

Incidence and Risk Factors for Ventilator-Associated Pneumonia in the Surgical Intensive Care Unit, Siriraj Hospital

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Background: Ventilator-associated pneumonia (VAP) is a serious illness with substantial morbidity and mortality resulting in increased costs of hospital care. Even though bundles of care to prevent VAP have been established, the incidence has not been shown to have improved.

Objective: To determine the incidence and risk factors of VAP in the general surgical intensive care unit, Siriraj Hospital (SICU).

Material and Method: During the period from June 1st, 2010 to June 30th, 2011, 228 adult patients admitted to the general SICU were recruited. All patients required ventilator support for more than 48 hours. Data were collected by reviewing patient medical records and the retrieval of information from the Nosocomial Infection Control, Siriraj Hospital.

Results: A total of 21 patients (9.21%) were diagnosed with VAP or an incidence of 8.21 cases/1,000 ventilator days. The onset of VAP was late in the majority of patients. The most common pathogens were *A. baumannii* (66%) followed by *P. aeruginosa* (19%). Multiple logistic regression analyses showed that the numbers of central venous catheter placements, intubations and surgeries and the use of muscle relaxants and steroids were independent risk factors for VAP. Median duration of ventilator and ICU lengths of stay were longer in the VAP group (25 vs. 6 days, 25 vs. 7 days, respectively; all $p < 0.0001$). In addition, the hospital mortality rates were significantly higher in the VAP group (33.33% vs. 12.07%; $p = 0.008$).

Conclusion: The incidence of VAP was high in the SICU. VAP bundles including weaning protocols and airway care should be implemented.

Keywords: Ventilator associated pneumonia, Incidence, Critically ill, Surgical

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Ventilator-associated pneumonia (VAP) is defined as a nosocomial pneumonia occurring in a patient after 48 hours of mechanical ventilation with an endotracheal tube or a tracheostomy tube⁽¹⁾. VAP has been recognized as one of the major causes of infection in intensive care units (ICUs) worldwide resulting in a high morbidity, a high mortality and additional health-care costs. In Thailand, over the past few decades, the incidence of VAP has been reported from some of the ICUs in teaching hospitals. Nevertheless, the incidence was different among reporting hospitals and was also different among the different types of ICUs. Apisartanarat et al⁽²⁾ has reported the incidence of

VAP as high as 20.6 cases per 1,000 ventilator-days in medical ICUs and 5.4 cases per 1,000 ventilator-days in surgical ICUs. In Ramathibodi Hospital, Kulvatunyou et al, demonstrated the incidence of VAP 39.7 per 1,000 ventilator-days in surgical ICUs⁽³⁾. The overall prevalence of VAP was at 75.3% among suspected nosocomial pneumonia patients between the year 2007 and 2009 in Siriraj Hospital⁽⁴⁾. In Siriraj general surgical ICUs (SICUs), the incidence ranges from 3 to 8 per 1,000 ventilator-days over the past three years and VAP has continued to be the most common nosocomial infection for SICUs' patients.

With regard to the high morbidity and mortality of VAP, early identification of high risk patients or recognition of the risk factors that can contribute to the development of VAP may prove to be beneficial. In addition, the implementation of the prevention protocols as bundles of care may help in reducing the

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incidence. Although risks factors for the development of VAP have been cited in several studies⁽⁵⁻⁸⁾, results have been controversial as a consequence of the differences in methodologies and the targeted populations. This study focuses on general surgical patients who underwent surgical procedures and strictly evaluate the risk factors in this particular population. Therefore, the objectives of the present study are to determine the incidence of VAP during the study period and to identify the independent risk factors associated with the development of VAP in Siriraj's general SICU.

Material and Method

The present study is a retrospective, observational study which had been conducted in Siriraj's general SICU between June 1st, 2010 and June 30th, 2011. All adult surgical patients (≥ 18 years) who required intubation longer than 48 hours were enrolled in the present study. Exclusion criteria included patients diagnosed with VAP within 48 hours of their SICU admission, referrals from other hospitals, terminally ill patients and patients who required permanent, ventilator assistance prior to their ICU admission. The sample size of patients was calculated by the estimation of a VAP rate of 5 per 1,000 ventilator days with a 95% confidence interval of ± 3 per 1,000 ventilator days. An equation is shown in Fig. 1.

