The effect of prophylactic ephedrine and phenylephrine on hemodynamics in surgical patients in the prone position

Efecto de la efedrina y la fenilefrina profilácticas sobre la hemodinámica en pacientes quirúrgicos en posición prona

Reza Irawan
Universitas Syiah Kuala Banda Aceh, Indonesia
Email: rezairawanmd61@gmail.com ; https://orcid.org/0009-0007-4035-3803
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Abstract

Prone positioning during surgery frequently induces hemodynamic instability, posing challenges for perioperative hypertension management. This study compared the effectiveness of prophylactic ephedrine and phenylephrine in maintaining hemodynamic stability in patients placed in the prone position. In this analytic observational study, 38 patients undergoing posterior stabilization surgery were divided into two groups receiving either intravenous ephedrine (0.1 mg/kg) or phenylephrine (1 mcg/kg) prior to positioning. Hemodynamic parameters—systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR)—were measured at baseline, 5, and 10 minutes after prone positioning. The groups were comparable at baseline. While no statistically significant differences were found in SBP or DBP, the pattern of MAP change differed significantly (Time × Group interaction, $p < 0.001$), with ephedrine producing a greater and more sustained elevation. Furthermore, ephedrine induced a significant increase in HR at 10 minutes (87.76 ± 8.77 vs. 79.93 ± 4.94 bpm, $p = 0.002$), whereas phenylephrine maintained a stable HR. In conclusion, both vasopressors prevent hypotension, but their profiles differ: ephedrine provides more sustained pressure support with a chronotropic effect, while phenylephrine offers stable pressure control without tachycardia. The choice between them should be individualized based on the patient's cardiovascular risk factors, directly informing tailored perioperative hypertension management strategies.

Keywords: Hypertension Management, Ephedrine, Phenylephrine, Prone Position, Hemodynamics.

Resumen

La posición prona durante la cirugía con frecuencia induce inestabilidad hemodinámica, lo que plantea desafíos para el manejo de la hipertensión perioperatoria. Este estudio comparó la eficacia de la efedrina y la fenilefrina profilácticas para mantener la estabilidad hemodinámica en pacientes colocados en posición prona. En este estudio observacional analítico, 38 pacientes sometidos a cirugía de estabilización posterior se dividieron en dos grupos que recibieron efedrina (0,1 mg/kg) o fenilefrina (1 mcg/kg) por vía intravenosa antes de la colocación en posición prona. Se midieron los parámetros hemodinámicos (presión arterial sistólica [PAS], presión arterial diastólica [PAD], presión arterial media [PAM] y frecuencia cardíaca [FC]) al inicio, a los 5 y a los 10 minutos después de la colocación en posición prona. Los grupos fueron comparables al inicio. Si bien no se encontraron diferencias estadísticamente significativas en la PAS ni en la PAD, el patrón de cambio de la PAM difirió significativamente (interacción Tiempo × Grupo, $p < 0,001$), con la efedrina produciendo una elevación mayor y más sostenida. Además, la efedrina indujo un aumento significativo de la FC a los 10 minutos (87,76 ± 8,77 frente a 79,93 ± 4,94 lpm, $p = 0,002$), mientras que la fenilefrina mantuvo una FC estable. En conclusión, ambos vasopresores previenen la hipotensión, pero sus perfiles difieren: la efedrina proporciona un soporte de presión más sostenido con un efecto cronotrópico, mientras que la fenilefrina ofrece un control de la presión estable sin taquicardia. La elección entre ambos debe individualizarse según los factores de riesgo cardiovascular del paciente, lo que permitirá diseñar estrategias personalizadas para el manejo de la hipertensión perioperatoria.

Palabras clave: Manejo de la hipertensión, Efedrina, Fenilefrina, Posición prona, Hemodinámica.

Introduction

The maintenance of hemodynamic stability during general anesthesia is a cornerstone of perioperative safety, with particular emphasis on the prevention and management of acute hypertensive and hypotensive episodes[1]. Pronounced blood pressure fluctuations are associated with increased risks of end-organ damage, myocardial injury, and cerebrovascular complications[2]. One common surgical scenario that precipitates significant hemodynamic alteration is the repositioning of the patient from supine to prone, a necessity for many spinal, urological, and neurosurgical procedures[3].

