

# Hemodynamic Effects of Ketamine Compared with Propofol as Continuous ICU Sedation in Mechanically Ventilated Patients: A Randomized Controlled Clinical Study

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## ABSTRACT

**Background:** Optimal sedation management for mechanically ventilated (MV) patients in the intensive care unit (ICU) remains essential for patient care.

**Objective:** This study aimed to compare the hemodynamic effects of ketamine and propofol on patient population.

**Patients and methods:** This parallel randomized controlled blind trial was conducted at Menoufia University Hospital, Egypt through the periode from October 2022 to October 2023. The study screened 145 mechanically ventilated ICU patients and only 100 patients who were randomized into two groups (50 in each group) and received continuous infusion sedation with either ketamine (Ketamin group) or propofol (Propofol group) for at least 48 hours. Baseline characteristics, sedation levels, pain control, and hemodynamic parameters were assessed.

**Results:** Baseline characteristics were similar between ketamine and propofol groups. Ketamine resulted in slightly higher heart rates at 45 minutes ( $80.08 \pm 9.18$  vs.  $75.78 \pm 8.92$ ,  $p = 0.019$ ) and 2 hours ( $77.42 \pm 9.52$  vs.  $73.42 \pm 9.33$ ,  $p = 0.036$ ). Mean arterial blood pressure was also slightly higher with ketamine at 45 minutes ( $85.8 \pm 8.57$  vs.  $80.96 \pm 9.83$ ,  $p = 0.010$ ) and throughout 48 hours. However, sedation scores and pain assessments were similar between groups, indicating comparable patient comfort. Ketamine showed lower incidences of hypotension (22% vs. 42%,  $p = 0.032$ ) and bradycardia (2% vs. 14%,  $p = 0.027$ ) but higher acute hypertension (38% vs. 16%,  $p = 0.013$ ) compared to propofol, suggesting a different safety profile.

**Conclusion:** This study provided evidence of the hemodynamic advantages of ketamine over propofol in ICU sedation for MV patients. Ketamine's ability to maintain stable cardiovascular parameters with fewer adverse events suggests its potential as an alternative sedative in this population. Further research is warranted to confirm these findings and optimize sedation strategies in critical care settings.

**Keywords:** Mechanical ventilation, Sedation, Ketamine, Propofol, Hemodynamic effects, ICU.

## INTRODUCTION

One essential component of the care of patients on MV is analgo-sedation, and optimizing sedation. These patients represents a dynamic and multifaceted challenge that demands a patient-centered approach, regular reassessment, and continuous research to enhance practices. That is because both mortality and morbidity rates in them remain notably high leading to significant costs within the healthcare system in addition to their suffering condition <sup>(1,2)</sup>.

Propofol, the recommended primary sedative for critically sick people undergoing mechanical ventilation (MV), does not come without risks. While, it has been connected to a lower incidence of delirium, shorter durations of MV, and shorter lengths of stay in the ICU, It is also linked to hypotension and bradycardia in 30%-60% of severely ill individuals. These dose-related hemodynamic abnormalities may have a negative impact on organ perfusion, especially in shock patients, where hypotension is closely connected to acute kidney injury and increased mortality <sup>(3,4,5)</sup>.

Ketamine, an N-methyl-D-aspartate (NMDA) antagonist, has found a new role as an ICU sedative. It exerts sedative and analgesic properties at low doses, and induces anesthesia at high doses <sup>(6)</sup>. Unlike propofol, ketamine triggers the sympathetic nervous system (SNS) by releasing catecholamines and inhibiting their absorption, which may improve heart rate (HR), blood

pressure (BP), and cardiac output (CO) <sup>(7)</sup>. Ketamine's versatility includes anesthetic, sedative, and dissociative properties via NMDA receptor antagonism, and agonism at  $\kappa$  and  $\mu$  opioid receptors. But what's truly exciting is its potential to benefit critically ill patients with respiratory failure. Ketamine exhibits neuroprotective and anti-inflammatory properties, a favorable hemodynamic profile, and bronchodilator effects, all of which could be game-changers in the ICU <sup>(8)</sup>. However, other studies found some negative effects, including a higher incidence of alarming neuropsychiatric issues including nightmares and hallucinations <sup>(9,10)</sup>.

