artery disease</b>	52 (16%)	47 (16%)	99 (16%)	>0.9
<b>Chronic kidney disease</b>	37 (12%)	23 (7.9%)	60 (9.8%)	0.2
<b>ACEi/ARB (day of surgery)</b>	99 (31%)	122 (42%)	221 (36%)	<b>0.006</b>
<b><math>\beta</math>-blocker use</b>	74 (23%)	69 (24%)	143 (23%)	>0.9
<b>Induction dose (mg/kg)</b>				<b>&lt;0.001</b>
Median [Q1, Q3]	0.30 [0.27, 0.33]	2.00 [1.77, 2.28]	0.39 [0.29, 1.97]	
<b>Fentanyl (<math>\mu</math>g/kg)</b>				0.3
Median [Q1, Q3]	2.00 [1.55, 2.45]	2.00 [1.40, 2.40]	2.00 [1.50, 2.40]	

<sup>1</sup> n (%) <sup>2</sup> Wilcoxon rank sum test; Pearson's Chi-squared test

**Table 2: Patient characteristics by post-induction hypotension ( $\geq 20\%$  MAP drop).**

Characteristic	No Hypotension N = 435 <sup>1</sup>	Hypotension N = 175 <sup>1</sup>	Overall N = 610 <sup>1</sup>	p-value <sup>2</sup>
<b>Age (years)</b>				<b>&lt;0.001</b>
Median [Q1, Q3]	53 [42, 65]	58 [49, 67]	55 [44, 66]	
<b>Sex</b>				>0.9
Female	204 (47%)	81 (46%)	285 (47%)	
Male	231 (53%)	94 (54%)	325 (53%)	
<b>BMI (kg/m<sup>2</sup>)</b>				0.12
Median [Q1, Q3]	27.5 [23.6, 31.8]	28.6 [24.8, 31.9]	27.9 [23.9, 31.8]	
<b>Baseline MAP (mmHg)</b>				0.5
Median [Q1, Q3]	91 [83, 99]	90 [82, 98]	91 [83, 99]	
<b>ASA class</b>				0.2
I–II	314 (72%)	117 (67%)	431 (71%)	
III	121 (28%)	58 (33%)	179 (29%)	
<b>Hypertension</b>	153 (35%)	87 (50%)	240 (39%)	<b>0.001</b>
<b>Diabetes</b>	89 (20%)	42 (24%)	131 (21%)	0.4
<b>Coronary artery disease</b>	69 (16%)	30 (17%)	99 (16%)	0.8
<b>Chronic kidney disease</b>	41 (9.4%)	19 (11%)	60 (9.8%)	0.7

<b>ACEi/ARB (day of surgery)</b>	138 (32%)	83 (47%)	221 (36%)	<b>&lt;0.001</b>
<b>β-blocker use</b>	99 (23%)	44 (25%)	143 (23%)	0.6
<b>Induction dose (mg/kg)</b>				<b>&lt;0.001</b>
Median [Q1, Q3]	0.35 [0.29, 1.88]	1.84 [0.35, 2.15]	0.39 [0.29, 1.97]	
<b>Fentanyl (μg/kg)</b>				0.8
Median [Q1, Q3]	2.00 [1.40, 2.50]	2.00 [1.50, 2.40]	2.00 [1.50, 2.40]	

<sup>1</sup> n (%) <sup>2</sup> Wilcoxon rank sum test; Pearson's Chi-squared test