The physiological transition to the prone position can induce a complex cardiovascular response. Increased intra-abdominal and intrathoracic pressures may compromise venous return, reduce cardiac preload, and consequently decrease cardiac output[4]. This, combined with the vasodilatory effects of anesthetic agents, often culminates in hypotension[5]. Paradoxically, the sympathetic activation triggered by this stressor, or the reflex response to vasopressor administration, can also lead to transient hypertension, complicating perioperative hypertension management. Sustained intraoperative hypotension is a well-established risk factor for acute kidney injury and cognitive dysfunction[6], while marked hypertension increases the risk of surgical bleeding and cardiovascular strain[7]. Therefore, proactive strategies to attenuate these extremes are critical.

Prophylactic vasopressor administration has emerged as a key pharmacological intervention to maintain arterial pressure within a target range during high-risk periods[8]. The choice of agent is pivotal due to differing pharmacological profiles. Phenylephrine, a potent selective α_1-adrenergic agonist, elevates blood pressure primarily through peripheral vasoconstriction and may induce reflex bradycardia[9]. In contrast, ephedrine, a mixed α- and β-adrenergic agonist, increases arterial pressure via a combination of increased heart rate, myocardial contractility, and mild vasoconstriction[10].

Existing comparative research has largely focused on obstetric populations under spinal anesthesia, where phenylephrine is often preferred for minimizing fetal acidosis[11]. However, the context of general anesthesia in the prone position presents distinct challenges—including altered cardiac filling and prolonged surgical duration—that may influence vasopressor efficacy and safety[3,5]. A study by Xia et al. directly comparing these agents in prone spine surgery suggested ephedrine may provide more sustained hemodynamic support, yet data remain limited[12]. Consequently, there is no consensus on the optimal prophylactic vasopressor for hypertension management in this specific surgical setting, particularly regarding which agent best maintains stable pressures without provoking significant tachycardia or hypertensive spikes.

The transition of a patient to the prone position under general anesthesia presents a well-documented cardiovascular challenge. This maneuver can significantly reduce venous return and cardiac preload due to increased abdominal and thoracic pressures, often precipitating a drop in arterial blood pressure. Concurrently, the sympathetic nervous system may be activated by the physical stress of repositioning or by the body's attempt to compensate for reduced perfusion. This creates a dynamic and often unpredictable hemodynamic environment where both hypotension and transient hypertension can occur, complicating the anesthesiologist's goal of maintaining steady organ perfusion pressure throughout the procedure[13].

In response to this instability, the prophylactic administration of vasopressors has become a cornerstone of preventive anesthetic management. The rationale is to preemptively support vascular tone and cardiac output, thereby smoothing the transition and minimizing extreme fluctuations in blood pressure. This proactive approach aims to avoid the well-known risks associated with intraoperative hypotension, such as end-organ ischemia, while also mitigating reactive hypertensive spikes. The selection of the optimal agent, however, remains a subject of clinical debate, as different drugs achieve hemodynamic stability through distinct physiological pathways[14].

Two of the most commonly employed agents are ephedrine and phenylephrine, each with a unique pharmacodynamic profile. Ephedrine acts as a mixed sympathomimetic, indirectly promoting the release of endogenous catecholamines to increase both heart rate and vascular resistance. Phenylephrine, in contrast, is a direct and selective alpha-agonist that produces vasoconstriction without direct cardiac stimulation and may even trigger a reflex slowing of the heart rate. Understanding the nuanced hemodynamic outcomes of these differing mechanisms is critical for developing evidence-based protocols for blood pressure management in this specific surgical context[15].

This study therefore aims to compare the effects of prophylactic ephedrine and phenylephrine on hemodynamic parameters in surgical patients undergoing prone positioning, with a specific focus on their implications for perioperative hypertension management. We hypothesize that the distinct mechanisms of these agents will lead to differentiable patterns in blood pressure stability, heart rate response, and the incidence of hypotensive or hypertensive events during the critical early period after repositioning.