Finally, in their comprehensive systematic review and metaanalysis about ketamine sedation in MV patients, **Manasco et al.** <sup>(1)</sup> concluded that there is a dearth of study data on ketamine usage in patients on mechanical ventilation in terms of both quantity and methodological quality, as well as clinical evidence of efficacy. Additionally, ketamine could be helpful as an alternative to sedatives, but it could also be harmful. Thus, before ketamine is widely used or adopted early in the sedative route, high-quality research investigations are needed <sup>(1)</sup>. Also, comparing of the hemodynamic effects of ketamine with those of propofol is highly needed for further clarification of these results, is essential for establishing the role of ketamine in sedating ICU patients who are mechanically ventilated.

Therefore, the main objective of this current randomized controlled trial was to compare the efficacy and safety of ketamine versus propofol in mechanically ventilated adult patients who are critically ill.

## PATIENTS AND METHODS

This parallel randomized controlled blind trial (RCT) was conducted on adult ill patients undergoing MV in the ICU at Menoufia University Hospital, Egypt from Oct-2022 to Oct-2023.

Stringent measures were implemented to ensure participant privacy, treating all patient data as confidential through the use of secret codes and individual private files were dedicated solely to ongoing medical research. Therefore, all data were de-identified following HIPAA Privacy Rule guidelines<sup>(11, 12)</sup>. To protect the patients' privacy and confidentiality, this required carefully deleting the patient's national identity number, medical record number, and other patient identifiers.

**Inclusion criteria:** Patients aged 18-65 years old who had been intubated within the preceding 24 hours, needed MV for more than 24 hours, and were on ICU sedation and pain protocol, with an associated infection required being in a septic state to participate in this study.

**Exclusion criteria:** Patients with a history of dementia or mental health issues, those taking antipsychotic or antidepressant medications at home, pregnant women, those anticipated to require MV < 24 hours, those on continuous infusion neuromuscular blockade and those using dexmedetomidine as the main sedative before randomization. Patients with cardiogenic shock, acute decompensated heart failure, or myocardial infarction, those with a history of end-stage liver failure (Child-Pugh score C), and those with a confirmed or suspected primary neurological injury (traumatic brain injury, ischemic stroke, intracranial hemorrhage, spinal cord injury and anoxic brain injury, or brain edema). Patients with persistent HR > 150 beats per minute (bpm) or SBP > 180 mmHg, patients identified as Do Not Resuscitate (DNR) and those expected to die within 24 hours. Patients on extracorporeal membrane oxygenation (ECMO), patients with refractory status epilepticus who are receiving ketamine infusion, patients with proven or suspected status asthmaticus and those in septic shock. Patients with daily opioid intake and presence of contraindications to any study drug, or on vasopressors.

**Randomization & blinding:** Randomization was done out using computer-generated random numbers and a predetermined randomization list established by an independent biostatistician and no stratification was performed<sup>(13)</sup>. The patients were randomized in 1:1 allocation to study group (ketamine group), which included 50 patients who received ketamine started at 0.5 mg/kg/hr and every 15 minutes titrated at 0.25 mg/kg/hr until the desired sedation level was reached at 4 mg/kg/hr. The control group (propofol group) included 50 patients who received propofol started at 0.3 to 0.6 mg/kg/hr and every 5 to 10 minutes titrated by 0.3 to 0.6

mg/kg/hr up to a maximum dosage of 4.5 to 4.8 mg/kg/hr to achieve the desired level of sedation.

Group allocation was concealed during the study. The study was double-blinded. The assessor who assessed the outcomes as well as the participant himself was blinded.

**Study procedures:** Upon admission to the ICU, intubated patients were linked to a MV operating in synchronized intermittent mandatory ventilation (SIMV) mode (Evita 4 Ventilator, Drägerwerk AG & Co. KGaA, Lübeck, Germany). Tidal volume parameters have been modified to 6-8 mL/kg for two-lung ventilation and 4-6 mL/kg for one-lung ventilation based on the calibrated body weight. The airway pressure was kept below 30cmH<sub>2</sub>O, while the inhaled oxygen concentration (FiO<sub>2</sub>) remained at 100%. Individual adjustments were made to the RR, inspiratory-expiratory time ratio, and positive end-expiratory pressure to maintain a PaCO<sub>2</sub> level of 35 to 45 mmHg. Comprehensive monitoring included capnography, 5-lead ECG, pulse oximetry, noninvasive BP, 12-lead ECG, chest radiography, and blood sample collection for analysis. Vital signs were monitored hourly.

Sedation levels were assessed using the Ramsay Sedation Score (RSS)<sup>(14)</sup>. Moreover, during the initial forty-eight hours, pain was evaluated every eight hours utilizing the Behavioral Pain Scale (BPS)<sup>(14)</sup>. The BPS includes three major components: facial status, upper limb movement, and moaning in non-intubated patients/patients on MV. The scale ranks pain from 3 to 12, with the patient's state being painless equals 3, mild from 4 to 6, moderate from 7 to 9, or severe pain from 10 to 12<sup>(15)</sup>.

