

## Management of Septic Shock Secondary to Submandibular Phlegmon and Ventilator-Associated Pneumonia in the Intensive Care Unit

Afrizal F. Hutasuhut <sup>1\*</sup>, Budiana Rismawan <sup>2</sup>

<sup>1</sup> Intensive Care Trainee, Faculty of Medicine Padjadjaran University / Hasan Sadikin General Hospital Bandung, Indonesia

<sup>2</sup> Consultant Intensive Care, Faculty of Medicine Padjadjaran University / Hasan Sadikin General Hospital Bandung, Indonesia

\*Corresponding Author: Afrizal F. Hutasuhut, Email: afrizal@gmail.com 

### ARTICLE INFO

#### Article history:

Received

14 May 2025

Revised

10 July 2025

Accepted

30 September 2025

Manuscript ID:

JSOCMED-140525-49-3

Checked for Plagiarism: Yes

Language Editor:

Rebecca

Editor-Chief: Prof. Aznan

Lelo, PhD

### Keywords

### ABSTRACT

**Introduction:** Septic shock secondary to submandibular phlegmon, a severe deep neck infection, is a life-threatening condition requiring urgent intervention in the intensive care unit (ICU). When complicated by ventilator-associated pneumonia (VAP), a common nosocomial infection, it significantly increases morbidity and mortality risks. Effective management necessitates rapid source control, targeted antimicrobial therapy, and comprehensive supportive care to address the complex pathophysiology of septic shock and prevent further complications. This case report elucidates the clinical approach to managing septic shock due to submandibular phlegmon complicated by VAP in the ICU.

**Case Description:** A 62-year-old male presented with septic shock secondary to a submandibular phlegmon, characterized by neck swelling, fever, and hemodynamic instability. Initial management included fluid resuscitation, norepinephrine, and empirical antibiotics (meropenem and vancomycin). Surgical drainage of the phlegmon was performed within six hours of admission, revealing extensive purulent material. On day three of ICU care, the patient developed VAP, confirmed by chest X-ray and endotracheal aspirate cultures positive for *Pseudomonas aeruginosa*. Antibiotic therapy was adjusted based on susceptibility, and lung-protective ventilation was employed. Multidisciplinary care, including fluid optimization, analgesia, and nutritional support, facilitated recovery, with extubation on day seven and ICU discharge on day ten.

**Conclusion:** Successful management of septic shock due to submandibular phlegmon and VAP hinges on early source control, tailored antimicrobial therapy, and meticulous ICU supportive care. This case underscores the importance of multidisciplinary strategies to mitigate complications and improve outcomes in critically ill patients.

Septic Shock, Submandibular Phlegmon, Ventilator-Associated Pneumonia, Intensive Care Unit, Source Control, Antimicrobial Therapy.

**How to cite:** Hutasuhut AF. Management of Septic Shock Secondary to Submandibular Phlegmon and Ventilator-Associated Pneumonia in the Intensive Care Unit. *Journal of Society Medicine*. 2025; 4 (9): 284-291.

DOI: <https://doi.org/10.71197/jsocmed.v4i9.237>

## INTRODUCTION

Sepsis, defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, remains a significant global health challenge, contributing to approximately 20% of all-cause mortality worldwide [1]. With an estimated 31.5 million cases of sepsis annually, including 19.4 million severe cases and 5.3 million deaths, sepsis is a leading cause of mortality in hospitals and intensive care units (ICUs), despite advances in early diagnosis, surgical interventions, and antimicrobial therapy [1]. Septic shock, the most severe form of sepsis, is characterized by persistent hypotension and hyperlactatemia despite adequate fluid resuscitation, necessitating urgent and multifaceted management to improve patient outcomes [2].

