Management of mechanical ventilation in patients with hospital-acquired pneumonia: A retrospective, observational study

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Background. Hospital-acquired pneumonia (HAP) in intensive care patients is a frequent reason for mechanical ventilation (MV). The management of MV and ventilator weaning vary, depending on the type of lung inflammation. This retrospective, observational study screened the data from all patients admitted to the intensive care unit (ICU) of the Department of Anaesthesiology and Intensive Care Medicine, Faculty of Medicine and Dentistry, Palacky University Olomouc between 2011 and 2016. The aims were to determine the parameters of pressure-controlled ventilation, the frequencies of tracheostomy, bronchoscopy, reconnection to MV, the length of ICU and hospital stay and the mortality in subgroups with early-/late-onset HAP compared to a subgroup with community-acquired pneumonia (CAP) and patients with MV without pneumonia. The primary outcome of this study was MV length.

Results. Over the study period, a total of 2672 patients were hospitalised. Excluded were 137 organ donors, 66 patient without MV and 20 patients placed on volume-controlled ventilation. The cohort comprised 2.447 patients requiring MV. A total of 1.927 patients (78.7%) were indicated for MV without signs of pneumonia. CAP was diagnosed in 131 patients (5.4%). The criteria for HAP were met by 389 patients (16.0%). Early-onset and late-onset HAP was diagnosed in 63 (2.6%) and 326 (13.3%) patients, respectively. In the subgroups without pneumonia, with CAP, early- and late-onset HAP, the median MV times were 3, 6, 6 and 12 days, respectively, and the median peak inspiratory pressure (Pinsp) of MV was 20, 25, 25 and 27 cm H_2O, respectively. The median positive end-expiratory pressure (PEEP) was 5, 8, 8 and 11 cm H_2O, respectively. The median inspired oxygen concentrations (FiO$_2$) were 0.45, 0.7, 0.7 and 0.8, respectively. The median length of hospital stays was 8, 15, 15 and 17 days. The mortality rates were 11.4%, 3.8%, 9.5% and 31.3%, respectively.

Conclusions. During MV, the late-onset HAP subgroup was shown to have the highest Pinsp, PEEP and FiO$_2$, the longest MV time, ICU and hospital stay, the highest frequency of tracheostomy, reconnection to MV, pulmonary hygiene bronchoscopy and the highest mortality compared to the early-onset HAP and CAP subgroups. The lowest values were found in the mechanically ventilated patients without pneumonia. The differences were due to the severity of lung damage that is graduated from CAP over early-onset HAP after late-onset HAP.

Key words: hospital-acquired pneumonia, mechanical ventilation, mortality, ventilator-associated pneumonia

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INTRODUCTION

One of the most common indications for admitting a patient to an intensive care unit (ICU) is the need for mechanical ventilation (MV) (ref.[1]). In most cases, the reasons for placing a patient on MV are not related to lung infection. However, patients receiving MV for either community-acquired pneumonia (CAP) or hospital-acquired pneumonia (HAP) require very different, more intensive MV to ensure adequate oxygenation and elimination of CO_2. From a pathophysiological perspective, the reasons for bronchial involvement are proliferative neutrophilic inflammation, obstruction with purulent mucus, alveoli filled with fibrinous exudate and cellular debris, lung tissue necrosis and alveolar disruption with loss of normal lung architecture. Higher MV settings and oxygen concentration (FiO$_2$) in the ventilator circuit are usually necessary in HAP compared with CAP. This is due to the greater incidence of multiple drug-resistant (MDR) strains, bacterial pathogens causing HAP (in particular late-onset HAP) (ref.[2]), leading to a clinically more severe course of lung inflammation, especially with frequent complications such as pleural effusions, empyema, acute respiratory distress syndrome (ARDS), septic shock and multiple organ failure[3]. Recent data show that the most frequently isolated etiological agents causing HAP are *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Burkholderia cepacia* complex and *Escherichia coli*[4]. These species were also shown to have the highest proportions of MDR strains[5]. Variations in the clinical course of different types of pneumonia not only require differences in MV management and setting of MV parameters, but also in weaning from prolonged MV; and so is the hospital stay. Moreover, treatment costs are higher in this group of patients[6,7]. Up to 50% of all deaths from nosocomial infections are related to nosocomial pneumonia[8]. The

overall mortality from HAP is 20-60% (ref.[9]), especially if severe sepsis develops[4]. The attributable mortality of HAP or ventilator-associated pneumonia (VAP) is approximately 13% (ref.[10]). The incidence of CAP with a severe clinical course requiring the use of MV is low, being approximately 1-2% of all CAP cases and 5-10% of hospitalised CAP cases (ref.[11]), with short-term MV in non-HAP complicated cases. By contrast, patients with a severe clinical course of HAP usually need to be placed on MV for a longer time, requiring more intensive parameters of ventilator setting, special techniques such as recruitment manoeuvres, the prone position, frequent use of bronchoscopy and more frequent tracheostomy. HAP and VAP account for almost one-half and one-third of all nosocomial infection cases in ICUs, respectively (ref.[11]). MV and intubation are risk factors for the development of HAP, increasing the risk 3- to 20-fold (ref.[12,13]). The incidence of VAP is 6-32% among MV patients (ref.[14]). According to the 2015 European Centre for Disease Prevention and Control annual epidemiological report, pneumonia was detected in 5.3% of ICU patients, of whom 93% were intubated[15]. The study describes the management of MV depending on the type of pneumonia compared to MV in patients without pneumonia. The aim of this study is to identify MV parameters, in particular MV length.