Tachycardia and bradycardia were addressed with appropriate measures. Hypotension was managed with noradrenaline, dopamine, or a combination based on blood pressure values. Hypertension was addressed with nitroglycerine infusion. Insufficient analgesia resulted in fentanyl administration. Recovery time was recorded, and sedation infusion discontinuation for extubation was contingent upon specific criteria. Various measurements were recorded, including demographic data, monitoring of MAP and HR. Side effects such as vomiting, nausea, bradycardia, hypotension, and respiratory depression.

**Assessment of prognosis:** The prognosis was assessed using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score. In order to offer a broad indication of the severity of the condition, the APACHE II score is determined using a point system that takes into account the patient's age, physiological data, and medical history. Because acute physiologic dysfunction and the likelihood of dying from disease are closely related, it can categorize a range of patients based on their prognosis<sup>(16, 17)</sup>.

**Primary outcome:** The primary outcome variable was the changes in hemodynamics in term of changes in HR and MAP throughout the first forty-eight hours. For the initial hour, measurements were performed at 15-minute intervals, for the subsequent six hours, measurements

were taken hourly and for the initial forty-eight hours, measurements were taken every six hours.

**Secondary outcomes:** The secondary outcome variables were sedation levels that were assessed using RSS and RASS every eight hours during the first 48 hours, pain assessment using the BPS every eight hours within the initial 48 hours, the incidence of adverse effects like acute hypertension, maximum HR, blood pressure, the prognosis and predicted mortality rate estimated by the APACHE II score.

**Sample size justification:** The determination of the sample size was conducted using G\*Power 3.1.9.2 (Universitat Kiel, Germany). A research of *Atchley et al.* (18) observed that patients in the ketamine group exhibited significantly fewer instances of clinically significant bradycardia or hypotension, accounting for 34.6%, compared to those who received propofol, with a prevalence of 63.5%. The calculation considered a 95% confidence limit, the research had 80% power, a 1:1 group ratio, and four extra cases in each group to account for anticipated dropouts. Consequently, each group had 50 patients.

**Ethical approval:** The Research Ethics Committee of the Institutional Review Board of Menoufia University Faculty of Medicine's approved the study (approval #: 1/2023ANET and The ClinicalTrials.gov ID # NCT06243822). Patients' first degree relative consent was obtained clearly. Helsinki Declaration

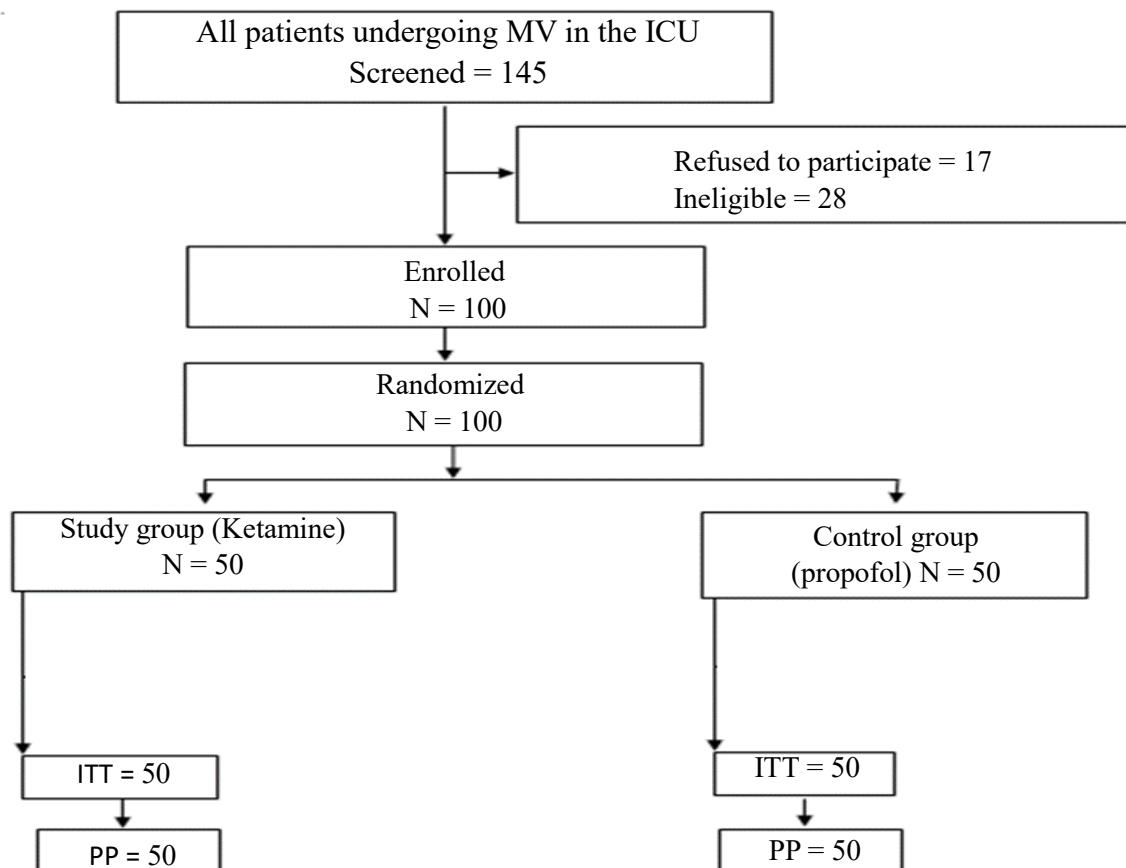
**was followed throughout the course of the investigation.**

