

Factors influencing lower respiratory tract infection in older patients after general anesthesia Journal of International Medical Research 49(9) 1–11 © The Author(s) 2021 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/03000605211043245 journals.sagepub.com/home/imr



### Tingting Chen, Yali Yasen, Jianjiang Wu and Hu Cheng

#### Abstract

**Objective:** Pulmonary complication is common in older patients after surgery. We analyzed risk factors of lower respiratory tract infection after general anesthesia among older patients.

**Methods:** In this retrospective investigation, we included older patients who underwent surgery with general anesthesia. Logistic regression analyses were performed to determine risk factors of lower respiratory tract infection.

**Results:** A total 418 postoperative patients with general anesthesia were included; the incidence of lower respiratory tract infection was 9.33%. Ten cases were caused by gram-positive bacteria, 26 cases by gram-negative bacteria, and 2 cases by fungus. We found significant differences in age, smoking, diabetes, oral/nasal tracheal intubation, and surgery duration. Logistic regression analysis indicated that age  $\geq$ 70 years (odds ratio [OR] 2.028, 95% confidence interval [CI] 1.115–3.646), smoking (OR 2.314, 95% CI 1.073–4.229), diabetes (OR 2.185, 95% CI 1.166–4.435), nasotracheal intubation (OR 3.528, 95% CI 1.104–5.074), and duration of surgery  $\geq$ 180 minutes (OR 1.334, 95% CI 1.015–1.923) were independent risk factors of lower respiratory tract infections.

**Conclusions:** Older patients undergoing general anesthesia after tracheal intubation have a high risk of lower respiratory tract infections. Clinical interventions should be provided to prevent pulmonary infections in patients with relevant risk factors.

#### Keywords

Infection, pulmonary, respiratory, surgery, general anesthesia, treatment, nursing

Date received: 29 December 2020; accepted: 26 July 2021

Department of Anesthesiology, The First Affiliated Hospital of Xinjiang Medical University, Urumqi, China

**Corresponding author:** 

Hu Cheng, No. 137, Liyushan Road, Xinshi District, Urumqi, Xinjiang Uygur Autonomous Region, China. Email: chenghu\_tiger@126.com

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).

### Introduction

General anesthesia produces temporary inhibition of the central system after the inhalation, intramuscular injection, or intravenous injection of anesthetics. This manifests as loss of consciousness, skeletal muscle relaxation, and reflex inhibition, which can alleviate the patient's pain and ensure the smooth progress of an operation.<sup>1</sup> Tracheal intubation is a common method of airway management after general anesthesia.<sup>2</sup> However, tracheal intubation destroys the natural barrier of the upper respiratory tract, causing the patient's nose and throat to become vulnerable to bacterial invasion and increasing the risk of lung infection.<sup>3</sup> Lower respiratory tract infections are usually caused by bacteria and viruses.<sup>4,5</sup> The wide application of antibacterial drugs has changed the types of pathogenic bacteria that can invade the lower respiratory tract; the number of drugresistant pathogen strains has gradually increased together with the level of drug resistance, and multidrug-resistant strains have appeared, bringing great challenges to clinical treatment.<sup>6</sup>

In recent years, with accelerated growth of the global aging population, the number of older patients undergoing surgical treatment has been increasing each year.<sup>7</sup> General anesthesia with tracheal intubation has the advantages of safe and effective management.<sup>8</sup> It is a widely used method of clinical anesthesia, but use of general anesthesia makes patients more prone to developing respiratory infections after surgery.<sup>9</sup> According to reports, patients undergoing tracheal intubation under general anesthesia have an approximately 8.12% to 21.36% probability of developing pulmonary infection.<sup>10,11</sup> With aging of the body, the immune function of older patients becomes weaker, making these patients more susceptible to infection with various pathogens.<sup>12</sup> At present, the reasons for older patients being at risk of developing lower respiratory tract infection after tracheal intubation under general anesthesia are not fully understood. Therefore, analysis of the clinical treatment in older patients with lower respiratory tract infections after general anesthesia is important to understand the relevant etiological characteristics and risk factors of lower respiratory tract infection. The findings of such investigation can provide evidence for the selection of clinically sensitive antibiotics and support the development of preventive measures against related risk factors to reduce the incidence of lower respiratory tract infections in this patient population.