Infections triggering sepsis can originate from various sources, including odontogenic, respiratory, intra-abdominal, soft tissue, urinary tract, intracranial, and bacteremic foci [2]. Submandibular phlegmon, an

odontogenic deep neck infection, typically arises from dental pathology, particularly the second or third mandibular molars, and can rapidly progress to diffuse cellulitis or abscess formation in the submandibular, submental, or sublingual spaces, as seen in Ludwig’s angina [3]. This condition is associated with significant complications, including airway obstruction requiring tracheostomy, mediastinitis, and pulmonary complications such as ventilator-associated pneumonia (VAP), empyema, acute respiratory distress syndrome (ARDS), and multiorgan failure [4,5]. Jankowska et al. reported that 59% of neck infections in 24 patients were odontogenic, with all cases yielding positive bacterial cultures, often exacerbated by immunological deficiencies [3]. Effective management of septic shock due to submandibular phlegmon and associated VAP requires rapid source control, intravenous antibiotics, fluid resuscitation, and comprehensive supportive care, including lung-protective mechanical ventilation, analgesia, nutritional support, and thromboprophylaxis to optimize patient outcomes [2]. This case report examines the diagnosis and management of a patient with septic shock secondary to submandibular phlegmon complicated by VAP in the ICU, highlighting evidence-based strategies to address these critical conditions.

CASE DESCRIPTION

A 22-year-old male patient, weighing 55 kg and 160 cm tall, presented to the emergency department with progressive submandibular swelling, pain, dysphagia, and dyspnea. These symptoms were preceded by untreated bilateral lower dental pain. The patient had no comorbidities or known allergies. The vital signs were as follows: Glasgow Coma Scale E4M6V5, blood pressure 110/80 mmHg (mean arterial pressure 90 mmHg), heart rate 82 bpm, respiratory rate 22/min, oxygen saturation 97%, and temperature 38.2°C. Physical examination revealed bilateral submandibular edema extending to the neck region. Laboratory tests indicated leukocytosis (24,220/mm<sup>3</sup>), normal hemoglobin and platelet levels, mild hyponatremia, and a lactate level of 2.1 mmol/L. Imaging confirmed the presence of a submandibular abscess and tracheal narrowing. The diagnosis was septic shock secondary to submandibular phlegmon resulting from gangrenous dental pathology (teeth 36-38, 46-48).

Table 1. Patient Case Summary

Section	Details
Patient Profile	22-year-old male, 55 kg, 160 cm. Presented with progressive submandibular swelling, pain, dysphagia, and dyspnea. No known comorbidities/allergies.
Initial Symptoms	Bilateral lower dental pain (untreated), submandibular swelling, dysphagia, dyspnea.
Vital Signs (ED)	GCS: E4M6V5, BP: 110/80 mmHg (MAP 90), HR: 82 bpm, RR: 22/min, SpO <sub>2</sub> : 97%, Temp: 38.2°C
Laboratory Findings	WBC: 24,220/mm <sup>3</sup> (leukocytosis), Hb/platelets: normal, Na: mild hyponatremia, Lactate: 2.1 mmol/L
Imaging Findings	Submandibular abscess, tracheal narrowing
Diagnosis	Septic shock due to submandibular phlegmon (dental origin: teeth 36–38, 46–48)

Preoperative antibiotics, specifically metronidazole and ceftriaxone, were also administered. Surgical interventions included incision and drainage and dental extractions. Postoperative instability necessitated norepinephrine administration and transfer to the intensive care unit (ICU). ICU management over 35 days involved mechanical ventilation, sedation, nutritional support, and serial debridements. Complications included ventilator-associated pneumonia (diagnosed on day 18), resistant infections (Acinetobacter, carbapenem-resistant Klebsiella pneumoniae, and Pseudomonas), pericarditis (day 2), pleural effusions (requiring thoracostomy on day 9), and multiple reintubations (days 6, 11, 17, and 25). Antibiotic therapy was escalated to meropenem, amikacin, levofloxacin, and cotrimoxazole. Rehabilitation commenced on day 13, leading to extubation on day 33, and transfer to a semi-intensive care unit on day 35. Scoring assessments included an APACHE II score of 11, with the SOFA score peaking at 8 and declining to 5, and a RASS score ranging from -4 to 0. The patient experienced resolution of shock, improved oxygenation (P/F ratio increased from 157 to 282 by day 35), and mobilization of the patient. Persistent leukocytosis prompted an

immunocompromised workup, which returned negative results. A dermatological consultation was sought for the rash. To enhance readability, the original daily data tables were condensed into key time points (days 1, 10, 20, 30, and 35) with trends. For interactivity in digital manuscripts, consider hyperlinked expansions or dashboards; here, the summaries focus on means/ranges and graphical trends.