METHODS

Study Design

A retrospective, observational study aimed to obtain clinical and epidemiological data of ICU patients requiring MV.

Setting

The primary outcome measure was MV length; secondary outcome measures were ICU length of stay, hospital length of stay and mortality. Other pre-specified outcome measures were MV Inspiratory pressure (Pinsp) and Positive end expiratory pressure (PEEP). The study was approved by the University Hospital Olomouc institutional ethics committee. The participants were not asked for informed consent. The study was registered in the ClinicalTrials.gov database (NCT03111303).

Participants

The study comprised patients staying in the ICU of the Department of Anaesthesiology and Intensive Care Medicine, Faculty of Medicine and Dentistry, Palacky University Olomouc and University Hospital Olomouc between 1 January 2011 and 31 December 2016.

Inclusion criteria were a minimum age of 18 years, pneumonia and the need of MV (Pressure controlled mechanical ventilation or Pressure support ventilation).

Exclusion criteria were organ donor, the need of Volume controlled ventilation and patients with no need of MV.

The participants were enrolled irrespective of their lower airway management (invasive/non-invasive), microbiological test results (positive/negative) for samples collected from the lower airways (endobronchial aspirate or bronchoalveolar lavage) or adequacy of initial empirical antibiotic therapy. The patients group with pneumonia was divided into subgroups according the following pneumonia types: CAP, early-onset HAP and late-onset HAP (ref.[16]). Patients with no signs of pneumonia required MV due to impaired consciousness, intoxication, trauma, delayed extubation following a major surgery, cerebral or myocardial infarction, pulmonary embolism, inadequate airway patency or considerable circulatory instability. The study included patients placed on pressure-controlled ventilation (PCV) using the bilevel positive airway pressure mode and receiving positive pressure support (PPS) during MV weaning. Tracheal or tracheostomy tube compensation was set at 80-90%. The ventilation parameters (peak inspiratory pressure – Pinsp, PPS, positive end-expiratory pressure – PEEP, FiO_2) were set so that blood gas levels reached at least the lower normal limit (pO_2 11.7 kPa = 88 mmHg, pCO_2 6.0 kPa = 45 mmHg) in arterial blood.

Definitions

Pneumonia is acute inflammation of the respiratory bronchioles, alveolar structures and pulmonary interstitium. Clinically, it is defined as the presence of newly developed or progressive infiltrates on chest radiographs plus at least two other signs of respiratory tract infection: temperature > 38 °C, chest pain, purulent sputum, leukocytosis or leucopoenia, signs of inflammation on auscultation, cough and/or respiratory insufficiency[17].

CAP is defined as pneumonia developing outside the hospital setting or within 48 h from the patient's hospital admission. HAP is defined as pneumonia that occurs 48 h or more after admission, which was not incubating at the time of admission[5]. According to the time of onset, HAP is classified as either early-onset pneumonia, developing within 48-96 h from hospital admission, or late-onset pneumonia, occurring on day five or later after admission[16]. If HAP develops more than 48 h after the patient is placed on MV using invasive airway management, it is referred to as VAP (ref.[12]). Nosocomial pneumonia was manifested both during spontaneous ventilation prior to initiation of MV and in the course of MV. Therefore, the cohort was not strictly divided into patients with HAP and those with VAP, with VAP being considered a subset of HAP.

Outcome Assessment

The primary outcome was length of MV in days. The crucial time of MV parameter assessment was the interval between the moment of fulfilling the criteria for pneumonia and definitive MV weaning or death. We assess the relationships between pneumonia types and the following MV parameters: Pressure controlled ventilation (PCV) time, Positive pressure support (PPS) time, overall MV time, Pinsp, PEEP, oxygen concentration in the ventilator circuit (FiO_2), need for tracheostomy (TS) – yes/no, need for reconnection to MV – yes/no, need for pulmonary hygiene bronchoscopy (BSC), length of stay (LOS)-ICU, LOS-hosp and Mortality (Mort).

Bias

No replacement of missing values or outliers was performed in order to minimise bias due to changed content of retrospective clinical records.

Data sources

All the data were obtained from medical records. These records are in accordance with the requirements of the accreditation commission of The ministry of health of Czech Republic.