#### Methods

#### Ethics

Our study followed a retrospective study design. The study was approved by the ethics committee of The First Affiliated Hospital of Xinjiang Medical University (MX20190112) and was carried out after receiving signed, written informed consent from all patients. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.<sup>13</sup>

#### Patients

We selected older patients who underwent surgery with general anesthesia at our hospital from 1 March 2019 to 30 September 2020 to participate in this study. The inclusion criteria were patients who (1) were age  $\geq$ 60 years; (2) underwent surgery with general anesthesia at our hospital; (3) had normal lung function before surgery; (4) agreed to participate in this study. Patients were excluded if they (1) were with pneumonia diagnosed before surgery; (2) had a history of pulmonary resuscitation within 3 months; (3) had severe cardiopulmonary disease, severe liver and kidney insufficiency, or severe immune deficiency; (4) did not agree to participant in this study.

## Diagnosis of lower respiratory tract infections

We referred to the 2016 American Society of Infectious Diseases Hospital Acquired Pneumonia guidelines<sup>14</sup> and relevant standards<sup>15,16</sup> for the diagnosis of lower respiratory tract infections. The specific diagnostic criteria were as follows: in physical examination, moist rales heard on chest auscultation; imaging (chest X-ray, chest computed tomography) suggesting inflammatory changes in the lungs; symptoms such as cough and sputum appearing within 3 days after surgery; body temperature >37.6°C; and white blood cells  $\geq 11.0 \times 10^9/L$ . According to the diagnosis of lower respiratory tract infection, patients were divided into the group with infection and the group with no infection.

#### Bacterial detection

We tested samples from all patients with lung infections for pathogenic bacteria. We collected sputum samples from patients and cultured the samples within 30 minutes. Pathogens were identified and screened in our laboratory using an automated bacterial identification instrument (VITEK-2; bioMérieux, Craponne, France).

#### Statistical analysis

We conducted statistical analysis for the incidence of lung infection after general anesthesia. We calculated the distribution of pathogenic bacteria for patients with lung infections. On this basis, we compared differences between the two groups in terms of basic characteristics (including age, sex, body mass index [BMI], alcohol consumption [defined as drinking  $\geq$ 200 mL beer or

wine per day for at least 3 months], smoking history [defined as smoking  $\geq$ 4 cigarettes for at least 1 month]), underlying diseases, duration of surgery, intraoperative blood infusion, and length of hospital stay.

We used IBM SPSS 20.0 software to analyze all the data (IBM Corp., Armonk, NY, USA). In univariate analysis, the enumeration data are expressed as number and percentage, and the  $\chi^2$  test was used. Variable data are expressed as mean  $\pm$ standard deviation, and comparisons between groups were carried out using the *t*-test. Multivariate logistic regression analysis was used to analyze independent risk factors. p < 0.05 was considered to indicate statistical significance.

#### Results

## Detected infections and patient characteristics

A total of 418 postoperative patients who underwent general anesthesia were included. Of these, 39 patients (mean age  $71.28 \pm 6.94$  years, 27 men) were diagnosed with lower respiratory tract infection. The incidence of lower respiratory tract infection in patients with general anesthesia was 9.33%. We conducted sputum analysis of samples from those 39 patients, and pathogens were detected in 38 samples. As presented in Table 1, there were 10 cases of infection caused by gram-positive bacteria, 26 cases caused by gram-negative bacteria, 2 cases of fungal infection. Pseudomonas aeruginosa was the most commonly detected bacterial species (36.84%) in patients with lower respiratory tract infection.

As shown in Table 2, there were significant differences among patients with lung infection with respect to age, smoking, diabetes, oral/nasal tracheal intubation, and duration of surgery (all p < 0.05). We found no significant differences in sex, BMI, alcohol consumption, hypertension,

hyperlipidemia, type of surgery, intraoperative blood infusion, and length of hospital stay.