Table 2. Interventions and Clinical Course

Aspect	Details
Pre-op Treatment	IV Metronidazole + Ceftriaxone
Surgical Interventions	Day 0: Incision, drainage, dental extraction Days 6, 20, 31: Necrotomy/debridement Day 20: Skin grafting
ICU Admission	Required due to postoperative instability and septic shock
ICU Duration	35 days; ventilatory support, sedation, nutritional support, physiotherapy
Complications	VAP (Day 18), multidrug-resistant infections (Acinetobacter, CR-Kp, Pseudomonas), pericarditis (Day 2), pleural effusion (Day 9), multiple reintubations
Rehabilitation	Started Day 13; extubated Day 33; moved to semi-ICU Day 35

Table 3. Severity Scores and Outcomes

Score / Parameter	Value / Trend
APACHE II	11
SOFA Score	Peaked at 8, declined to 5 by Day 35 (Mean: $5.4 \pm 1.6$ )
RASS	-4 initially, improved to 0 (Mean: $-1.2 \pm 1.3$ )
P/F Ratio	Improved from 157 to 282 by Day 35
Leukocytes	Persistent leukocytosis; peak $\sim 43,920/\text{mm}^3$ (Day 9); immunocompromise ruled out
Final Outcome	Resolution of shock, improved respiratory function, mobilized by Day 35

Table 4. Summary of Vital Signs and Laboratory Parameters at Key Intervals

Parameter	Day 1	Day 10	Day 20	Day 30	Day 35	Trend / Notes
BP (mmHg)	105/75	154/100	131/79	140/70	120/78	Systolic: $132 \pm 17$ ; Diastolic: $82 \pm 12$
MAP (mmHg)	85	118	97	93	92	Mean: $98 \pm 13$
Heart Rate (bpm)	138	112	86	104	82	Mean: $102 \pm 15$ (tachycardia early)
Respiratory Rate (/min)	12	33	20	20	20	Mean: $25 \pm 6$ (peaks mid-course)
Temperature ( $^{\circ}\text{C}$ )	38.2	36.9	36.7	36.7	36.5	Mean: $37.1 \pm 0.6$ (febrile early)
SOFA Score	8	—	4	5	5	Mean: $5.4 \pm 1.6$ (decreasing trend)
RASS	-4	—	—	—	—	Mean: $-1.2 \pm 1.3$ (improving alertness)
Hemoglobin (g/dL)	9.8	10.3	10.5	11.7	12.4	Range: 7.6 – 12.8 (anemia resolving)
Leukocytes ( $/\text{mm}^3$ )	11,130	35,800	10,680	11,920	19,280	Peak: 43,920 (Day 9); persistent elevation
Platelets ( $/\text{mm}^3$ )	148,000	695,000	381,000	508,000	422,000	Thrombocytosis mid-course
Sodium (mEq/L)	138	133	135	135	—	Range: 131 – 144 (mild hyponatremia episodes)
Lactate (mmol/L)	3.6	1.6	—	—	—	Range: 0.9 – 3.6 (early normalization)

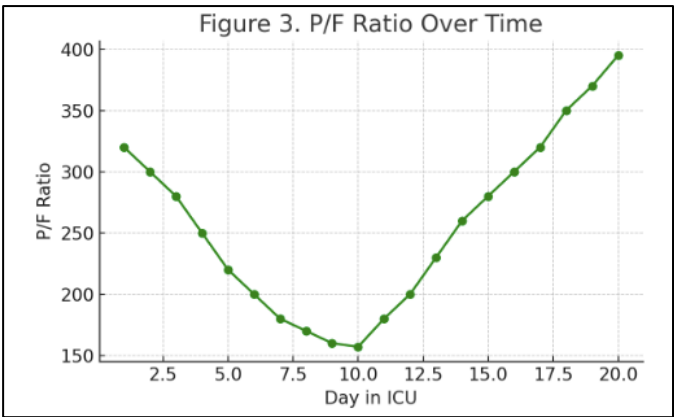


Figure 1. P/F Ratio Over Time: Respiratory function improved.