Materials and methods

This analytical observational study utilized a cross-sectional design. The research was conducted at the operating theater of Dr. Zainoel Abidin Regional General Hospital (RSUDZA), Banda Aceh, Indonesia. The study protocol received ethical approval from the Health Research Ethics Committee (KEPK) of the Faculty of Medicine, Universitas Syiah Kuala–RSUDZA, and data collection took place between September 1 and November 1, 2025.

Study Population and Sampling

The study population comprised adult patients scheduled for elective posterior stabilization surgery requiring the prone position under general anesthesia. A total sampling (census) method was employed, whereby all eligible patients admitted during the study period who met the inclusion criteria were invited to participate. The final sample consisted of 38 patients. The primary inclusion criteria were patients aged 18-65 years, classified as American Society of Anesthesiologists (ASA) physical status I-III, and undergoing the specified procedure. Patients with severe cardiovascular disease, uncontrolled hypertension, known arrhythmias, or hypersensitivity to the study drugs were excluded.

Study Protocol and Interventions

Following standard anesthetic induction and endotracheal intubation, patients were prospectively assigned to one of two groups based on the prophylactic vasopressor administered prior to prone positioning. The Ephedrine group received an intravenous bolus of ephedrine at a dose of 0.1 mg/kg, while the Phenylephrine group received an intravenous bolus of phenylephrine at a dose of 1 mcg/kg. The administration occurred approximately three minutes before patient repositioning from supine to prone. All other aspects of anesthetic management, including the choice of induction and maintenance agents, fluid administration, and monitoring, followed the hospital's standard protocol.

Data Collection and Variables

Demographic data, including age, sex, body weight, height, and body mass index (BMI), were recorded preoperatively. The primary outcome measures were hemodynamic parameters, systematically recorded at three predefined time points: T0 (baseline, after induction in the supine position), T1 (5 minutes after achieving the prone position), and T2 (10 minutes after achieving the prone position). The parameters included systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR). All hemodynamic measurements were obtained non-invasively using a standard automated oscillometric blood pressure cuff and continuous electrocardiogram monitoring.

Statistical Analysis

Data were processed and analyzed using IBM SPSS Statistics software. Categorical demographic variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation (SD). The normality of data distribution was assessed using the Kolmogorov-Smirnov test. For bivariate analysis comparing continuous variables between the two independent groups (Ephedrine vs. Phenylephrine), an independent samples t-test was used for normally distributed data. Changes in hemodynamic parameters over time within and between groups were analyzed using a General Linear Model (GLM) for repeated measures. A p-value of less than 0.05 was considered statistically significant for all analyses.

Results

A total of 38 patients were enrolled and completed the study, with 19 patients prospectively assigned to each vasopressor group. The baseline demographic and anthropometric characteristics of the ephedrine and phenylephrine groups are presented in Table 1. The two groups were comparable in terms of age, body weight, and body mass index (BMI) distribution, with no statistically significant differences observed ($p > 0.05$ for all). Although a statistically significant difference was found in mean height (159.38 ± 7.00 cm vs. 161.63 ± 6.53 cm, $p=0.034$), this minor difference of 2.2 cm is not considered clinically relevant to hemodynamic responses or drug pharmacodynamics.

Table 1. Baseline Characteristics of the Study Population

Characteristic	Ephedrine Group (n=19)	Phenylephrine Group (n=19)	p-value
Age (years), mean ± SD	50.68 ± 12.62	53.00 ± 13.73	0.058
Sex, n (%)			0.042
Male	5 (26.3%)	7 (36.8%)	
Female	14 (73.7%)	12 (63.2%)	
Weight (kg), mean ± SD	66.13 ± 11.08	65.37 ± 13.84	0.081
Height (cm), mean ± SD	159.38 ± 7.00	161.63 ± 6.53	0.034
BMI Category, n (%)			0.290
Normal	10 (52.6%)	9 (47.4%)	
Overweight	2 (10.5%)	6 (31.6%)	
Obesity I	3 (15.8%)	2 (10.5%)	
Obesity II	3 (15.8%)	2 (10.5%)	