# Logistic regression analysis for risk factors of lower respiratory tract infection

Table 3 shows the variable assignment in multivariate logistic regression. As shown

**Table 1.** Pathogen distributions in patients withlower respiratory tract infection.

Pathogens	Cases	Percent
Gram-positive bacteria	10	26.32%
Staphylococcus aureus	5	13.17%
Streptococcus	2	5.26%
Enterococcus	3	7.89%
Gram-negative bacteria	26	68.42%
Pseudomonas aeruginosa	14	36.84%
Acinetobacter baumannii	5	13.16%
Klebsiella pneumoniae	7	18.42%
Fungus	2	5.26%
Candida albicans	2	5.26%
Total	38	100%

in (Table 4), logistic regression analysis indicated that age  $\geq$ 70 years (odds ratio [OR] 2.028, 95% confidence interval [CI] 1.115–3.646), smoking (OR 2.314, 95% CI 1.073–4.229), diabetes (OR 2.185, 95% CI 1.166–4.435), nasotracheal intubation (OR 3.528, 95% CI 1.104–5.074), and duration of surgery  $\geq$ 180 minutes (OR 1.334, 95% CI 1.015–1.923) were independent risk

Table 3.	Variable	assignment	of	multivariate
logistic re	gression.			

Factors	Variable	Assignment
Infection Age (years) Smoking	Y X <sub>1</sub> X <sub>2</sub>	yes = 1, no = 2 $\geq 70 = 1$ , $<70 = 2$ yes = 1, no = 2
Diabetes Nasotracheal intubation	X <sub>3</sub> X <sub>4</sub>	yes = 1, no = 2 yes = 1, no = 2
Duration of surgery (minutes)	X <sub>5</sub>	$\geq$ 180 = 1, <180 = 2

Table 2. Characteristics of included patients.

Variable	Infection group (N = 39)	No-infection group (N = 379)	$t/\chi^2$	p-value
Male/female, n	27/12	265/114	1.321	0.091
Age (years)	$71.28\pm6.94$	67. 13 $\pm$ 9.22	1.213	0.016
BMI (kg/m <sup>2</sup> )	$\textbf{23.39} \pm \textbf{1.09}$	$\textbf{24.01} \pm \textbf{1.45}$	1.242	0.082
Alcohol consumption	19 (48.72%)	148 (39.05%)	1.118	0.069
Smoking	30 (76.92%)	101 (26.65%)	1.093	0.007
Hypertension	20 (51.28%)	172 (45.38%)	1.239	0.074
Diabetes	19 (48.72%)	88 (23.21%)	1.187	0.023
Hyperlipidemia	8 (20.51%)	71 (18.73%)	1.216	0.089
Oral/nasal tracheal intubation	18/21	23/356	1.128	0.002
Type of surgery			2.066	0.054
Abdominal surgery	13 (33.33%)	8 (3 . 3%)		
Ear, nose and throat surgery	10 (25.64%)	95 (25.07%)		
Thoracic surgery	7 (17.95%)	74 (19.53%)		
Orthopedic surgery	5 (12.82%)	59 (15.57%)		
Neurosurgery	4 (10.26%)	33 (8.71%)		
Duration of surgery (minutes)	$\textbf{208.73} \pm \textbf{38.52}$	$173.22 \pm 30.94$	1.106	0.035
Intraoperative blood infusion	21 (53.85%)	178 (46.97%)	1.218	0.095
Length of hospital stay (d)	$5.73 \pm 1.15$	$\textbf{5.13} \pm \textbf{1.24}$	1.177	0.102

Variables	β	SE	OR	95% CI	p-value
Age $\geq$ 70 years	0.128	0.119	2.028	1.115–3.646	0.025
Smoking	0.119	0.184	2.314	1.073-4.229	0.039
Diabetes	0.123	0.114	2.185	1.166-4.435	0.033
Nasotracheal intubation	0.131	0.124	3.528	1.104-5.074	0.017
Duration of surgery $\geq$ 180 minutes	0.173	0.306	1.334	1.015-1.923	0.041

Table 4. Logistic regression analysis of risk factors for lower respiratory tract infection.

SE, standard error; OR, odds ratio; CI, confidence interval.

factors of lower respiratory tract infection (all p < 0.05).