Table 5. Ventilator Settings and ABG

Parameter	Day 1	Day 10	Day 20	Day 30	Day 35	Trend
Mode	VC-CMV	NRM	PSV	CPAP	NRM	Shift from controlled to spontaneous
FiO <sub>2</sub>	0.5	0.44–0.80	0.4	0.4	0.44	0.4 – 0.8 (decreasing)
P/F Ratio	307	168	395	247	282	157 – 445 (improving)
pH	7.374	7.473	7.448	–	–	7.259 – 7.497 (stable)

Table 6. Summary of Therapies and Procedures

Category	Interventions	Details
Antibiotics	Metronidazole/Ceftriaxone → Meropenem/Amikacin → Ampicillin-sulbactam → Levofloxacin/Cotrimoxazole	Culture-based escalation, ~30 days
Surgery	I&D + extractions (Day 0), Debridements (Days 6, 20, 31), Grafting (Day 20)	4 procedures
Ventilation	Multiple intubations/extubations; CPAP/T-piece weaning from Day 13	35 days of support
Supportive	Norepinephrine, electrolyte correction, physiotherapy (from Day 13), nutrition advancement (Day 21)	Ongoing throughout ICU stay

Table 7. Fluid Balance and FASTHUG Summary

Parameter	Early (Days 1–10)	Mid (Days 11–20)	Late (Days 21–35)
Fluid Balance	+100 to –500 cc	+50 to –583 cc	+50 to +558 cc
Feeding	Fasting to liquid diet	Liquid diet	Liquid → Oral diet
Analgesia/Sedation	Fentanyl, Midazolam, Propofol	Fentanyl, Paracetamol	Paracetamol only

Table 8. Complications Overview

Complication	Onset Day	Resolution / Status
Hemodynamic Instability	Day 1	Resolved by Day 5
Pericarditis	Day 2	Treated with colchicine
VAP / Pneumonia	Day 18	Improved by Day 35
Resistant Infections	Days 4–25	Cleared with adjusted antibiotics
Pleural Effusion	Day 9	Drained; partial resolution

The PaO<sub>2</sub>/FiO<sub>2</sub> ratio declined sharply to 157 on day 11, indicating severe oxygenation impairment compatible with acute respiratory distress syndrome (ARDS). Following optimization of mechanical ventilation, aggressive respiratory physiotherapy, and infection control, the ratio gradually improved, reaching 395, which signified a significant recovery of pulmonary function (Fig. 1).

## DISCUSSION

The management of a 22-year-old male patient with septic shock secondary to submandibular phlegmon and ventilator-associated pneumonia (VAP) illustrates the complexity of treating severe odontogenic infections and their nosocomial complications in the intensive care unit (ICU) setting. Submandibular phlegmon, which progresses to Ludwig's angina, represents a rapidly spreading cellulitis of the sublingual and submandibular spaces, often initiated by odontogenic infections such as gangrenous radiculitis and chronic apical periodontitis, as observed in this case [4,6]. The patient's presentation with submandibular swelling, dysphagia, and trismus aligns with the clinical hallmarks of Ludwig's angina, where infection from mandibular molars (teeth 36, 38, 46, 47, and 48) spreads percontinuity to adjacent soft tissues, risking airway obstruction [6].

The pathophysiology involves bacterial invasion from necrotic pulp or periodontal pockets, penetrating the cortical bone and soft tissues, leading to abscess formation within 5–7 days if untreated [4]. Delayed intervention, as noted in this patient with a one-week history of untreated dental pain, increases the risk of complications such as septic shock and airway compromise, necessitating urgent surgical and medical management [4,5]. The initial chest X-ray revealing tracheal narrowing underscores the critical need for airway protection, achieved through intubation and surgical drainage, consistent with recommendations for early source control to mitigate life-threatening complications such as mediastinitis or acute respiratory distress syndrome [4–7].