### Statistical analysis

SPSS version 25.0 was used to perform the statistical analysis. The intent-to-treat population was the subject of the statistical analysis for safety and effectiveness. A 95% significance threshold was used for all statistical tests. Histograms and the Shapiro-Wilks test were used to assess the data distribution's normality. When applicable, the  $\chi^2$ -test or Fisher's exact test were used to analyze the qualitative variables, which were shown as frequency and percentage (%). The unpaired student t-test was used to assess quantitative parametric data, which were presented as mean  $\pm$  SD. The Mann-Whitney test was used to assess and show the median and IQR for quantitative non-parametric data. P-values with two tails  $\leq 0.05$  were deemed statistically significant.

### RESULT

A total of 145 patients undergoing MV in the ICU were invited to participate. The CONSORT diagram (Figure 1) showed that 17 cases refused to participate, and 28 were excluded before randomization because they did not meet the inclusion criteria, leaving 100 patients for randomization with 50 assigned to each group as follows: The study (Ketamine) group included 50 patients. The control (Propofol) group included 50 patients. None is excluded after randomization. Therefore, the intent-to-treat (ITT) population was 100 individuals, 50 patients in each group.



**Figure (1):** CONSORT diagram.

**Baseline characteristics:** The average age for the ketamine group was  $42.8 \pm 13.38$  years, but the propofol group had an average age of  $45.1 \pm 12.97$  years, with insignificant difference ( $p = 0.385$ ). In terms of gender distribution, the ketamine group had 38% females and 62% males, whereas the propofol group had 46% females and 54% males, with an insignificant difference ( $p = 0.418$ ). Additionally, there were insignificant differences among the groups in terms of weight, height, and BMI ( $p$  values  $> 0.05$ ) (Table 1).