#### Discussion

General anesthesia for tracheal intubation is widely used in clinical practice because of its good anesthesia effect, mild intraoperative response, low physical and mental trauma to patients, and high level of acceptance.<sup>17,18</sup> However, postoperative lower respiratory tract infections are a common complication after general anesthesia.<sup>19</sup> In clinical nosocomial infections related to general anesthesia with tracheal intubation, lower respiratory tract infections account for more than 70% of cases.<sup>20</sup> The process of tracheal intubation breaks the natural barriers of the nasal cavity and throat. These then lose their protection against external pathogenic infectious agents, causing the trachea and bronchi of the respiratory tract to become vulnerable to exposure and colonization with bacteria in the oropharynx, which can migrate to the lower respiratory tract.<sup>21</sup> Additionally, general anesthesia destroys the mucous membrane of the respiratory tract and produces local secretions, which can promote bacterial growth and reproduction.<sup>22</sup>

With aging, the immune function of the body gradually weakens and the function of various organs gradually declines.<sup>23</sup> Several studies<sup>24,25</sup> have reported that pathogens commonly found in the lower respiratory tract infection after general anesthesia

with tracheal intubation mainly comprise gram-negative bacteria, which is consistent with the results of this study. It is particularly important to identify which factors can increase the risk of lung infection and take timely measures to treat and prevent pulmonary infections.<sup>26</sup> The results of previous studies<sup>27,28</sup> have shown that in clinical nosocomial infections related to general anesthesia for tracheal intubation, lower respiratory tract infections account for more than 59% of nosocomial surgical infections. We have found that the incidence of lower respiratory tract infections in patients with general anesthesia was 9.33%. A previous study<sup>29</sup> found that 48 out of 400 older patients had lower respiratory tract infections, with an incidence of 12.0%, which is higher than that of our results. This difference may be owing to the different study populations. In the present study, we found that age  $\geq 70$  years, smoking, diabetes, nasotracheal intubation, and duration of surgery >180 minutes were independent risk factors of lower respiratory tract infections. Therefore, early intervention is needed for patients who have these risk factors.

We found that older age was an independent risk factor for lower respiratory tract infection after general anesthesia. Many studies<sup>30,31</sup> have also shown that older age is an independent risk factor for pulmonary infection. This may be related to the progressive loss of functional reserves in various organ systems among older patients,

which includes changes in the patient's heart and lung function as well as changes in the lung structure, which cause lung elastic recoil to decrease.<sup>32</sup> With aging, the cross-sectional area of the pulmonary capillary bed diminishes, resulting in increased pulmonary vascular resistance and pulmonary artery pressure.<sup>33</sup> These changes increase the risk of perioperative lung complications in patients.<sup>34</sup> At the same time, the respiratory tract mucosa shrinks in older individuals, the function of phagocytic cells is weakened, and the motility of respiratory tract cilia declines, resulting in poor mucous clearance and reduced ability of the respiratory tract to clear pathogenic bacteria, which can then multiply rapidly in the respiratory tract.<sup>35</sup> Moreover, the immune function of older people is reduced, with poor immune system defense and a weakened immune response to infection. Tolerance for aggressive operations is low in older people; thus, lung infections are more likely to occur in these patients.<sup>36</sup>

Long-term heavy smoking weakens the motor ability of bronchial mucosal cilia, which weakens the capacity for airway self-purification, stimulates airway glands to secrete more mucus, and hinders the function of alveolar phagocytes.<sup>37</sup> These are all related to the high incidence of postoperative pulmonary infections in patients who undergo surgery.<sup>38</sup> Smoking can also induce chronic obstructive pulmonary disease (COPD).<sup>39</sup> Quitting smoking for more than 4 weeks before surgery can alleviate clinical symptoms in patients with COPD, reduce pulmonary inflammation, and lower the incidence of postoperative pulmonary complications.<sup>40</sup> It has been reported that smoking can increase the incidence of perioperative respiratory complications, and detecting the level of carbon monoxide exhaled by patients before surgery can serve to assess their risk of perioperative respiratory complications.<sup>41</sup> Quitting smoking 48 hours before surgery can reduce the Hamilton Anxiety Rating Scale score and the need for anesthetic drugs, improve patient comfort, reduce the level of nicotine in the blood, and gradually improve mucociliary function and airway hypersensitivity.<sup>42,43</sup> Therefore, it is important for patients who are smokers and require surgery to quit smoking prior to undergoing any surgical procedure.