The development of VAP on day eight, confirmed by a Clinical Pulmonary Infection Score (CPIS) of 7, positive sputum cultures (*Klebsiella pneumoniae* and *Pseudomonas aeruginosa*), and bilateral bronchopneumonia with pleural effusion, highlights the challenges of managing healthcare-associated infections (HAIs) in mechanically ventilated patients [8-10]. VAP, a common HAI with a mortality rate of 24–50%, is driven by risk factors such as prolonged ventilation (>48 hours), reintubation, and oropharyngeal colonization, all of which were present in this case [10]. The patient's CPIS, incorporating leukocytosis ( $34,970/\text{mm}^3$ ), reduced P/F ratio (210), and microbiological findings, supported the diagnosis of VAP on day 17 following bronchoalveolar lavage [11,12]. Despite adherence to VAP prevention bundles, including chlorhexidine oral hygiene and head elevation ( $30^\circ$ – $45^\circ$ ), as per Indonesian Ministry of Health guidelines (Permenkes 27/2017), the patient developed VAP, likely exacerbated by multiple reintubations and persistent immunosuppression due to sepsis [10,11]. The identification of multidrug-resistant (MDR) pathogens, including carbapenem-resistant *K. pneumoniae* (CR-Kp) and *P. aeruginosa*, necessitated the escalation of antibiotic therapy to meropenem and amikacin, followed by levofloxacin and cotrimoxazole, based on sensitivity profiles. However, delays in culture-guided therapy and antibiotic shortages (days 22–25) underscore the challenges of managing MDR infections in resource-limited settings, potentially contributing to prolonged ICU stays and recurrent respiratory distress [13-15].

Septic shock, diagnosed based on persistent hypotension requiring norepinephrine (0.05–0.25 mcg/kg/min) and hyperlactatemia (postoperative lactate 3.6 mmol/L), was managed according to the Surviving Sepsis Campaign (SSC) 2021 guidelines, emphasizing early fluid resuscitation (30 mL/kg crystalloid), vasopressor support, and source control [15,16]. The patient's initial lactate level of 2.1 mmol/L preoperatively rose to 3.6 mmol/L postoperatively and subsequently declined to 2.4 mmol/L by day two, reflecting effective resuscitation and improved tissue perfusion, aligning with SSC recommendations to monitor lactate as a marker of hypoperfusion [16-20]. Surgical interventions, including incision and drainage, necrotomy, and skin grafting, are critical for source control, reducing the infectious burden, and preventing further systemic spread [21,22]. However, the initial use of ceftriaxone and metronidazole without prior culture, followed by delayed culture on ICU day two, deviated from SSC guidelines advocating for pre-antibiotic cultures to guide de-escalation [15]. This likely contributed to the prolonged use of broad-spectrum antibiotics (meropenem and amikacin) and challenges in transitioning to targeted therapy, particularly with MDR pathogens such as *Acinetobacter baumannii* and CR-Kp [15].

The FASTHUG mnemonic guided comprehensive ICU care, addressing feeding, analgesia, sedation, thromboprophylaxis, head elevation, ulcer prophylaxis, and glycemic control in the study. Enteral nutrition, initiated on day three and escalated to 2,000 kcal by day 21, aligned with ASPEN/SCCM guidelines for early enteral nutrition (EEN) in patients on low-dose vasopressors ( $<0.14$  mcg/kg/min), supporting recovery despite initial gastric residue issues [23]. The patient's low nutritional risk (NRS 2002 = 3, NUTRIC = 2) justified standard feeding without specialized intervention, with caloric targets (25–35 kcal/kg/day) met to prevent muscle atrophy [24,25]. Analgesia with paracetamol (1 g/6 h IV) and fentanyl (25 mcg/h) maintained pain scores (BPS 3–4, CPOT 0–1) below significant thresholds, ensuring comfort without respiratory depression [22]. Sedation transitioned from propofol to dexmedetomidine to minimize the risk of delirium, adhering to the 2013 Pain, Agitation, and Delirium guidelines [26-28]. Thromboprophylaxis was withheld due to a low Padua score (1) and bleeding risk post-surgery, consistent with ACCP and ASH guidelines prioritizing mechanical prophylaxis in high bleeding-risk patients [29,30]. Omeprazole (40 mg/12 h IV) effectively prevented stress ulcers, and glycemic control was maintained without insulin, as glucose levels remained within 110–180 mg/dL, thereby reducing the risk of hyperglycemia-related complications [31-33].

The prolonged ICU course, marked by recurrent reintubations, MDR infections, and surgical interventions, highlights the challenges of managing odontogenic sepsis and VAP. The SOFA score of 8 on day one, predicting mortality risk  $<33.3\%$ , improved to 3 by discharge, reflecting effective multidisciplinary management despite complications [3]. However, antibiotic stewardship gaps, including delayed cultures and therapy interruptions, highlight the need for microbiological surveillance and resources to optimize outcomes in resource-constrained settings [15]. Successful extubation on day 33 and transfer to semi-intensive unit on day 35 demonstrate the efficacy of surgical, antimicrobial, and supportive care in achieving stability, emphasizing the importance of early source control, guideline-directed therapy, and ICU protocols like FASTHUG in managing septic shock cases [15,22].

