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VIEWPOINT

Hemodynamic Effects of Propofol

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Sedation is a fundamental and routine component of care provision in the cardiac intensive care unit (CICU). It is employed for multiple purposes, including the induction of anesthesia and endotracheal intubation during bedside procedures, facilitation of mechanical ventilation, and suppression of refractory ventricular tachycardia, among others. Despite its ubiquitous use, the optimal sedative agents for patients with cardiac critical illness remain unknown. Many commonly used agents have hemodynamic effects that may influence their selection in this population. Emerging consensus from clinical trials in general critically ill populations suggests that nonbenzodiazepine continuous sedation strategies may be associated with shorter duration of mechanical ventilation, shorter intensive care unit (ICU) lengths of stay, and possibly lower rates of delirium.[1] Such approaches often favor the use of propofol, a sedative γ-aminobutyric acid A receptor agonist. However, concerns about potential adverse hemodynamic effects of propofol, particularly hypotension and negative inotropy, lead some to limit the use of this particular agent or altogether avoid it in the CICU.[2] These concerns may conflict with the potential benefits of nonbenzodiazepine sedation in the ICU. Accordingly, we examine the evidence regarding acute hemodynamic effects of propofol in patient populations relevant to the CICU to determine whether current avoidance practices are justified.

Propofol is administered intravenously, can be given as a bolus for induction or as a continuous infusion for maintenance of sedation, and has multiple advantages, including rapid onset, short duration of effect, and quick elimination. Its pharmacokinetic profile is particularly attractive in the CICU setting, where sedation interruption is frequently necessary and rapid clearance of sedative metabolites is often desired. Another strength of propofol is its rapid metabolism via multiple cytochrome P450 isoforms, which renders propofol less dependent on renal or hepatic clearance than midazolam (a benzodiazepine). Propofol's metabolic profile can be particularly beneficial as it typically does not require significant dosage adjustment for renal or hepatic injury, unlike many other sedatives.

Propofol's most notable hemodynamic effects include hypotension and bradycardia. The incidence of hypotension was reported to be up to 42% and may be especially pronounced when bolused during anesthesia induction.[3] Compared with other anesthetics, propofol is associated with increased risks for bradycardia—in certain CICU patients, such as those with myocardial ischemia, this effect may be beneficial, while in others, such as those with aortic insufficiency, it may be undesirable.[4] The mechanisms underlying hypotension are multifactorial. One proposed pathway is the inhibition of the L-type calcium channels and activation of nitric oxide synthetase, resulting in relaxation of the vascular smooth muscle and therefore a reduction of systemic vascular resistance.[5] However, clinical data regarding propofol's hemodynamic consequences remain inconsistent and are mostly from retrospective studies.

One significant concern regarding the use of propofol in CICU pertains to potential negative inotropy. Observational studies have reported decreases, increases, or neutral effects on cardiac output (CO) and stroke volume (**Figure 1**).[6] Such variability may be