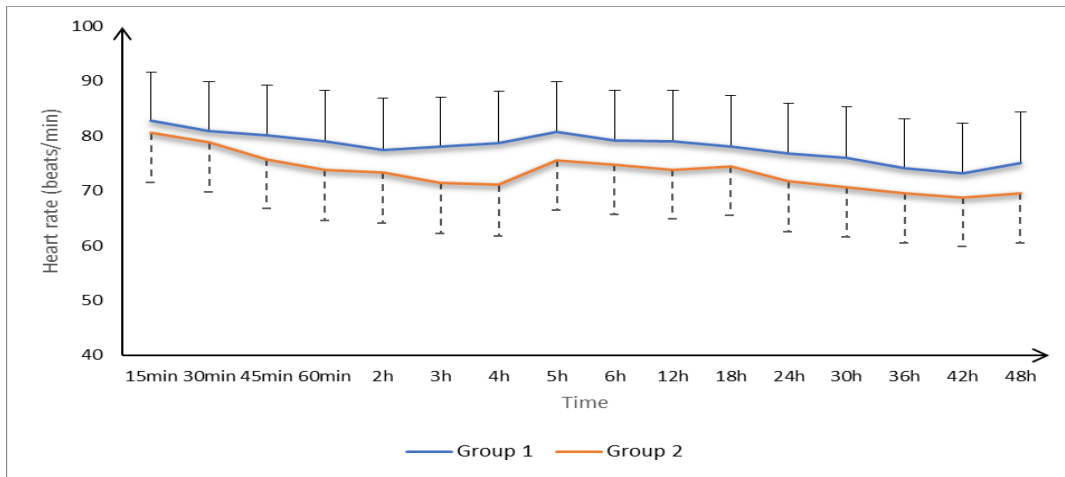
**Table (1):** Baseline characteristics

	Ketamine (N = 50)	Propofol (N = 50)	P value
	Mean $\pm$ SD	Mean $\pm$ SD	
Age (years)	$42.8 \pm 13.38$	$45.1 \pm 12.97$	0.385
Weight (Kg)	$72.38 \pm 8.8$	$70.6 \pm 10.1$	0.350
Height (m)	$1.7 \pm 0.07$	$1.69 \pm 0.07$	0.316
BMI (Kg/m <sup>2</sup> )	$25.12 \pm 4.01$	$24.81 \pm 3.73$	0.684
	n (%)	n (%)	P value
Gender			
Male	31 (62%)	27 (54%)	0.418
Female	19 (38%)	23 (46%)	

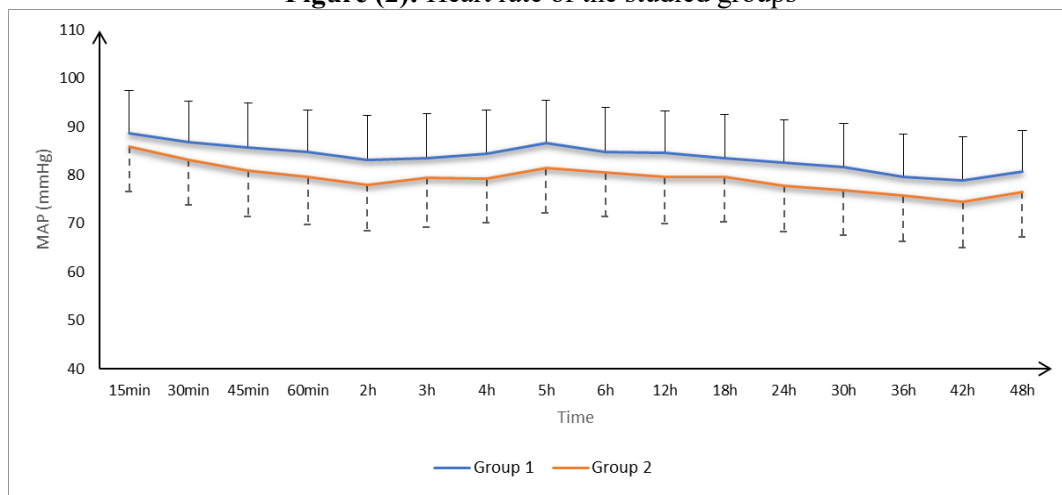
**Hemodynamic parameters during the study:** Comparison of hemodynamic parameters between the ketamine group and the propofol group revealed notable significant differences. Regarding heart rate (HR), ketamine consistently demonstrated significantly higher values at various time points, including 45 minutes ( $80.08 \pm 9.18$  vs.  $75.78 \pm 8.92$ ,  $p = 0.019$ ), 2 hours ( $77.42 \pm 9.52$  vs.  $73.42 \pm 9.33$ ,  $p = 0.036$ ), and up to 48 hours. In contrast, propofol exhibited lower HR across these intervals. Similarly, mean arterial blood pressure (MAP) showed significant differences, with ketamine resulting in higher values at 45 minutes ( $85.8 \pm 8.57$  vs.  $80.96 \pm 9.83$ ,  $p = 0.010$ ) and maintaining these differences up to 48 hours (Table 2 and figures 2 & 3).