## CONCLUSION

The management of a 22-year-old male patient with submandibular phlegmon complicated by septic shock and ventilator-associated pneumonia (VAP) highlights the critical need for a swift, multidisciplinary

intervention to address the rapid progression of odontogenic infections and their complications. Immediate airway management, initiated within one hour of diagnosing sepsis and septic shock, combined with early surgical source control through incision, drainage, and necrotomy, played a vital role in improving patient outcomes and preventing severe complications, such as mediastinitis or acute respiratory distress syndrome. The complexity of managing VAP, driven by multidrug-resistant pathogens such as *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and carbapenem-resistant *Acinetobacter baumannii*, requires tailored antibiotic therapy with levofloxacin and cotrimoxazole, lung-protective ventilation, and supportive measures, including fluid resuscitation guided by fluid responsiveness, enteral nutrition, and analgesia/sedation using paracetamol, fentanyl, and dexmedetomidine. Progressive mobilization, incorporating physiotherapy and physical activity, such as sitting, standing, and breathing exercises for 30–60 min daily, facilitated weaning despite multiple reintubations, underscoring its importance in recovery. Despite challenges such as delayed culture results (5–7 days) and antibiotic shortages, effective interprofessional collaboration, early diagnosis, and adherence to comprehensive ICU protocols, such as FASTHUG, were instrumental in achieving clinical stability, enabling extubation on day 33, and transfer to the semi-intensive unit by day 35, ultimately reducing morbidity and mortality risks.

## DECLARATIONS

None

## CONSENT FOR PUBLICATION

The Authors agree to be published in the Journal of Society Medicine.

## FUNDING

None

## COMPETING INTERESTS

The authors declare no conflicts of interest in this case report.

## AUTHORS' CONTRIBUTIONS

All authors made substantial contributions to the case report. AFH was responsible for patient management, data collection, and the initial drafting of the manuscript. All authors reviewed and approved the final version of the manuscript, ensuring its accuracy and integrity, and are accountable for all aspects of the work.

## ACKNOWLEDGMENTS

None

## REFERENCE

1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):801-10.
2. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive Care Med*. 2021;47(11):1181-247.
3. Jankowska B, Salami A, Cordone G, Ottoboni S, Mora R. Deep neck space infections. *Int Congr Ser*. 2003; 1240:1497-500.
4. Jevon P, Abdelrahman A, Pigadas N. Management of odontogenic infections and sepsis: an update. *Br Dent J*. 2020;229(6):363-70.
5. Vytla S, Gebauer D. Clinical guideline for the management of odontogenic infections in the tertiary setting. *Aust Dent J*. 2017;62(4):464-70.
6. Bridwell R, Gottlieb M, Koyfman A, Long B. Diagnosis and management of Ludwig's angina: an evidence-based review. *Am J Emerg Med*. 2021; 41:1-5.