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ABBREVIATIONS AND ACRONYMS

CICU = cardiac intensive care unit

CO = cardiac output

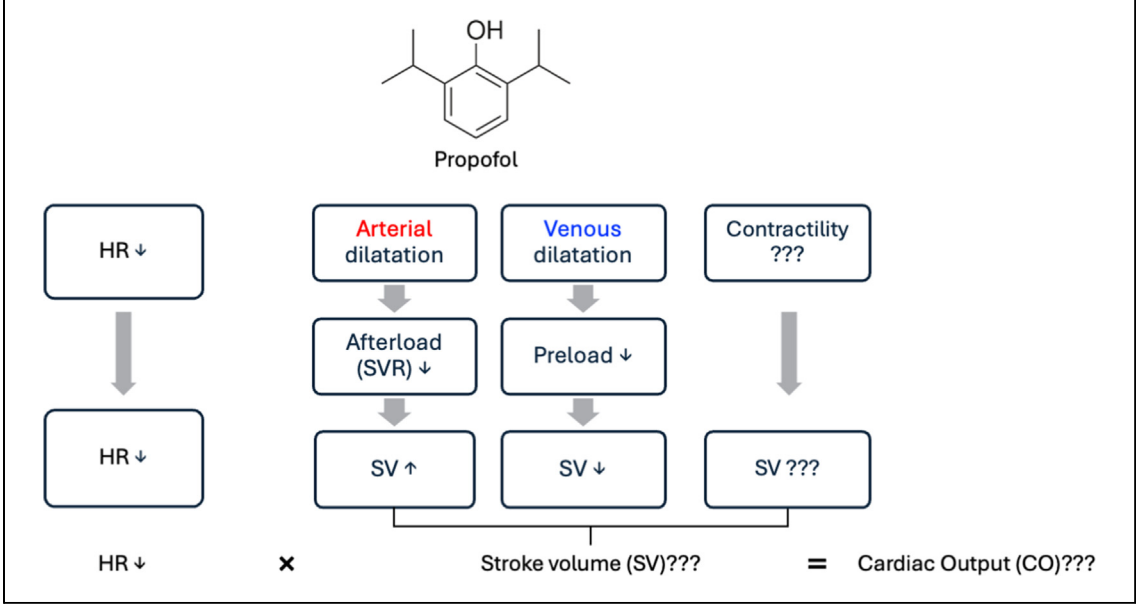
ICU = intensive care unit

attributable to differences in dosing, patient populations, and frequent coadministration with other sedatives or analgesics, which confound interpretations. Some effects on CO likely reflect a reduction in preload due to propofol-induced venodilatation, which decreases venous return and subsequently cardiac preload, potentially leading to a decrease in CO. By contrast, a reduction in afterload may augment stroke volume and thus potentially increase CO in some patients. Additionally, propofol inhibits the sympathetic nervous system, contributing to bradycardia—potentially lowering CO as well,[4] although such sympatholytic effect may reduce myocardial oxygen demands and in turn myocardial ischemia. Thus, although propofol may be associated with a reduction in CO, particularly at higher doses, the extent to which this effect is driven by changes in preload vs direct myocardial effects remains unclear. Several animal studies have demonstrated a dose-dependent decrease in myocardial contractility; however, these changes were seen at supra-therapeutic concentrations, largely exceeding the clinical range at which propofol is typically used for continuous sedation.[7] Furthermore, experimental evidence from animal studies of propofol-related infusion syndrome (a rare toxicity infrequently seen with high doses for long-duration infusions) suggests that propofol-related mitochondrial toxicity may produce direct cardiotoxic effects.[8] While microscopic and histological examination of myocardial tissue of propofol-related infusion syndrome patients indicates myocardial mitochondrial involvement,[9] definitive clinical evidence of direct negative inotropy at standard sedative doses remained limited.

Few clinical studies have evaluated the association between sedation with propofol on clinical outcomes in the CICU. However, most recently published retrospective studies have suggested that cardiac patients receiving propofol had lower propensity-matched mortality rates when compared with those receiving other sedatives,[1,10] suggesting that its direct negative inotropy, at standard sedative doses, may be less clinically relevant than initially suggested.

In summary, the benefits of propofol as a continuous sedative in the critically ill are increasingly compelling and offer several evidence-based and theoretical potential advantages in the CICU population. Studies have shown nonbenzodiazepine strategies are associated with shorter ICU stays, reduced mechanical ventilation duration, and lower rates of delirium.[1] Although concerns regarding negative inotropy stem from limited and conflicting data, the available evidence in the literature does not strongly support a direct negative inotropic effect of propofol at the lower doses used for continuous sedation in the CICU, suggesting it may have limited relevance to clinical practice. Nonetheless, the hemodynamic effects of propofol through hypotension (via reduced vascular tone) and bradycardia are important considerations in any critically ill patient. As such, they should be anticipated and mitigated when possible.

FIGURE 1 Hemodynamic Effects of Propofol



The literature is constrained by small sample sizes and confounding from coadministration of other agents. Ideal future research should be well-designed, prospective studies focusing on the hemodynamic effects of propofol, particularly on the question of whether it has negative inotropic effects at the doses used in usual care continuous sedation among high-risk populations such as those in cardiogenic shock and acute myocardial infarction. Clarifying mechanisms underlying propofol-associated hypotension and clarifying potential cardio- and neuro-protective effects could critically inform optimal sedation practices in the CICU. Until more definitive evidence is available, prudent clinical judgment—including careful patient selection, dose titration, and hemodynamic monitoring—is advised when maintaining any sedative in the CICU.

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