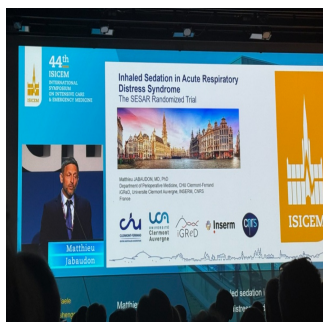


SESAR Trial: Inhaled Sedation in Acute Respiratory Distress Syndrome



Acute respiratory distress syndrome (ARDS) is common in ICU patients and has high mortality rates (35%-46%). Mechanical ventilation is essential for ARDS management and often requires sedation, though the optimal sedative choice remains unclear. Guidelines suggest light sedation with nonbenzodiazepine sedatives like propofol or dexmedetomidine, but specific recommendations for ARDS are lacking. Deep sedation and neuromuscular blockade may be needed for lung-protective ventilation in severe cases.

Inhaled volatile anaesthetics, such as sevoflurane, are emerging as alternatives to intravenous sedatives. A pilot study found sevoflurane improved oxygenation and reduced lung injury markers compared to midazolam, while other trials showed that inhaled sedation led to faster awakening and extubation. However, evidence specific to ARDS patients remains limited.

The Sevoflurane for Sedation in ARDS (SESAR) trial, presented at the ISICEM Congress in Brussels, aimed to evaluate whether early sedation with inhaled sevoflurane could improve outcomes, specifically increasing ventilator-free days, compared to propofol in patients with moderate to severe ARDS.

The SESAR trial was conducted from May 2020 to October 2023, with a 90-day follow-up. It enrolled adults with early moderate to severe ARDS across 37 French ICUs.

Patients were randomised to receive either inhaled sevoflurane (intervention) or intravenous propofol (control) for sedation up to 7 days. The primary outcome was ventilator-free days at 28 days, with 90-day survival as a key secondary outcome.

The trial enrolled 687 patients (mean age 65 years, 30% female), with 346 receiving sevoflurane and 341 receiving propofol. Both groups had a median sedation duration of 7 days. Ventilator-free days at 28 days were similar but slightly lower in the sevoflurane group. The 90-day survival rate was lower with sevoflurane (47.1% vs. 55.7%). Sevoflurane was also associated with higher 7-day mortality (19.4% vs. 13.5%) and fewer ICU-free days at 28 days.

In this trial, inhaled sedation with sevoflurane resulted in fewer ventilator-free days at 28 days and lower 90-day survival compared to intravenous propofol. The potential benefits of inhaled sedation in ARDS were previously suggested by studies showing the anti-inflammatory and lung-protective effects of volatile anaesthetics. However, the current findings contrast with earlier evidence suggesting benefits for volatile anaesthetics in non-ARDS patients.

The use of sevoflurane was associated with increased serum lactate, higher norepinephrine doses, and higher rates of acute kidney injury and nephrogenic diabetes insipidus, which may explain the worse clinical outcomes. This was consistent with previous studies on prolonged sevoflurane use, though some results were unexpected.

The study's design, involving early deep sedation with neuromuscular blockade followed by lighter sedation, might also have influenced outcomes. Despite this, the findings are relevant to contemporary ARDS management. The trial highlights the need for more research on the duration of sevoflurane use and the effects of other volatile anaesthetics like isoflurane. The ongoing SAVE-ICU trial will provide additional safety data on inhaled anaesthetics in ICU patients.

Overall, in this trial of patients with moderate to severe ARDS, inhaled sedation with sevoflurane led to fewer ventilator-free days and lower 90-day survival compared to intravenous propofol.

Source: [JAMA](#); ISICEM 2025 Presentation
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