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Review Article

# Anesthesia on Sepsis

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**Abstract**

Sepsis is defined as the life-threatening organ dysfunction by the third international consensus. To explore the difference between sepsis patient and normal patient about method of anesthesia, induction and maintain of anesthesia, we reviewed the articles and made a conclusion.

**Keywords:** Sepsis; Septic shock; Anesthesia

## Introduction

The initial Surviving Sepsis Campaign (SSC) guideline was firstly published in 2004. At that time, the guideline mentioned early goal-directed resuscitation of the septic patient during the first 6h after recognition [1]. In 2016, the Third International Consensus Definition for Sepsis and Septic Shock (Sepsis-3) defined sepsis as life-threatening organ dysfunction resulting from dysregulated host responses to infection. Septic shock is a subset of sepsis with circulatory and cellular/metabolic dysfunction associated with a higher risk of mortality [2]. The sepsis has increasing reported in hospital mortality by 13% to 13.3% in United States from 2004 to 2009, [3] and were associated with substantially increased ICU mortality rates greater than 40% [4]. From 2006 to 2015, the other survey demonstrated that, the annual sepsis incidence increased 50.5% from 31.5/100,000 to 47.4/100,000 persons [5]. In china, the most population nation, reported 8.68% developing serve sepsis in ICU [6]. The Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score used to assess the organ dysfunction [7]. Recently, the new measurement of organ dysfunction Quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) has been used in clinic, which performed greater predictive validity than SOFA (AUROC = 0.79; 95% CI, 0.78-0.80;P< .001) [2] However, the other study presented qSOFA has limited utility for predicting mortality in an ICU setting [8]. The therapy of sepsis is mainly focus on anti-infection and organ function support. Therefore, early antibiotic agent's administration and surgical necrotic tissue excision should be considered to perform during the first 3-6h. Hence, the anesthesiologists have to face the challenge about perioperative management of sepsis or septic shock patients. The difference of sepsis patient and normal patient about anesthesia is still undefined. We reviewed the articles and explained the issue.

## Method of Anesthesia

Based on limited clinical evidence about which type of anesthesia was benefited for patients with sepsis or septic shock, we should choose the appropriate method of anesthesia according to location and duration of the procedure [9]. Neuraxial Anesthesia (NA) and General Anesthesia (GA) were both adapted for abdomen and low extremity surgery. Tyagi A et al. compared General Anesthesia (GA) *vs*. general anesthesia plus thoracic epidural anesthesia (GT) for emergency laparotomy for small intestinal perforation peritonitis. They found the number of patients with major morbidity or 30-day mortality was statistically similar between the two groups (group GT, 0/33; group GA 4/33; P = 0.114). Nevertheless, GT group shortened the time to pass stools and oral feeding (4 ± 2 *vs*. 3 ± 1 days) (P = 0.006 and 0.012, respectively) [10]. Another cohort study reviewed 16,555 patients (9167 patients receiving GA and 7388 patients receiving NA). There was no statistically different between the two groups, but NA group showed low incidences of pneumonia (P = 0.035) and composite systemic infection (P = 0.006) with in 30 days [11]. Some physicians afraid of aggravating central nervous system CNS infection after neuraxial puncture. Recent publications show a low incidence (0.007% to 0.6%) of infection of the CNS after neuraxial puncture in patients at risk of or with ongoing bacteremia [12]. Similarly, in patients with preexisting infection or immunosuppression, a low incidence of infections following regional anesthetic techniques has been reported. Single-puncture techniques can be safe in sepsis or septic patients, it is only presence of infection at the puncture site or catheter insertion may be contraindicated [13]. In spite of this, considering unstable hemodynamics of sepsis patients, NA still will be performed prudently. Because of ultrasound used in anesthesia in recent years, Nerve block (NA) performed increasingly in anesthesia practice and postoperative analgesia. The benefit of NA was reduced systemic opiate agents and sufficient analgesia [14]. It seems performed the advantage of patient with sepsis. Nonetheless, further clinical evidence should prove the safety of NA utilized in patients with sepsis. GA still performed at most in anesthesia with sepsis because of the surgical site and appropriate analgesia. Generally, for unstable patient, etomidate and ketamine were selected to be induction medication as the ideal agents. Because of suppressed adrenal function, etomidate used in septic patient controversially [15]. Compared with thiopentone (5mg/kg), patients who administrated etomidate (0.26mg/kg) for induction have been found descending plasma cortisol levels and increasing peak ACTH in 120, 150, 180, 210, and 240 minutes post induction [16]. Another