When $\alpha = 0.05$, $1 - \alpha = 0.95$ (confidence interval), $\mu = 0.005$ (Incidence of VAP per 1,000 ventilator days in; adult, critically ill, surgical patients who were admitted in the Siriraj surgical intensive care unit). The value of d (distance from proportion to limit) = 0.003. Type I and type II errors are 0.05 and 0.2 respectively. This person-days-at-risk should be divided by the length of the follow-up period. The averaged ventilator days were approximately 10 days in this population. Therefore, the sample of patients would be at least 214 patients.

Data collection

Data were collected by reviewing patient medical records and by laboratory assessments. From each patient, the following data were collected during ICU stay: age, gender, co morbidities, acute physiological age and chronic health evaluation (APACHE) II score, the type and duration of the surgical procedure, length of time under anesthesia, the onset of VAP and the type of organisms found. The current ICU admission was classified as an emergency or elective surgery or non-surgical. Specific medical

care processes were examined as potential risk factors for the development of VAP. These included the use of tracheotomies; dialysis; the use of sedation; corticosteroids, inotropes and/or vasopressors; the administration of blood transfusions; number and duration of central venous catheter (CVC) placements; and the types of nutritional support (enteral, EN or parenteral, PN). The occurrence of aspiration, reintubation within 48 hours and incidences of self extubation were also recorded. VAP outcomes were measured by mechanical ventilator days, ICU and hospital lengths of stay and mortality within a 28-day period.

Definition

VAP, as defined by the Centers for Disease Control and Prevention (CDC)⁽⁹⁾ and the requirements that the patients meet all the following criteria within three days are; 1) Radiological: new infiltrates or cavitation with air-fluid levels persisting for at least 24 hours, 2) Clinically: febrile ($\geq 38.3^\circ\text{C}$) or hypothermic ($\leq 36.0^\circ\text{C}$) and $\text{WBC} > 10^5$ or $< 4 \times 10^3$ or $> 25\%$ increasing above the last value or with bands $> 10\%$. 3) Bacteriologic confirmation as demonstrated by at least one: positive blood cultures with infection by the same organism as identified in sputum or other respiratory cultures, an OR protected brush specimen with $\geq 10^3$ cfu/ml pathogen or bronchoalveolar lavage (BAL) exhibiting $> 10^4$ cfu/ml pathogens, non-bronchoscopy BAL with $> 10^3$ cfu/ml pathogen, positive gram stain with $\geq 3+$ of one type of bacteria or positive semi quantitative sputum culture with $\geq 3+$ growth of one type of pathogenic organism. If unable to assess quantitatively, all results must show 'moderate' or 'heavy' growth.

The APACHE II score was calculated based on clinical data available from the first 24 hours of the ICU admission. The worst value found in the first 24 hours was selected for each of the 12 APACHE II variables.

Statistical analysis

Incidence of VAP would be presented as percentages per 1,000 ventilator days. Continuous data were presented as a median with an interquartile range (IQR) or the mean \pm SD. Categorical data were presented as ratios and percentages. Continuous variables were compared using the student's t-test for normally distributed data and the Mann-Whitney U test for abnormally distributed data. The Chi-square test was used to compare patients with and without VAP for

categorical data. The results of these tests were confirmed with multiple logistic regression analysis while controlling specific patient characteristics and the severity of the patients' illnesses. Forward stepwise selection of $p < 0.2$ was used after univariate testing in order to assess the independent effect of each variable on the development of VAP. Results of this test were reported as adjusted odds ratios (AORs) with their 95% confidence intervals (CIs). All p -values of ≤ 0.05 were considered to indicate statistically significant results.

Results

During the 12-month period, 242 adult surgical patients requiring ventilator support for more than 48 hours were evaluated. Fourteen patients were excluded due to incomplete medical records (7 patients), terminal status (5 patients) and those referred from other hospitals (2 patients). Finally, there were 228 adult surgical patients included in the analysis.

Of the 228 patients, 21 patients (9.21%) developed VAP during their ICU stays or the incidence of VAP was 8.21 per 1,000 ventilator-days. The majority of patients (90.5%) had an onset of VAP after day six of the initiation of mechanical ventilation (referred as late onset VAP). Median onset of VAP followed the 10th day, post intubation. One-fourth of these patients had concomitant bacteremia and two-thirds of these patients had septic shock and acute kidney injuries. Other VAP features are shown in Table 1.