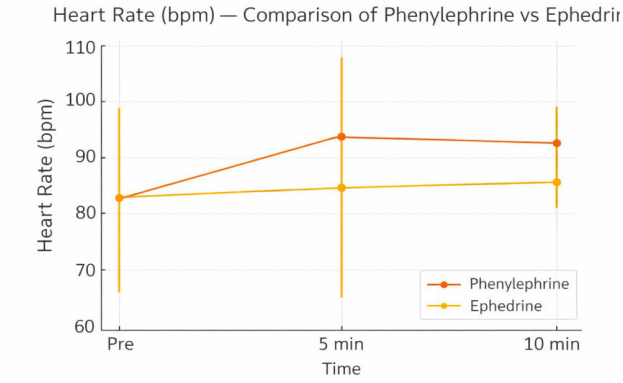
The effects of the two vasopressors on heart rate are summarized in Table 2. Baseline HR was similar between groups ($p=0.843$). A marked divergence was observed following prone positioning. While the phenylephrine group maintained a stable HR, the ephedrine group exhibited a significant increase.

Table 2. Comparison of Heart Rate (HR) Between Study Groups

Time Point	Ephedrine Group (bpm), mean ± SD	Phenylephrine Group (bpm), mean ± SD	p-value
Pre-induction (Baseline)	78.56 ± 20.71	77.34 ± 16.70	0.843
5 min Post-Prone	88.84 ± 19.60	77.84 ± 17.11	0.074
10 min Post-Prone	87.76 ± 8.77	79.93 ± 4.94	**0.002**

At 10 minutes post-positioning, the HR in the ephedrine group was significantly higher than in the phenylephrine group (87.76 ± 8.77 vs. 79.93 ± 4.94 bpm, p=0.002), confirming the chronotropic effect of ephedrine. The trend of HR changes over time is visually depicted in Figure 1.

Figure 1. Heart rate trends from baseline to 10 minutes after prone positioning in the ephedrine and phenylephrine groups

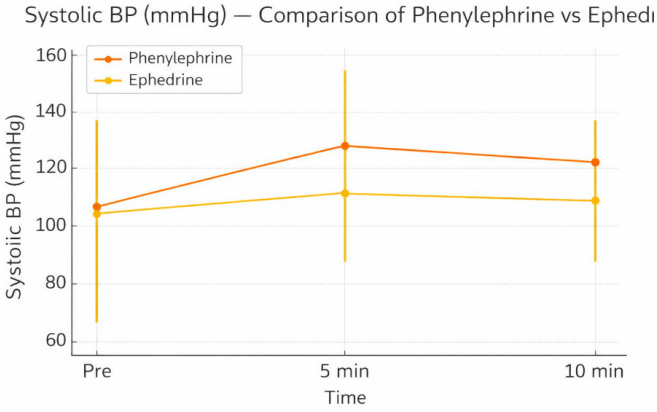


The comparative effects on systolic (SBP) and diastolic (DBP) blood pressure are shown in Table 3 and illustrated in Figure 2 and Figure 3.

Table 3. Comparison of Systolic and Diastolic Blood Pressure Between Study Groups

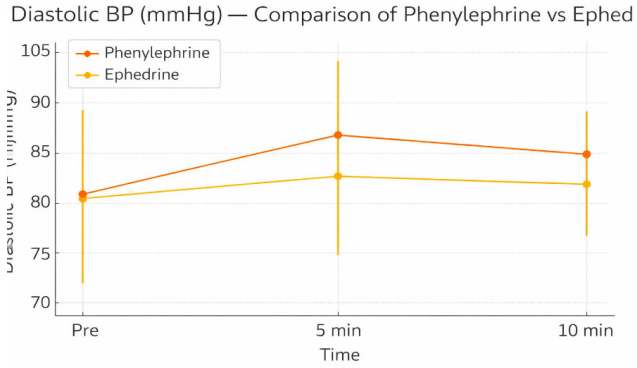
Parameter & Time Point	Ephedrine Group (mmHg), mean ± SD	Phenylephrine Group (mmHg), mean ± SD	p-value
Systolic BP - Baseline	133.08 ± 21.55	126.63 ± 18.32	0.327
Systolic BP - 5 min Post-Prone	143.65 ± 21.05	131.93 ± 18.35	0.075
Systolic BP - 10 min Post-Prone	136.15 ± 21.01	126.24 ± 18.50	0.132
Diastolic BP - Baseline	85.40 ± 14.33	84.28 ± 7.37	0.763
Diastolic BP - 5 min Post-Prone	90.68 ± 13.87	87.38 ± 7.43	0.366
Diastolic BP - 10 min Post-Prone	87.13 ± 13.58	84.15 ± 7.74	0.411