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study also presented significant differences in adrenocortical function measured at 4 hours after intubation in patients received etomidate (0.3mg/kg) in contrast with midazolam (0.05-0.1mg/kg). However, there was no significant difference in 12h and 24h [17]. Inversely, evidences also found despite of transient insufficiency of adrenal function, single etomidate seemed not increase the morbidity and mortality of sepsis or septic shock [18-24]. Ketamine has been reported to improve survive and delay the mortality because of decreased serum interleukin 6 (IL-6) in rat model [25]. Recent study demonstrated ketamine protects rats against HMGB1-RAGE activation in a rat model of sepsis-induced ALI [26]. Jabre, P. et al compared etomidate and ketamine for intubation in critically patients. They found the mean maximum SOFA score between the two groups did not differ significantly (10.3 [SD 3.7] for etomidate *vs* 9.6 [3.9] for ketamine; mean difference 0.7 [95% CI 0.0-1.4], p=0.056). Intubation conditions did not differ significantly between the two groups (median intubation difficulty score 1 [IQR 0-3] in both groups; p=0.70). The percentage of patients with adrenal insufficiency was significantly higher in the etomidate group than in the ketamine group (OR 6.7, 3.5-12.7) [27]. Ketamine was significantly associated with hypotension immediately after intubation and at 15, 30, and 60 min post-RSI [RR = 1.78 (1.36–2.35)] in sepsis patients [24]. Propofol which was found the characteristic of antiinflammation can improve the survival rate of sepsis, reducing tissue damage and the release of cytokines [28-32]. However, because of suppressing circulation, Propofol should be administrated by titration as an induction agent. Limited researches focus on the benefit of maintain agents for sepsis patients by inhalation or intervein anesthetic.

One study compared Propofol and three types of inhalation in animals for 24h. The result indicated that volatile anesthetics dramatically improved survival and attenuate systemic inflammation as compared to Propofol. The main mechanism responsible for adverse Propofol effects could be an enhanced plasma endotoxin concentration, leading to profound hypotension, which was unresponsive to fluid resuscitation [33]. In addition, dexmedetomidine has been researched increasingly in recent year. Tasdogan, M et al. presented dexmedetomidine infusion decreases TNF-a, IL-1, and IL-6 levels and Intra-Abdominal Pressure (IAP) more than a Propofol infusion in sepsis [34]. Compared with midazolam, dexmedetomidine-treated patients spent less time on the ventilator, experienced less delirium, and developed less tachycardia and hypertension [35]. Bollen, P. J. et al. found the consumption of Propofol and fentanyl was significantly reduced in pigs with endotoxin-induced sepsis [36]. It is noteworthy that study demonstrated Propofol depressed H(2)O(2) production by blood and peritoneal neutrophils at clinical concentrations compared with midazolam in rats [37]. Opioid administration presented less influence in sepsis patients about the parameters including body temperature, body weight, water and food ingestion, mortality, analgesia, blood leukocytes, mean arterial blood pressure, vascular reactivity to phenylephrine, lung myeloperoxidase activity, and plasma levels of IL1-beta, glutamic-oxaloacetic, glutamic-pyruvic, lactate, creatinine and urea [38]. D-Ala2-D-Leu5-enkephalin (DADLE), a synthetic delta-opioid receptor agonist, has been shown to protect rats from sepsis probably by decreasing the serum level of HMGB1 [39]. Similar with Propofol, fentanyl also reduced inflammatory responses in septic mice [40]. Which opioid agent could be benefit for sepsis patient was still unclear. It needs more evidence further.

## Conclusion

There was no significant difference between Neuraxial Anesthesia (NA) and General Anesthesia (GA) in 30-day mortality. NA seemed to reduce the incidence of pneumonia and composite systemic infection. Single-puncture techniques can be safe in sepsis or septic patients, without the increasing incidence of infection. Etomidate and ketamine is benefit for unstable patients. Single etomidate seemed not increase the morbidity and mortality of sepsis or septic shock. Propofol should be administrated by titration as an induction agent. Dexmedetomidine developes less tachycardia and hypertension. Opioid agents influence less in sepsis patient and reduce the inflammatory responses.

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