Acinetobacter baumannii was the leading microorganism cultured for the patients who developed VAP (66.66%) followed by *Pseudomonas aeruginosa* (19.04%). Methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia was found in only 9.5%. Other organisms are shown in Fig. 2.

Table 2 shows the baseline demographic data and types of medical care between the two groups. Patients who developed VAP had significantly higher APACHE II scores (18.3 ± 5.3 vs. 13.1 ± 5.4 ; $p < 0.0001$), required emergency surgery (66.6% vs. 35.8%; $p = 0.006$) and a greater number of surgeries (2.2 ± 1.2 vs. 1.2 ± 0.8 ; $p = 0.001$). These patients also had more blood transfusions (95.2% vs. 75.3%; $p = 0.039$), a higher incidence of CVC use (3 vs. 1; $p < 0.0001$), and were indicated for neuromuscular blocking agent (NMB) use (42.8% vs. 3.3%; $p < 0.0001$), sedative agent use (85.7% vs. 50.7%; $p = 0.02$) and steroid use (33.3% vs. 3.8%; $p < 0.0001$). Moreover, patients who developed VAP have shown instances of multiple intubations (2 ± 1 vs. 1.0 ± 0.2 ; $p < 0.0001$), self extubation (9.5% vs. 1.4%; $p = 0.016$), reintubation within 48 hours (38.1% vs. 4.8%;

$p < 0.0001$) and tracheostomies (76.1% vs. 19.8%; $p < 0.0001$).

Risk factors for the development of VAP are shown in Table 3. Selected risk factors were entered into a logistic regression analysis, it revealed that NMB used, the number of intubations ≥ 2 , the number of surgeries ≥ 3 , steroid use and multiple sites of CVC placements were identified as independent risk factors for the development of VAP (Table 4).

Similarly, the duration of mechanical ventilation, ICU and hospital lengths of stay were significantly longer in patients with VAP. In this study,

$$n = \frac{Z_{1-\alpha}^2 \cdot p \cdot q}{d^2}$$

$$n = \frac{1.96^2 (0.005)}{0.003^2} = 2135 \text{ ventilator days}$$

Fig. 1 An equation used for the calculation of sample size.

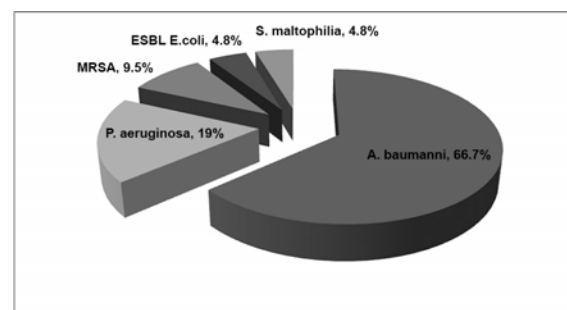


Fig. 2 Percentage of organism isolated from tracheal aspiration.

Table 1. VAP characteristics

Characteristic	VAP group (n = 21)
Onset of VAP, day [median (IQR)]	10 (7-18)
Late onset VAP ⁺ (%)	19 (90.5%)
Bacteremia (%)	5 (23.8%)
PaO ₂ /FiO ₂ ratio (mean ± SD)	210.4 ± 57.2
Shock required vasopressor	16 (76.2%)
Presence of AKI* (%)	16 (76.2%)
Required RRT** (%)	10 (47.6%)

*AKI acute kidney injury, **RRT renal replacement therapy.
⁺Late onset VAP referred to VAP occurred > day six after mechanical ventilation

Table 2. Baseline demographic data and types of medical care between patients with and without VAP