Many clinical factors can cause lower respiratory tract infections in patients after general anesthesia. Previous studies<sup>44,45</sup> have shown that damage to the lower respiratory tract mucosa after tracheal intubation and interaction between the lower respiratory tract and the exterior environment are the main causes of lower respiratory tract infections in postoperative patients. Р. aeruginosa, Acinetobacter baumannii, Klebsiella pneumoniae. *Staphylococcus* aureus. and Streptococcus pneumoniae are common causative agents of lower respiratory tract infections, and different strains have different levels of resistance to antibiotics.<sup>46</sup> In clinical practice, antibiotics should be used rationally in accordance with the results of testing and characteristics of the causative pathogen. Diabetes can cause metabolic disorders in the body and increase the risk of complicated infections.<sup>47</sup> Such infections can easily induce cardiac insufficiency, lead to respiratory and circulatory failure, and affect the patient's prognosis.48

The advantages of oral endotracheal intubation are that it is a simple and rapid procedure, with minimal trauma, thorough sputum and mucus excretion, and a low risk of complications.<sup>49</sup> However, the disadvantage is that the patient may not tolerate intubation and must be extubated early.<sup>50</sup> The indwelling time with oral intubation is short; however, performing oral care is inconvenient, and it is impossible to eat. The advantages of nasal endotracheal intubation are that it is especially suitable for patients who are awake,<sup>51</sup> is easy to

tolerate, and can remain in place for a long time. Nasal intubation is more convenient for performing oral care, but sputum suction is not easy and strict airway management is required.<sup>52</sup> With a greater amount of secretions, the tube can easily become blocked; the incidence of infection-related complications is high; and the intubation procedure time is relatively long, which can easily cause hypoxia.<sup>53</sup> Both oral endotracheal intubation and transnasal endotracheal intubation have their own advantages and disadvantages. In the intensive care unit, the patient should be treated according to the patient's state of consciousness, volume of respiratory secretions, and the severity of disease.54,55

For patients undergoing general anesthesia for tracheal intubation in clinical practice, management of the respiratory tract is particularly important. For risk factors of lower respiratory tract infection, preoperative education among medical professionals should be improved, patients who smoke should quit smoking before surgery, and patients should be trained in breathing and coughing to increase vital capacity.<sup>56</sup> Furthermore, improving oropharyngeal care is necessary prior to surgery, according to the pH value of the patient's oral cavity. If necessary, local antibacterial treatment or sterilization of the oropharynx may be carried out.<sup>57</sup> Additionally, it is necessary to strictly follow anesthesia and intraoperative procedures and conduct regular training of anesthesiologists. Individualized anesthesia and surgical treatment plans should be developed for different patients, which include ways to avoid deep intubation and repeated intubation so as to perform timely extubation.<sup>58</sup> Sputum suctioning as needed is essential to prevent pulmonary infection. Postoperative care should be strengthened; patients should be instructed in how best to cough and expectorate, and if necessary, family members should be taught how pat the patient's back to promote sputum

production. Patients must also be encouraged to get out of bed as soon as possible to prevent the occurrence of pneumonia.<sup>59</sup>

This study has certain limitations that must be addressed. The patients included in this study were limited to those undergoing general anesthesia at our hospital during the past year. The case dataset was small and the sample size was relatively limited. We did not find differences for the risk of infection and types of surgery, which may be because the sample size was not sufficiently powered to detect group differences. Multicenter data are needed for further verification. Additionally, this was a retrospective study, and some observational indicators may not have been included. Potential influencing factors of lower respiratory infection, such as the results of blood gas analysis or prognostic indicators, should be included in future studies.

#### Conclusions

The results of our study showed that in older patients who received general anesthesia, age >70 years, smoking, diabetes, nasotracheal intubation, and duration of surgery >180 minutes were the independent risk factors of lower respiratory tract infection. In clinical practice, medical health care providers should focus on the risk factors related to pulmonary complications after general anesthesia, formulate reasonable plans on the basis of these risk factors, and adopt targeted treatment strategies and nursing care to reduce the risk of pulmonary complications after surgery.

#### **Declaration of conflicting interest**

The authors declare that there is no conflict of interest.

#### Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Our study

has been funded by Natural Science Foundation of Xinjiang Uygur Autonomous Region (2019D01C305). The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

#### **Author contributions**

TC and HC designed the research; TC, YY, and HC conducted the research; TC, YY, and JW analyzed the data; HC wrote the first draft of the manuscript; HC had primary responsibility for the final content. All authors read and approved the final manuscript.