**Table (2):** Hemodynamic parameters during the study: heart rate and mean arterial blood

	Heart rate, beat per minute			Mean arterial blood, mmHg		
	Ketamine (N = 50)	Propofol (N = 50)	P value	Ketamine (N = 50)	Propofol (N = 50)	P value
	Mean $\pm$ SD	Mean $\pm$ SD		Mean $\pm$ SD	Mean $\pm$ SD	
15min	$82.86 \pm 8.86$	$80.6 \pm 9.06$	0.210	$88.64 \pm 8.4$	$85.94 \pm 9.36$	0.132
30min	$80.94 \pm 8.98$	$78.86 \pm 9.06$	0.252	$86.84 \pm 9.05$	$83.2 \pm 9.42$	0.052
45min	$80.08 \pm 9.18$	$75.78 \pm 8.92$	<b>0.019</b>	$85.8 \pm 8.57$	$80.96 \pm 9.83$	<b>0.010</b>
60min	$79.1 \pm 9.2$	$73.84 \pm 9.22$	<b>0.005</b>	$84.86 \pm 9.12$	$79.62 \pm 9.55$	<b>0.006</b>
2h	$77.42 \pm 9.52$	$73.42 \pm 9.33$	<b>0.036</b>	$83.2 \pm 9.16$	$78 \pm 10.32$	<b>0.009</b>
3h	$78.08 \pm 9.02$	$71.46 \pm 9.28$	<b>&lt;0.001</b>	$83.56 \pm 8.96$	$79.54 \pm 9.09$	<b>0.028</b>
4h	$78.72 \pm 9.53$	$71.06 \pm 9.28$	<b>&lt;0.001</b>	$84.44 \pm 8.93$	$79.26 \pm 9.17$	<b>0.005</b>
5h	$80.78 \pm 9.09$	$75.58 \pm 9.11$	<b>0.005</b>	$86.64 \pm 9.23$	$81.42 \pm 9.12$	<b>0.005</b>
6h	$79.12 \pm 9.22$	$74.82 \pm 9.06$	<b>0.021</b>	$84.78 \pm 8.69$	$80.5 \pm 9.52$	<b>0.021</b>
12h	$78.98 \pm 9.42$	$73.82 \pm 8.97$	<b>0.006</b>	$84.62 \pm 8.97$	$79.58 \pm 9.33$	<b>0.007</b>
18h	$78.14 \pm 9.21$	$74.5 \pm 8.97$	<b>0.048</b>	$83.58 \pm 8.91$	$79.64 \pm 9.5$	<b>0.035</b>
24h	$76.86 \pm 9.04$	$71.72 \pm 9.21$	<b>0.006</b>	$82.56 \pm 8.94$	$77.86 \pm 9.2$	<b>0.011</b>
30h	$76.02 \pm 9.3$	$70.74 \pm 9.07$	<b>0.005</b>	$81.7 \pm 8.91$	$76.82 \pm 9.42$	<b>0.009</b>
36h	$74.08 \pm 9.07$	$69.62 \pm 9.1$	<b>0.016</b>	$79.6 \pm 8.99$	$75.72 \pm 9.39$	<b>0.037</b>
42h	$73.12 \pm 9.27$	$68.84 \pm 9$	<b>0.021</b>	$78.9 \pm 8.56$	$74.48 \pm 9.42$	<b>0.016</b>
48h	$75.08 \pm 9.3$	$69.62 \pm 9.12$	<b>0.004</b>	$80.74 \pm 8.84$	$76.58 \pm 9.39$	<b>0.025</b>



**Figure (2):** Heart rate of the studied groups



**Figure (3):** MAP of the studied groups.

**Analgo-sedation during the study:** As shown in table (3), the comparison of sedation scores between ketamine and propofol groups revealed variations in both RSSs and BPS measurements. In the RSSs, no statistically significant differences were observed at 1, 8, 16, 24, 32, 40, and 48 hours between the two groups. The median scores consistently ranged from 3 to 4 in both groups, indicating a comparable level of sedation. Similarly, when assessing pain using the BPS, no significant differences were found at various time points. The median BPS scores ranged from 4 to 5 in both groups, reinforcing the similarity in analgesic effects.

**Table (3):** Comparison among the two studied groups regarding Ramsay sedation score measurements and BPS measurements.

	Ramsay sedation score			Behavioral pain scale (BPS)		
	Ketamine (N = 50)	Propofol (N = 50)	P value	Ketamine (N = 50)	Propofol (N = 50)	P value
	Median (IQR)	Median (IQR)		Median (IQR)	Median (IQR)	
1h	3 (3 - 4)	4 (3 - 4)	0.061	4 (3 - 5)	5 (4 - 6)	0.083
8h	3 (3 - 4)	3 (3 - 4)	0.453	4 (3 - 5)	5 (4 - 5.75)	0.126
16h	3 (3 - 4)	4 (3 - 4)	0.321	4 (3 - 5)	4 (4 - 6)	0.309
24h	3 (3 - 4)	4 (3 - 4)	0.107	4 (4 - 5)	5 (4 - 6)	0.267
32h	3 (3 - 4)	4 (3 - 4)	0.259	4 (3 - 5)	4 (3 - 5)	0.838
40h	3 (3 - 4)	4 (3 - 4)	0.404	4 (4 - 5)	4.5 (4 - 5)	0.665
48h	3 (3 - 4)	4 (3 - 4)	0.284	4 (3 - 5)	5 (4 - 6)	0.348