Characteristic	VAP group (21)	No VAP group (207)	p-value
Age (mean \pm SD)	68.3 \pm 12.8	65.1 \pm 16.9	0.290
Male	12 (57%)	104 (50.2%)	0.550
APACHE II (mean \pm SD)	18.3 \pm 5.3	13.1 \pm 5.4	<0.001
History of surgery (%)	21 (100%)	176 (85.0%)	0.056
Abdominal surgery	16 (76.1%)	118 (67.0%)	0.390
Emergency surgery	14 (66.6%)	63 (35.8%)	0.006
Number of surgery (mean \pm SD)	2.2 \pm 1.2	1.2 \pm 0.8	0.001
Blood transfusion (%)	20 (95.2%)	156 (75.3%)	0.039
Central line used	20 (95.2%)	161 (77.7%)	0.059
Number of catheter used [median (IQR)]	3 (2-4)	1 (0-2)	<0.001
PPI	21 (100%)	205 (99.0%)	0.650
Sedative agent used	18 (85.7%)	105 (50.7%)	0.020
NMB agent used	9 (42.8%)	7 (3.3%)	<0.001
Steroid used	7 (33.3%)	8 (3.8%)	<0.001
History of dialysis	11 (47.6%)	24 (11.1%)	<0.001
Number of intubation (mean \pm SD)	2 \pm 1	1.09 \pm 0.29	<0.001
Reintubation in 48 hrs	8 (38.1%)	10 (4.8%)	<0.001
Self extubation	2 (9.5%)	3 (1.4%)	0.016
Tracheostomy	16 (76.1%)	41 (19.8%)	<0.001

Table 3. Risk factors for development of VAP

Risk factor	Odds ratio	95% CI	p-value
Catheter used \geq 3	35.60	11.90-106.10	<0.001
Number of surgery \geq 3	31.00	9.00-106.80	<0.001
NMB used	21.40	6.80-67.40	<0.001
Number of intubation \geq 2	18.70	6.70-51.70	<0.001
Tracheotomy	12.90	4.40-37.40	<0.001
Steroid used	12.40	3.90-39.20	<0.001
Reintubation in 48 hrs.	12.10	4.00-35.90	<0.001
Required dialysis	7.27	2.79-18.99	<0.001
Self extubation	7.16	1.13-45.52	0.016
APACHE II >16	6.58	2.43-17.79	<0.001
Blood transfusion	6.54	0.86-49.94	0.017
Sedative drug used	5.83	1.67-20.39	0.001
Previous antibiotic used	5.53	2.16-14.15	<0.001
Emergency surgery	3.59	1.38-9.35	0.007

Table 4. Risk factors for development of VAP by logistic regression analysis

Characteristic	Adjusted odds ratio	95% CI	p-value
NMB used	96.8	6.0-1,561.0	0.001
Number of intubation \geq 2	40.5	3.2-511.1	0.004
Number of surgery \geq 3	33.9	2.6-439.7	0.007
Steroid used	31.1	2.4-403.7	0.008
Multiple site of catheters (\geq 3)	20.8	1.6-261.5	0.019

the 28 day mortality rate of patients with VAP was 33.3%. That is significantly higher than patients who did not develop VAP as shown in Table 5.

Discussion

The important findings of this study are 1) the incidence of VAP was 9.2% and it was mainly of the late onset category. Incidence of VAP in this present study is 9.21% or 8.12 per 1,000 ventilator days. That is lower when compared to what has been mentioned in previous studies which had ranged from 18% to 32%^(2,3,10). As previously mentioned, the incidences of VAP varied depending on many reasons. These include; the target population, the definitions used and the differences in methodology. The majority of the population in the present study was surgical and all of patients who developed VAP underwent at least one operation. However, even in surgical ICUs in educational hospitals, the incidence of VAP was not consistent e.g. the present study demonstrates an incidence of 8.12 per 1,000 ventilator days, Thammasart hospital⁽²⁾ reported 5.4 cases per 1000 ventilator days and Ramathibodi hospital⁽³⁾ showed 39.7 per 1,000 ventilator days. The bottom line is; how do we diagnose VAP or what specifically is the definition we will use. Radiologic and clinical parameters have been shown to lack sensitivity and specificity⁽¹¹⁾. In the present study, the author not only uses clinical and radiological criteria for diagnosing VAP but also uses microbiological criteria to confirm the diagnosis.

The majority of patients who developed VAP had an onset later than one week and *Acinetobacter baumannii* is the most common pathogen followed by *P. aureginosa* and MRSA. In previous studies^(2,3,12), the most frequently isolated organisms from patients with VAP were *P. auruginosa* and MRSA. Nevertheless, when considering late onset of VAP, El-Saed et al⁽¹³⁾ demonstrated that *Acinetobacter baumannii* was the most common and an increasingly important pathogen associated with VAP in late-onset and recurrent VAP associated with prolonged ventilation. The causative organisms were similar in our findings and can be

extrapolated that health care providers should be more vigilant in regard to this pathogen which is associated with a high morbidity and mortality. In the present study, the authors found that nearly 80% of the patients who developed VAP had experienced acute kidney injury and concomitantly used vasopressors. Not surprisingly, VAP patients also have higher ventilator days, extended ICU and hospital lengths of stay and show a resulting higher mortality when compared with patients who do not develop VAP.