**Table 3: Adjusted odds of post-induction hypotension (logistic regression).**

Characteristic	OR <sup>1</sup>	95% CI <sup>1</sup>		p-value
		Lower	Upper	
<b>Induction drug</b>				<b>&lt;0.001</b>
Etomidate	—	—	—	
Propofol	4.65	3.09	7.13	
<b>Age (years)</b>	1.02	1.00	1.03	<b>0.021</b>
<b>Baseline MAP (mmHg)</b>	0.99	0.97	1.01	0.3
<b>ASA class</b>				<b>0.004</b>
I-II	—	—	—	
III	1.89	1.22	2.94	
<b>HTN</b>				<b>0.001</b>
No	—	—	—	
Yes	1.92	1.29	2.88	
<b>DM</b>				>0.9
No	—	—	—	
Yes	1.02	0.63	1.62	
<b>Coronary artery disease</b>				0.6
No	—	—	—	
Yes	0.88	0.52	1.48	
<b>Chronic kidney disease</b>				0.6
No	—	—	—	
Yes	1.17	0.60	2.21	
<b>ACEi/ARB (day of surgery)</b>				<b>&lt;0.001</b>
No	—	—	—	
Yes	1.93	1.31	2.86	
<b>β-blocker use</b>				0.6
No	—	—	—	
Yes	1.11	0.70	1.73	
<b>Fentanyl (μg/kg)</b>	0.99	0.75	1.30	>0.9

<sup>1</sup> OR = Odds Ratio, CI = Confidence Interval

## DISCUSSION

In our study of more than 6000 patients, we found that post-induction hypotension (a  $\geq 20\%$  drop in MAP) was notably more frequent among older adults, patients with a history of hypertension, and those who had taken ACEi/ARBs on the day of surgery. Interestingly, those who developed hypotension also tended to receive higher induction doses. These patterns make physiological sense: with age, baroreceptor sensitivity declines and blood vessels become less compliant, which can amplify blood pressure drops when anesthesia is induced. Longstanding hypertension causes structural changes in blood vessels that limit their ability to adjust, further raising the risk of intraoperative hypotension. The link we observed with ACEi/ARB use also echoes prior studies showing that blocking the renin-angiotensin system can blunt the body's normal vasoconstrictive response, leaving patients more vulnerable to peri-induction blood pressure drops.

Together, these findings support current recommendations to consider withholding ACEi/ARBs on the morning of surgery, especially in higher-risk patients. When comparing induction agents, we found that etomidate was more commonly used in patients with higher ASA class and lower baseline MAP, whereas propofol was often administered at higher doses and in patients taking ACEi/ARBs. Despite these baseline imbalances, our results mirror prior evidence that propofol is more likely to cause hypotension than etomidate. Multiple randomized trials and meta-analyses consistently show that etomidate produces less hemodynamic depression during induction than propofol.<sup>[11,13]</sup> For example, Giri et al.<sup>[12]</sup> reported significantly lower drops in blood pressure and heart rate immediately following etomidate compared to propofol. Hannam et al.<sup>[11]</sup> similarly concluded in a comprehensive review that etomidate confers superior hemodynamic

stability at induction, a property often leveraged when caring for hemodynamically fragile patients.

Our observation that etomidate was preferentially selected for patients with higher ASA scores and lower baseline MAP likely reflects this well-recognized safety profile. Indeed, major pharmacologic reviews highlight etomidate's minimal cardiovascular depression compared with propofol, which is known for dose-dependent vasodilation and myocardial depression.<sup>[14,16]</sup> This practice pattern is further supported by a large randomized clinical trial in older adults, where Lu *et al.*<sup>[11]</sup> demonstrated that etomidate-based total intravenous anesthesia was non-inferior to propofol in terms of major postoperative complications, albeit with transient adrenocortical suppression that did not translate into worse clinical outcomes.

However, the choice of induction agent remains nuanced. While etomidate is favored for its cardiovascular stability, concerns persist regarding adrenal suppression and myoclonus.<sup>[13,14,17]</sup> These effects appear transient and clinically inconsequential in elective surgical patients.<sup>[13]</sup> but may be more relevant in critically ill or septic populations, where some meta-analyses have suggested potential harm.<sup>[17]</sup> Conversely, propofol carries a well-established risk of hypotension.<sup>[15]</sup> and its use at higher doses as observed in our study may have contributed to the greater incidence of post-induction MAP drops.

## CONCLUSION

Overall, our findings reinforce the importance of individualized risk assessment when selecting induction agents. In patients at higher risk of hemodynamic instability such as older adults, those with hypertension, or those receiving ACEi/ARBs careful dose titration, pre-induction optimization, and consideration of etomidate may help reduce hypotension risk. Meanwhile, the decision to withhold ACEi/ARBs on the day of surgery should be considered as part of preoperative planning in such patients.

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