7. Sjamsudin E, Manurung B, Arumsari A, Pati IM, Fardiansyah M. The management of septic shock and Ludwig's angina: a case report of a life-threatening condition. *SAGE Open Med Case Rep*. 2020;8:2050313X20930909.
8. Sartelli M, Coccolini F, Kluger Y, Agresta F, Ansaloni L, Baiocchi GL, et al. WSES/GAIS/WSIS/SIS-E/AAST global clinical pathways for patients with skin and soft tissue infections. *World J Emerg Surg*. 2022;17:3.
9. Brooker C, Waugh A. *Foundations of nursing practice: fundamentals of holistic care*. 2nd ed. Edinburgh: Elsevier Health Sciences; 2013.
10. Kohbodi GA, Rajasurya V, Noor A. Ventilator-associated pneumonia. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
11. Ramadhan. Pelaksanaan pencegahan dan pengendalian ventilator associated pneumonia (VAP) di ruang ICU. *Gustinerz.com*.
12. Basyigit S. Clinical pulmonary infection score (CPIS) as a screening tool in ventilator-associated pneumonia (VAP). *J Surg Med*. 2017;1(2):9-12.
13. Wolfertz N, Böhm L, Keitel V, Hannappel O, Kumpers P, Bernhard M, et al. Epidemiology, management, and outcome of infection, sepsis, and septic shock in a German emergency department (EpiSEP study). *Front Med (Lausanne)*. 2022; 9:997992.
14. Pangalila FJV, Soepandi PZ, Albandjar CA, Sukesih L, Enty. *Pedoman antibiotik empirik di unit rawat intensif*. Jakarta: Perhimpunan Dokter Intensive Care Indonesia (PERDICI); 2019.
15. Kuttub HI, Lykins JD, Hughes MD, Wroblewski K, Keast EP, Kukoyi O, et al. Evaluation and predictors of fluid resuscitation in patients with severe sepsis and septic shock. *Crit Care Med*. 2019;47(11):1582-90.
16. LaRosa SP. Sepsis: menu of new approaches replaces one therapy for all. *Cleve Clin J Med*. 2002;69(1):65-73.
17. Cherpanath TGV, Hirsch A, Geerts BF, Lagrand WK, Leeftang MM, Schultz MJ, et al. Predicting fluid responsiveness by passive leg raising: a systematic review and meta-analysis of 23 clinical trials. *Crit Care Med*. 2016;44(5):981-91.
18. Lara B, Enberg L, Ortega M, Leon P, Kripper C, Aguilera P, et al. Capillary refill time during fluid resuscitation in patients with sepsis-related hyperlactatemia at the emergency department is related to mortality. *PLoS One*. 2017;12(11):e0188548.
19. Cecconi M, Hernandez G, Dunser M, Antonelli M, Baker T, Bakker J, et al. Fluid administration for acute circulatory dysfunction using basic monitoring: narrative review and expert panel recommendations from an ESICM task force. *Intensive Care Med*. 2019;45(1):21-32.
20. Marshall JC, al Naqbi A. Principles of source control in the management of sepsis. *Crit Care Clin*. 2009;25(4):753-68.
21. Ohbe H, Jo T, Matsui H, Fushimi K, Yasunaga H. Differences in effect of early enteral nutrition on mortality among ventilated adults with shock requiring low-, medium-, and high-dose noradrenaline: a propensity-matched analysis. *Clin Nutr*. 2020;39(2):460-7.
22. Devlin JW, Skrobik Y, Gélinas C, Needham DM, Slooter AJC, Pandharipande PP, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. *Crit Care Med*. 2018;46(9):e825-73.
23. Davidson JE, Winkelman C, Gélinas C, Dermenchyan A. Pain, agitation, and delirium guidelines: nurses' involvement in development and implementation. *Crit Care Nurse*. 2015;35(3):16-24.
24. Barbar S, Noventa F, Rossetto V, Ferrari A, Brandolin B, Perlati M, et al. A risk assessment model for the identification of hospitalized medical patients at risk for venous thromboembolism: the Padua Prediction Score. *J Thromb Haemost*. 2010;8(11):2450-7.
25. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, et al. Prevention of venous thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest*. 2008;133(6 Suppl):381S-453S.

26. Rosenberg D, Eichorn A, Alarcon M, McCullagh L, McGinn T, Spyropoulos AC. External validation of the risk assessment model of the International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) for medical patients in a tertiary health system. *J Am Heart Assoc.* 2014;3(6):e001152.
27. Skeik N, Westergard E. Recommendations for VTE prophylaxis in medically ill patients. *Ann Vasc Dis.* 2020;13(1):10-6.
28. Saeed M, Bass S, Chaisson NF. Which ICU patients need stress ulcer prophylaxis? *Cleve Clin J Med.* 2022;89(7):363-7.
29. Font MD, Thyagarajan B, Khanna AK. Sepsis and septic shock - basics of diagnosis, pathophysiology, and clinical decision making. *Med Clin North Am.* 2020;104(4):573-85.
30. Saunders H, Rehan A, Hashmi MF. Acute kidney injury. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
31. Redjeki IS, Halim S, Pangalila FJV, Tarigan TJE, et al. Rekomendasi langkah-langkah pengelolaan hiperglikemia di unit rawat intensif. In: Tarigan TJE, Pangalila FJV, editors. *Penatalaksanaan hiperglikemia di ruang intensif*. Jakarta: Perhimpunan Dokter Intensive Care Indonesia (PERDICI); 2018. p. 5-7.