Other findings include: 2) independent risk factors for the development of VAP in critically ill surgical patients are if NMB agents are used, the number of intubations ≥ 2 , the number of surgeries ≥ 3 , concurrent steroid used and multiple sites of CVC placement. Risk factors for a nosocomial pneumonia that have been identified in previous studies^(14,15) include: reintubation, gastric aspiration, high APACHE II scores, advanced ages, history of COPD, depressed consciousness or coma, use of antacids or cimetidine, tracheostomies, bronchoscopies, tube thoracotomies and multiple line insertions. Some of these risk factors were also present in this study. Although the use of NMB agents was considered one of the strongest risk factors, the overall administered rate of these agents was only 7%. It is hard to explain the association of this with the development of VAP. However, use of NMB agents to assist ventilator synchrony in severely ill pneumonia patients could possibly increase the risk of aspiration. Not surprisingly, reintubation is another important predictor for the development of VAP. Bacterial colonization of the aero digestive tract and the entry of contaminated secretions into the lower respiratory tract during re-intubation in critically ill patients who have low protective mechanisms can definitely be considered into the etiology of VAP.

Almost 60% of our patients underwent complicated abdominal surgeries that frequently required more than one surgery or radiological intervention. More than two surgeries correlate with the contraction of VAP. It might as well be correlated with the transporting of the patients from ICUs to

Table 5. Comparison of patient outcome between patient with and without VAP

Characteristic	VAP group (21)	No VAP group (207)	p-value
Ventilator days [median (IQR)]	25 (21-52)	6 (3-11)	<0.001
ICU LOS [median (IQR)]	25 (21-52)	7 (5-13)	<0.001
Hosp. LOS [median (IQR)]	48 (25.5-64.5)	28 (15-52)	0.027
28 day mortality	7 (33.3%)	25 (12.0%)	0.008

operating suites or radiology departments with endotracheal tubes that result in an increased risk for tube misplacement and aspiration. As in the use of NMB agents, corticotherapy was used less than 7% of the time and the indications include septic shock and adrenal insufficiency. In regard to its well-known anti-inflammatory and immunosuppressor effects, previous studies had addressed the association between steroid used and the development of pulmonary infections^(16,17). More than two-thirds of the patients in our surgical ICUs required central venous catheters. The indications varied. These include: for the purpose of measuring central venous pressures and as a route for vasopressor/inotropic agents and parenteral nutrition. If the patients need renal replacement therapy (RRT), another site for a temporary dialysis catheter may be required in the case of patients who are not end-stage renal disease patients and who already have arterial-venous grafts in place. VAP patients tended to have a higher numbers of RRTs and CVCs, however, the information regarding catheter related blood stream infections was not provided.

A number of limitations for the present study should be addressed. The calculated sample size came originally from the estimation of the incidence of VAP in surgical ICUs. The independent risk factors for VAP from this calculated sample size would be one considerable interpretation. The present study was a retrospective study that used information from electronic medical records and from The Center for Nosocomial Infection Control, Siriraj hospital. Some confounding factors or otherwise important information may not have been addressed. However the diagnosis of VAP was provided by the Nosocomial Infection Control, Siriraj Hospital in accordance to the CDC guidelines. Finally, these stated independent risk factors may not be the causative factors of contracting VAP but merely associated with the development of VAP.

In conclusion, the incidence and the risk factors for ventilator-associated pneumonia depend on the target population and the definitions used. The major risk factors are possibly different from hospital to hospital. Although some bundles of prevention have been implemented, the incidence of VAP has not decreased in some institutions as the care bundles do not correlate well with the risk factors. In order to improve the rates of infection, health care providers should realize the key factors that contribute to specific infections and create bundles of care that are practical and correlate with the findings. Finally, infections' control would not assuredly be improved without

delineated monitoring of strict adherence to the bundles of care.

Potential conflicts of interest

None.