#### ORCID iD

Hu Cheng D https://orcid.org/0000-0001-7128-5742

#### References

- Smith G, D'Cruz JR, Rondeau B, et al. General Anesthesia for Surgeons. In: StatPearls. edn. Treasure Island (FL); 2020.
- Kolb CM, Tinley-Strong D, Rangarajan R, et al. General anesthesia risk across pediatric surgical specialties: Low in otolaryngology. *Int J Pediatr Otorhinolaryngol.* 2020; 129: 109780.
- 3. Chia WT, Liu YC and Wong TW. Optimize General Anesthesia for a Dystrophic Epidermolysis Bullosa Patient That Cannot Be Intubated. *Asian J Anesthesiol.* 2020; 58: 111–114.
- 4. Cabrini L, Baiardo Redaelli M, Filippini M, et al. Tracheal intubation in patients at risk for cervical spinal cord injury: A systematic review. *Acta Anaesthesiol Scand.* 2020; 64: 443–454.
- Wang J, Lu F, Zhou M, et al. [Tracheal intubation in patients with severe and critical COVID-19: analysis of 18 cases]. *Nan Fang Yi Ke Da Xue Xue Bao* 2020; 40: 337–341.
- Kilic Y, Bas SS, Aykac O, et al. Nonoperating Room Anesthesia for Interventional Neuroangiographic Procedures: Outcomes of 105 Patients. J Stroke Cerebrovasc Dis. 2020; 29: 104495.
- 7. Kissel M, Rambeau A, Achkar S, et al. Challenges and advances in cervix cancer

treatment in elder women. Cancer Treat Rev. 2020; 84: 101976.

- Tung A, Fergusson NA, Ng N, et al. Medications to reduce emergence coughing after general anaesthesia with tracheal intubation: a systematic review and network meta-analysis. *Br J Anaesth.* 2020; S0007-0912(20)30012-X.
- Mushambi MC, Athanassoglou V and Kinsella SM. Anticipated difficult airway during obstetric general anaesthesia: narrative literature review and management recommendations. *Anaesthesia* 2020; 75: 945–961.
- Toure T, Williams SR, Kerouch M, et al. Patient factors associated with difficult flexible bronchoscopic intubation under general anesthesia: a prospective observational study. *Can J Anaesth.* 2020; 67: 706–714.
- 11. Hammer M, Santer P, Schaefer MS, et al. Supraglottic airway device versus tracheal intubation and the risk of emergent postoperative intubation after general anaesthesia in adults: a retrospective cohort study. *Br J Anaesth.* 2021; 126: 738–745.
- Estebsari F, Dastoorpoor M, Khalifehkandi ZR, et al. The Concept of Successful Aging: A Review Article. *Curr Aging Sci.* 2020; 13: 4–10.
- von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med.* 2007; 147: 573–577.
- 14. Kalil AC, Metersky ML, Klompas M, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis* 2016; 63: e61–e111.
- Martin-Loeches I, Rodriguez AH and Torres A. New guidelines for hospitalacquired pneumonia/ventilator-associated pneumonia: USA vs. Europe. *Curr Opin Crit Care*. 2018; 24: 347–352.
- Lu M and Kang Y. [Clinical practice guidelines of HAP/VAP in 2016: the updates]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue*. 2017; 29: 769–773.

- Nakamoto H, Kayama S, Harada M, et al. Airway emergency during general anesthesia in a child with plastic bronchitis following Fontan surgery: a case report. *JA Clin Rep.* 2020; 6: 6.
- Lv L, Yan L, Liu X, et al. Effectiveness of lidocaine/prilocaine cream on cardiovascular reactions from endotracheal intubation and cough events during recovery period of older patients under general anesthesia: prospective, randomized placebo-controlled study. *BMC Geriatr.* 2020; 20: 157.
- Zdravkovic M, Podbregar M and Kamenik M. Near-infrared spectroscopy for assessing microcirculation during laparoscopic gynaecological surgery under combined spinalgeneral anaesthesia or general anaesthesia alone: a randomised controlled trial. J Clin Monit Comput. 2020; 34: 943–953.
- Du H, Tong X, Sun X, et al. Effect of anesthesia strategy during endovascular therapy on 90-day outcomes in acute basilar artery occlusion: a retrospective observational study. *BMC Neurol* 2020; 20: 398.
- 21. Kaur G, Gupta S, Mehta N, et al. Comparative Evaluation of McGrath MAC, Truview Video Laryngoscopes and Macintosh Laryngoscope for Endotracheal Intubation in Patients Undergoing Surgery under General Anaesthesia. *Anesth Essays Res.* 2020; 14: 20–24.
- Lieber SR, Heller BJ, Martin CF, et al. Complications of Anesthesia Services in Gastrointestinal Endoscopic Procedures. *Clin Gastroenterol Hepatol.* 2020; 18: 2118–2127.e4.
- Kim SH, Choi YS, Lee SK, et al. Comparison of general anesthesia and conscious sedation in procedure-related complications during esophageal endoscopic submucosal dissection. *Surg Endosc.* 2020; 34: 3560–3566.
- Rezoagli E, Zanella A, Cressoni M, et al. Pathogenic Link Between Postextubation Pneumonia and Ventilator-Associated Pneumonia: An Experimental Study. *Anesth Analg.* 2017; 124: 1339–1346.
- 25. Zhong G, Chen J and Wei M. Analysis and research on risk factors of pulmonary infection in elderly patients undergoing general