IQR: interquartile range

**Assessment of severity and safety:** Complications were systematically assessed in both the ketamine and propofol groups, revealing significant differences in the incidence of hypotension, bradycardia, and acute hypertension. Hypotension was observed in 11 patients (22%) in the ketamine group compared to 21 patients (42%) in the propofol group, with a statistically significant difference ( $p = 0.032$ ). The majority of patients did not experience hypotension, accounting for 78% in the ketamine group and 58% in the propofol group. Bradycardia was noted in only 1 patient (2%) in the ketamine group, contrasting with 7 patients (14%) in the propofol group, which was statistically significant ( $p = 0.027$ ). Additionally, the incidence of acute hypertension was significantly higher in the ketamine group at 38% ( $n=19$ ) compared to 16% ( $n=8$ ) in the propofol group ( $p = 0.013$ ). Concerning the APACHE II scores at baseline and at the end of the study, there were no statistically significant differences observed between ketamine and propofol groups in terms of baseline APACHE II scores (median 9.5, IQR 6-14.75 vs. median 7.5, IQR 5-12.75,  $p = 0.227$ ) or end-of-study APACHE II scores (median 10, IQR 4.5-15 vs. median 6.5, IQR 5-14,  $p = 0.555$ ). These findings suggest that there was no significant discrepancy in APACHE II scores between patients treated with ketamine compared to those treated with propofol (Table 4).

**Table (4):** Comparison among the two studied groups regarding complications of the studied groups

	<b>Ketamine (N = 50)</b>	<b>Propofol (N = 50)</b>	<b>P value</b>
	<b>n (%)</b>	<b>n (%)</b>	
Hypotension	11 (22%)	21 (42%)	<b>0.032</b>
Bradycardia	1 (2%)	7 (14%)	<b>0.027</b>
Acute hypertension	8 (16%)	17 (34%)	<b>0.038</b>
	<b>Median (IQR)</b>	<b>Median (IQR)</b>	<b>P value</b>
Baseline APACHE II	9.5 (6-14.75)	7.5 (5-12.75)	0.227
End of study APACHE II	10 (4.5-15)	6.5 (5-14)	0.555

## DISCUSSION

Propofol has long been the standard sedative in ICU settings. Still, ketamine's utilization for ICU sedation is on the rise due to its well-established safety, sedative effects, and adequate analgesia at lower doses<sup>(2)</sup>. Ketamine's unique ability to stimulate the sympathetic nervous system (SNS) by inhibiting catecholamine reuptake that lead to beneficial effects on BP, CO, and heart rate<sup>(5)</sup>. This randomized controlled trial aimed to evaluate the hemodynamic effects of ketamine versus propofol as sedatives in mechanically ventilated ICU patients.

Our study revealed that ketamine significantly increased HR and BP measurements 45 minutes after

the start of infusion, while propofol demonstrated a higher incidence of hypotension, bradycardia, and acute hypertension. Both drugs provided effective sedation and analgesia without significant differences in efficacy. These results suggested that ketamine may offer hemodynamic advantages over propofol in maintaining stable cardiovascular parameters during sedation. The findings indicated that ketamine consistently demonstrated higher HR values at various time points, including 45 minutes ( $80.08 \pm 9.18$  vs.  $75.78 \pm 8.92$ ,  $p = 0.019$ ) and 2 hours ( $77.42 \pm 9.52$  vs.  $73.42 \pm 9.33$ ,  $p = 0.036$ ), extending up to 48 hours. Similarly, mean arterial blood pressure (MAP) showed significant differences, with ketamine resulting in higher values at 45 minutes ( $85.8 \pm 8.57$  vs.  $80.96 \pm 9.83$ ,  $p = 0.010$ ) and maintaining these differences for up to 48 hours. These findings highlighted ketamine's potential to maintain more favorable cardiovascular parameters during sedation. These results are in line with a research by **Atchley *et al.***<sup>(18)</sup> who examined the hemodynamic effects of ketamine as a continuous ICU sedative compared to dexmedetomidine or propofol. The study reported that ketamine was related with a decreased incidence of clinically relevant bradycardia or hypotension. That aligns with our observation that ketamine causes fewer adverse hemodynamic events than propofol. However, our results differ from those of **Sephri Nour *et al.***<sup>(19)</sup> who studied the impact of propofol and ketamine on brain oxygenation and hemodynamic markers in children having heart catheterization. They discovered that there were no appreciable variations in hemodynamic parameters between the 2 groups. This discrepancy could be attributed to the differences in patient populations and clinical settings between the studies. Similarly, **Hui *et al.***<sup>(20)</sup> conducted a retrospective study and found that ketamine when combined with another sedative, resulted in reduced vasopressor needs in mechanically ventilated patients compared to the conventional use of propofol and fentanyl. This confirms our results that ketamine can maintain hemodynamic stability more effectively than propofol.