Figure 2. Comparison of blood pressure against Ephedrine and Phenylephrine (consolidated view)



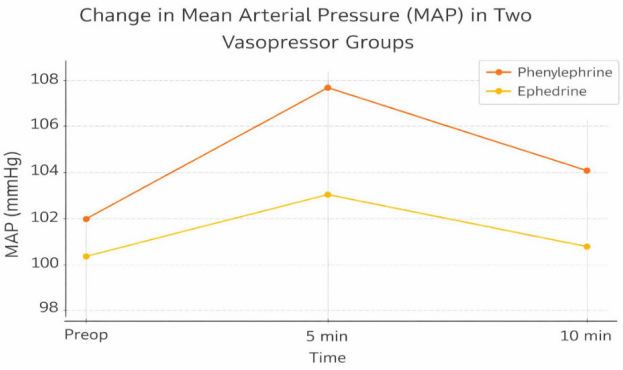
At baseline, both SBP and DBP were comparable. Although the ephedrine group showed a numerically greater increase in SBP at 5 minutes post-positioning (143.65 vs. 131.93 mmHg), the inter-group differences at all time points did not reach statistical significance ($p > 0.05$). Similarly, no statistically significant differences were observed in DBP between the groups throughout the observation period.

Figure 3. Systolic and diastolic blood pressure trends from baseline to 10 minutes after prone positioning (detailed view).



The analysis of MAP, a key parameter for organ perfusion and hypertension management, revealed distinct dynamic patterns between the groups (Table 4). The baseline MAP values for both groups are presented in Figure 4. Repeated-measures ANOVA demonstrated a highly significant main effect of time ($p < 0.001$) and, crucially, a significant Time × Group interaction effect ($p < 0.001$).

Figure 4. Pre-induction mean arterial pressure (MAP) in the phenylephrine and ephedrine groups



This indicates that the pattern of MAP change over time was different for each vasopressor. Ephedrine produced a more pronounced and sustained elevation in MAP, particularly evident at the 5-minute mark (108.34 ± 15.80 vs. 102.23 ± 10.39 mmHg). By 10 minutes, while MAP in both groups declined from the 5-minute peak, it remained higher in the ephedrine group (103.47 ± 15.71 vs. 98.18 ± 10.70 mmHg).

Table 4. Comparison of Mean Arterial Pressure (MAP) Between Study Groups

Time Point	Ephedrine Group (mmHg), mean ± SD	Phenylephrine Group (mmHg), mean ± SD	p-value (Between Groups)
Pre-induction (Baseline)	101.29 ± 16.43	98.40 ± 10.45	0.327
5 min Post-Prone	108.34 ± 15.80	102.23 ± 10.39	0.075
10 min Post-Prone	103.47 ± 15.71	98.18 ± 10.70	0.132
Statistical Effects (Repeated Measures ANOVA)			
Effect of Time	$p < 0.001$		
Time × Group Interaction	$p < 0.001$		
Between-Subjects Effect (Group)	$p = 0.283$		

Despite these dynamic differences, the overall between-subjects effect (comparing the grand mean of all measurements between groups) was not statistically significant (p=0.283), likely due to substantial inter-individual variability.

Discussion

Discussion

This study provides a comparative analysis of the hemodynamic profiles induced by prophylactic ephedrine and phenylephrine in surgical patients during the critical transition to the prone position. The findings underscore their distinct mechanisms of action and offer insights for tailored perioperative hypertension management[13].