anesthesia after tracheal intubation. *Chinese Medical Science* 2019; 9: 255–257.

- 26. Lian Y, Jiang H, Zhou H, et al. Analysis of pathogenic bacteria distribution and risk factors of lung infection in patients with esophageal cancer after tracheal intubation general anesthesia. *Chinese Journal of Nosocomial Infection* 2015; 18: 209–211.
- 27. Cernada M, Aguar M, Brugada M, et al. Ventilator-associated pneumonia in newborn infants diagnosed with an invasive bronchoalveolar lavage technique: a prospective observational study. *Pediatr Crit Care Med.* 2013; 14: 55–61.
- Parker CM, Kutsogiannis J, Muscedere J, et al. Canadian Critical Care Trials G. Ventilator-associated pneumonia caused by multidrug-resistant organisms or Pseudomonas aeruginosa: prevalence, incidence, risk factors, and outcomes. J Crit Care. 2008; 23: 18–26.
- Taiping C, Jie Z, and Lingjun K. The etiological characteristics and risk factors of lower respiratory tract infections after general anesthesia and tracheal intubation in elderly patients. *Chinese Journal of Nosocomial Infection* 2017; 27: 4908–4911.
- Sipka S, Toth A, and Sipka S Jr. Age-dependent possible role of contact-activated blood coagulation factor XII as a potential contributor to the "bradykinin storm" in COVID-19 patients. *Orv Hetil.* 2020; 161: 2099–2103.
- Zandkarimi E, Moradi G and Mohsenpour B. The Prognostic Factors Affecting the Survival of Kurdistan Province COVID-19 Patients: A Cross-sectional Study From February to May 2020. Int J Health Policy Manag. 2020. PMID: 32861230
- 32. Lee CH, Wang JY, Lin HC, et al. Treatment delay and fatal outcomes of pulmonary tuberculosis in advanced age: a retrospective nationwide cohort study. *BMC Infect Dis.* 2017; 17: 449.
- 33. Sapey E, Patel JM, Greenwood HL, et al. Pulmonary Infections in the Elderly Lead to Impaired Neutrophil Targeting, Which Is Improved by Simvastatin. *Am J Respir Crit Care Med.* 2017, 196: 1325–1336.
- 34. Qi Z, Yang W and Wang YF. Epidemiological analysis of pulmonary

tuberculosis in Heilongjiang province China from 2008 to 2015. *Int J Mycobacteriol*. 2017; 6: 264–267.