Conversely, **Manasco *et al.***<sup>(4)</sup> demonstrated that ketamine was linked to a higher prevalence of cardiovascular problems such as tachycardia and hypertension. Variations in patient groups, dosage regimens, and research designs might be the cause of this discrepancy. Supporting our results, **Benken *et al.***<sup>(21)</sup> conducted a study that compared the hemodynamic effects of continuous infusions of propofol and dexmedetomidine in septic patients without shock. They found that propofol was associated with statistically significant adverse hemodynamic events, corroborating our finding that propofol increases the risk of hypotension and bradycardia.

In terms of sedation and pain control, our study found no statistically significant differences in RSSs or BPS measurements between the ketamine and propofol

groups. The median scores consistently ranged from 3 to 4 and 4 to 5, respectively. This suggests that both drugs achieve comparable sedation and analgesic effects in mechanically ventilated patients. Similar results were published by **Midega *et al.*** <sup>(22)</sup> who conducted a comparative study on ICU sedation using ketamine and propofol. They found that both agents provided effective sedation and analgesia with no significant differences in sedation scores or pain control metrics. This reinforces the conclusion that ketamine and propofol are equally effective in managing sedation and pain in ICU patients.

Complications were systematically assessed in both groups, revealing significant differences in the incidence of hypotension, bradycardia, and acute hypertension. Hypotension was observed in 22% of patients in the ketamine group compared to 42% in the propofol group ( $p = 0.032$ ). Bradycardia was noted in only 2% of patients in the ketamine group versus 14% in the propofol group ( $p = 0.027$ ). Conversely, acute hypertension was significantly higher in the ketamine group at 38% compared to 16% in the propofol group ( $p = 0.013$ ).

**Midega *et al.*** <sup>(22)</sup> also discussed the hemodynamic effects of ketamine, noting that ketamine tends to maintain cardiovascular stability better than other sedatives due to its sympathomimetic effects, which can lead to increased heart rate and blood pressure. This corroborates our findings of a lower incidence of hypotension and bradycardia in the ketamine group, alongside a higher incidence of acute hypertension. These hemodynamic properties of ketamine may be particularly advantageous in critically ill patients where maintaining stable BP and HR is crucial.

#### Strengths and weaknesses of our study:

Our study, a thorough evaluation of ketamine and propofol in a critical care setting, had several strengths. Conducted as a randomized controlled trial (RCT), it minimizes bias and establishes causality. Using a CONSORT diagram enhances transparency and reproducibility, and the study's sizable sample of 100 patients ensures sufficient power to detect differences. The comprehensive assessment of hemodynamic parameters, sedation levels, pain control, and intention-to-treat (ITT) analysis strengthens the validity of our findings.

However, there are limitations, the single-center design may limit generalizability to other ICU settings with different patient populations and practices. The short follow-up duration (48 hours) may not capture long-term outcomes and complications. Additionally, the absence of a cost-effectiveness analysis is a significant limitation for clinical decision-making in resource-limited settings. The study also did not assess other relevant outcomes such as delirium, long-term cognitive function, and patient satisfaction, highlighting areas for future research to provide a more comprehensive understanding.

## CONCLUSION

In summary, our study underscored the hemodynamic advantages of ketamine over propofol in ICU sedation. While, both drugs provided effective sedation and analgesia, ketamine maintained stable cardiovascular parameters with fewer incidences of hypotension and bradycardia, making it a valuable alternative. These findings highlighted the need for further research to confirm ketamine's optimal use in various clinical settings.

Our study contributed valuable insights by comparing the hemodynamic effects of propofol and ketamine in mechanically ventilated ICU patients. Ketamine demonstrated a more favorable impact on BP and HR than propofol, emphasizing its potential benefits as a supplementary sedative. However, more research is required to understand the broader clinical implications and optimize sedation strategies for improved patient outcomes. We recommend integrating ketamine into sedation protocols for mechanically ventilated ICU patients, focusing on careful dosing and continuous monitoring to ensure safety. Additionally, large-scale, multicenter trials are necessary to compare ketamine with other sedatives, enhancing understanding of its efficacy and safety. Future research should explore outcomes beyond hemodynamics, such as delirium prevention and long-term cognitive function, and tailor sedation approaches based on individual patient characteristics for optimized critical care.

**Conflict of interest:** None.

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