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อัตราและปัจจัยเสี่ยงของการติดเชื้อระบบทางเดินหายใจส่วนล่างจากการใช้เครื่องช่วยหายใจในผู้ป่วยหนักทางศัลยกรรมโรงพยาบาลศิริราช

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ภูมิหลัง: ภาวะปอดติดเชื้อจากการใส่เครื่องช่วยหายใจเป็นการติดเชื้อที่พบได้บ่อยในหออภิบาล และนำไปสู่ภาวะแทรกซ้อนร้ายแรงต่างๆ ได้ถึงแม้ว่าจะมีการใช้แนวทางการป้องกันต่างๆ มาเป็นเวลานาน อัตราการเกิดภาวะปอดติดเชื้อจากการใส่เครื่องช่วยหายใจยังอยู่ในอัตราสูงและมีความแตกต่างในหออภิบาลแต่ละที่

วัตถุประสงค์: เพื่อที่จะหาอัตราการเกิดภาวะปอดติดเชื้อจากการใส่เครื่องช่วยหายใจรวมถึงปัจจัยเสี่ยงในหออภิบาลศัลยกรรมทั่วไปโรงพยาบาลศิริราช

วัสดุและวิธีการ: เป็นการศึกษาโดยเก็บข้อมูลย้อนหลังในผู้ป่วยที่เข้ารับการรักษาในหออภิบาลศัลยกรรมทั่วไปที่มีการใส่เครื่องช่วยหายใจมากกว่า 48 ชั่วโมง ระหว่างวันที่ 1 มิถุนายน พ.ศ. 2553 ถึง 30 มิถุนายน พ.ศ. 2554 ข้อมูลได้จากเวชระเบียนและหน่วยควบคุมการติดเชื้อโรงพยาบาลศิริราช การวิเคราะห์ทางสถิติใช้ multiple logistic regression analysis สำหรับการวิเคราะห์แบบกลุ่ม ค่าความแตกต่างอย่างมีนัยสำคัญทางสถิติเมื่อ $p < 0.05$

ผลการศึกษา: ผู้ป่วย 21 ราย (ร้อยละ 9.21 หรือ 8.21/1,000 ventilator days) เกิดภาวะปอดติดเชื้อจากการใส่เครื่องช่วยหายใจและโดยส่วนใหญ่เกิดในช่วงหลังของการอยู่หออภิบาล *A. baumannii* เป็นเชื้อก่อโรคที่พบมากเป็นอันดับหนึ่งตามมาด้วย *P. aeruginosa* (ร้อยละ 66 และ ร้อยละ 19 ตามลำดับ) จากการวิเคราะห์แบบ multiple logistic regression analysis พบว่าจำนวนสายสวนที่ใส่ในเส้นเลือดดำใหญ่ จำนวนครั้งของการใส่ท่อหายใจและการผ่าตัด การใช้ยาหย่อนกล้ามเนื้อและยาสแตียรอยด์เป็นปัจจัยเสี่ยงของการเกิดภาวะปอดติดเชื้อจากการใส่เครื่องช่วยหายใจ ผู้ป่วยที่เกิดภาวะปอดติดเชื้อจากการใส่เครื่องช่วยหายใจมีระยะเวลาการใส่เครื่องช่วยหายใจ (25 vs. 6 วัน, $p < 0.0001$) ระยะเวลาการอยู่หออภิบาล (25 vs. 7 วัน, $p < 0.0001$) รวมถึงอัตราตายในโรงพยาบาล (ร้อยละ 33.3 vs. 12.1, $p = 0.008$) สูงกว่ากลุ่มที่ไม่เกิดภาวะปอดติดเชื้อจากการใส่เครื่องช่วยหายใจอย่างมีนัยสำคัญ

สรุป: อัตราการเกิดภาวะปอดติดเชื้อจากการใช้เครื่องช่วยหายใจในหออภิบาลศัลยกรรมทั่วไป โรงพยาบาลศิริราชยังคงสูง การใช้แนวทางป้องกันการเกิดภาวะปอดติดเชื้อจากการใช้เครื่องช่วยหายใจที่รวมถึงการดูแลทางเดินหายใจ การหย่าเครื่องช่วยหายใจน่าจะมีส่วนช่วยในการลดอัตราการเกิดภาวะปอดติดเชื้อ จากการใส่เครื่องช่วยหายใจในหออภิบาลศัลยกรรมทั่วไป