The most salient difference was the significant chronotropic effect of ephedrine, evidenced by the marked increase in heart rate at 10 minutes post-positioning (Table 2, Figure 1). This is a direct pharmacological consequence of its β-adrenergic receptor agonism, which increases sinoatrial node automaticity and myocardial contractility[10]. In contrast, phenylephrine, a pure α_1-agonist, maintained heart rate stability. This absence of tachycardia is advantageous in patients where increased myocardial oxygen demand is a concern, such as those with coronary artery disease, and aligns with a key goal in hypertension management—controlling pressure without exacerbating cardiac strain[6,7]. The reflex bradycardia often associated with phenylephrine's pressor effect was not pronounced in our cohort, possibly due to the concurrent effects of general anesthesia on baroreceptor reflexes[9].

Regarding blood pressure stabilization, our results present a nuanced picture. While no statistically significant differences were found in systolic or diastolic pressures at individual time points (Table 3), the analysis of mean arterial pressure (MAP) dynamics revealed a critical distinction. The significant Time × Group interaction for MAP (Table 4) indicates that ephedrine produced a more robust and sustained pressor response compared to the more transient effect of phenylephrine. This can be attributed to ephedrine's dual mechanism: increasing cardiac output (via β_1-effects) while also causing peripheral vasoconstriction (via α-effects)[10]. Phenylephrine's action is solely vasoconstrictive, which may lead to a quicker compensatory adjustment or be more sensitive to the vasodilatory milieu of general anesthesia[9]. This sustained effect of ephedrine, visualized in Figure 4, suggests it may be more effective in preventing prolonged hypotensive episodes during prone surgeries, a factor crucial for maintaining spinal cord and renal perfusion[4,6].

Our findings corroborate the work of Xia et al., who also reported a more prolonged elevation in blood pressure with ephedrine during prone spine surgery[12]. This consistency across studies strengthens the evidence for its use in this specific context. However, our results contrast with the established preference for phenylephrine in obstetric spinal anesthesia, where it is favored for minimizing maternal tachycardia and resulting fetal acidosis[11]. This divergence highlights a fundamental principle: the

optimal vasopressor is context-dependent. The hemodynamic goals in a young, healthy parturient under spinal anesthesia differ markedly from those in an older patient undergoing prolonged prone surgery under general anesthesia. The prone position itself introduces unique challenges—reduced venous return and increased intrathoracic pressure—that may alter drug pharmacokinetics and hemodynamic responses[3,4]. Therefore, protocols for hypertension management cannot be extrapolated directly from one surgical setting to another.

From a hypertension management perspective, these profiles present a strategic choice. Ephedrine's stronger and longer-lasting pressor effect might be preferable in procedures with a high and sustained risk of positional hypotension or in patients where a higher perfusion pressure is deemed critical. Conversely, phenylephrine's milder, shorter-lived effect offers easier titratability and potentially a lower risk of inducing rebound hypertension once the surgical stimulus diminishes. The choice must be individualized, balancing the need for hemodynamic stability against the patient's tolerance for tachycardia.

Study Limitations and Future Directions

The observational design and lack of randomization limit the strength of causal inference. The sample size, while adequate for detecting the primary heart rate difference, may have been underpowered to identify subtler differences in blood pressure endpoints. Reliance on non-invasive blood pressure monitoring precluded the assessment of advanced hemodynamic variables like stroke volume variation or cardiac output, which would have provided a more complete picture of each drug's impact. Future research employing a randomized controlled trial (RCT) design with invasive hemodynamic monitoring is warranted to confirm these findings and elucidate the underlying effects on cardiac performance and vascular tone.

Conclusions

In conclusion, this study demonstrates that prophylactic ephedrine and phenylephrine confer distinct hemodynamic advantages relevant to hypertension management during surgery in the prone position. Ephedrine is associated with a more sustained increase in mean arterial pressure and a significant rise in heart rate, making it suitable for scenarios requiring robust and prolonged hemodynamic support. Phenylephrine provides effective pressure stabilization without causing tachycardia, offering a favorable profile for patients in whom increased heart rate is undesirable. The decision between these agents should be guided by a careful assessment of the patient's cardiovascular comorbidities and the specific hemodynamic goals of the surgical procedure. These findings contribute to the growing body of evidence supporting context-specific vasopressor selection in anesthetic practice.

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