- 35. Machida Y, Motono N, Matsui T, et al. Successful endovascular coil embolization in an elder and asymptomatic case of anomalous systemic arterial supply to the normal basal segment. *Int J Surg Case Rep.* 2017; 34: 103–105.
- Mannemuddhu SS, Clapp W, Modica R, et al. End-stage renal disease secondary to anti-glomerular basement membrane disease in a child with common variable immunodeficiency. *Clin Nephrol Case Stud.* 2019; 7: 1–6.
- Tashkin DP and Roth MD. Pulmonary effects of inhaled cannabis smoke. *Am J Drug Alcohol Abuse* 2019; 45: 596–609.
- Hamid S, Alvares da Silva MR, Burak KW, et al. WGO Guidance for the Care of Patients With COVID-19 and Liver Disease. J Clin Gastroenterol. 2021; 55: 1–11.
- Ji X, Cui W, Zhang B, et al. Effect of lung protective ventilation on perioperative pulmonary infection in elderly patients with mild to moderate COPD under general anesthesia. J Infect Public Health. 2020; 13: 281–286.
- Hogea SP, Tudorache E, Fildan AP, et al. Risk factors of chronic obstructive pulmonary disease exacerbations. *Clin Respir J*. 2020; 14: 183–197.
- Sun X, Shang J, Wu A, et al. Identification of dynamic signatures associated with smoking-related squamous cell lung cancer and chronic obstructive pulmonary disease. *J Cell Mol Med.* 2020; 24: 1614–1625.
- 42. Duffney PF, Embong AK, McGuire CC, et al. Cigarette smoke increases susceptibility to infection in lung epithelial cells by upregulating caveolin-dependent endocytosis. *PLoS One* 2020; 15: e0232102.
- 43. Cai G, Bosse Y, Xiao F, et al. Tobacco Smoking Increases the Lung Gene Expression of ACE2, the Receptor of SARS-CoV-2. *Am J Respir Crit Care Med.* 2020; 201: 1557–1559.
- Huang T, Wang G, Xu Q, et al. [Preventing Infection Measures of COVID-19 Patients during Mechanical Ventilation]. *Zhongguo Yi Liao Qi Xie Za Zhi* 2020; 44: 453–456.

- Wunsch H. Mechanical Ventilation in COVID-19: Interpreting the Current Epidemiology. Am J Respir Crit Care Med. 2020; 202: 1–4.
- 46. Otsuji K, Fukuda K, Ogawa M, et al. Dynamics of microbiota during mechanical ventilation in aspiration pneumonia. *BMC Pulm Med.* 2019; 19: 260.
- 47. Sartorius A, Lu Q, Vieira S, et al. Mechanical ventilation and lung infection in the genesis of air-space enlargement. *Crit Care* 2007; 11: R14.
- 48. Bluhmki T, Allignol A, Ruckly S, et al. Estimation of adjusted expected excess length-of-stay associated with ventilationacquired pneumonia in intensive care: A multistate approach accounting for timedependent mechanical ventilation. *Biom J*. 2018; 60: 1135–1150.
- 49. Xue FS, Liao X, Liu KP, et al. The circulatory responses to tracheal intubation in children: a comparison of the oral and nasal routes. *Anaesthesia* 2007; 62: 220–226.
- Jagannathan N, Sequera-Ramos L, Sohn L, et al. Randomized comparison of experts and trainees with nasal and oral fibreoptic intubation in children less than 2 yr of age. *Br J Anaesth.* 2015; 114: 290–296.
- Jazayeri-Moghaddas OP, Tse W, Herzing KA, et al. Is nasotracheal intubation safe in facial trauma patients? *Am J Surg.* 2017; 213: 572–574.
- 52. Holzapfel L, Chevret S, Madinier G, et al. Influence of long-term oro- or nasotracheal intubation on nosocomial maxillary sinusitis and pneumonia: results of a prospective, randomized, clinical trial. *Crit Care Med.* 1993; 21: 1132–1138.
- 53. Holzapfel L. Nasal vs oral intubation. *Minerva Anestesiol.* 2003; 69: 348–352.
- Patel A, Saadi R and Lighthall JG. Securing the Airway in Maxillofacial Trauma Patients: A Systematic Review of Techniques. *Craniomaxillofac Trauma Reconstr.* 2021; 14: 100–109.
- 55. Jubran A, Grant BJB, Duffner LA, et al. Long-Term Outcome after Prolonged Mechanical Ventilation. A Long-Term Acute-Care Hospital Study. *Am J Respir Crit Care Med.* 2019; 199: 1508–1516.

- Thorburn K, Jardine M, Taylor N, et al. Antibiotic-resistant bacteria and infection in children with cerebral palsy requiring mechanical ventilation. *Pediatr Crit Care Med.* 2009; 10: 222–226.
- Phua GC and Govert J. Mechanical ventilation in an airborne epidemic. *Clin Chest Med.* 2008; 29: 323–328, vii.
- 58. Bickenbach J, Schoneis D, Marx G, et al. Impact of multidrug-resistant bacteria on

outcome in patients with prolonged weaning. BMC Pulm Med. 2018; 18: 141.

59. Pena-Lopez Y, Ramirez-Estrada S, Eshwara VK, et al. Limiting ventilator-associated complications in ICU intubated subjects: strategies to prevent ventilator-associated events and improve outcomes. *Expert Rev Respir Med.* 2018; 12: 1037–1050.