Statistical Methods

No replacement of missing values or outliers was performed in order to minimise bias due to changed content of retrospective clinical records. Standard descriptive statistics were applied to summarise the primary data; continuous variables as means and 95% confidence intervals or median and range; categorical variables by absolute and relative frequencies. The selection of variables for the multivariate model was based on univariate $P<0.1$ and redundancy analysis of these preselected predictors. $P<0.05$ was adopted as the level of statistical significance for all analyses. Data were described using measures of descriptive statistics (median, minimum and maximum values, mean and standard deviation). The Shapiro-Wilk test showed that the data were not normally distributed. The groups were compared using the non-parametric Kruskal-Wallis test; subsequently, multiple-comparison post hoc tests were performed. The independent predictors were PCV time, MV time, Pinsp, PEEP, FiO_2, TS, reconnection to MV, BSC, LOS-ICU, LOS-hosp and Mort. The dependent variable was CAP and HAP (early-/late-onset). To compare qualitative descriptors, data were entered into a contingency table and compared with the chi-squared test. Subsequently, multiple pair-wise comparison with the Bonferroni correction was carried out. The model was built in 4 steps using the Forward Stepwise method. SPSS 21 (IBM Corporation, 2012) was the software used.

RESULTS

Patients

Over the study period, a total of 2,670 patients were admitted to the ICU, accounting for 15,770 hospital days. Excluded from the cohort were 137 organ donors, 66 patients without MV and 20 patients placed on volume-controlled ventilation (VCV). The final cohort comprised 2,447 patients requiring PCV. 1,927 patients (78.7%) were indicated for MV without having signs of pneumonia; the remaining 520 patients met the criteria for pneumonia. CAP was diagnosed in 131 patients (5.4%), HAP in 389 patients (16.0%). Early-onset and late-onset HAP was diagnosed in 63 (2.6%) and 326 (13.3%) patients, respectively. The flow chart is shown in Figure 1.

Descriptive data

The mean age of the final cohort was 58.9 ± 17.4 years (median, 63 years), the mean APACHE II score was 21.5. The participants were admitted on the grounds of internal (54.5%, 1,444 patients) or surgical (45.5%, 1,003 patients) diagnosis.

Main results and mortality

In final cohort (n=2,447) median MV length was 4 (mean 5.6) days, median pressure-controlled ventilation time was 3 (mean 4.2) days, median Pinsp was 21 (mean 22.2) cm H_2O, median PEEP was 6 (mean 6.6) cm H_2O, median FiO_2 was 50 (mean 54.3)%. Patients' median LOS-ICU and LOS-hosp were 5 (mean 6.4) and 9 (mean 11.7) days, respectively. The mortality rate was 18.6% (454 patients).
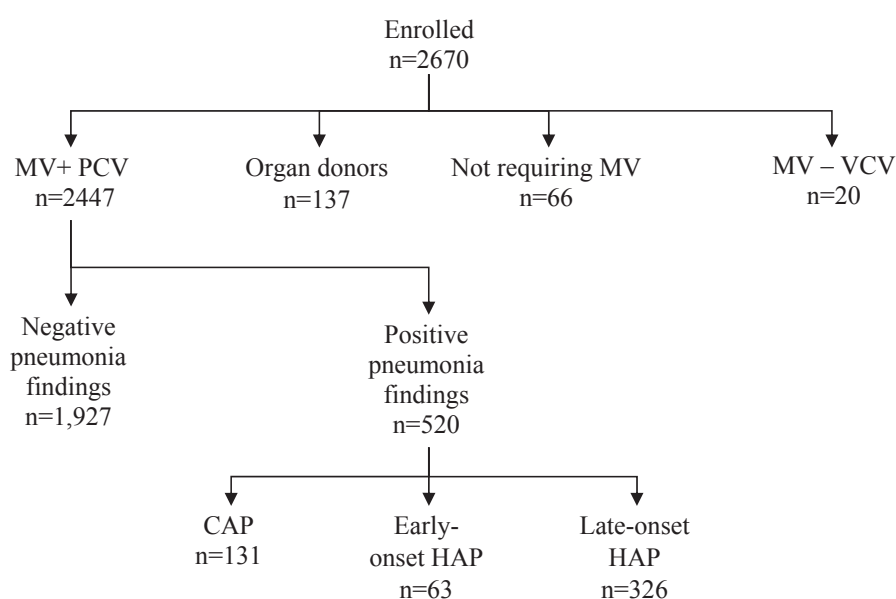

Fig. 1. Study flow chart.
MV-PCV: mechanical ventilation-pressure controlled ventilation, MV-VCV: mechanical ventilation-volume controlled ventilation, CAP: community-acquired pneumonia, HAP: hospital-acquired pneumonia

Table 1. Parameters of mechanical ventilation and frequency of selected diagnostic and therapeutic interventions in patients with pneumonia (n=520).

	Median (min-max)	Mean	SD	P
PCV	7 (3-22)	8.8	5.1	<0.0001
MV	10 (3-24)	10.9	6.2	<0.0001
Pinsp	26 (18-34)	25.4	3.9	<0.0001
PEEP	10 (5-14)	9.5	2.5	<0.0001
FiO$_2$	80 (50-100)	75.8	16.3	<0.0001
TS	0 (0-1)	0.3	0.4	<0.0001
re MV	0 (0-1)	0.3	0.4	<0.0001
BSK	0 (0-1)	0.3	0.4	<0.0001
LOS-ICU	11 (3-26)	12.1	6.5	<0.0001
LOS-Hosp	15 (3-45)	18.2	9.8	<0.0001

Legend: PCV – pressure-controlled ventilation time (days), MV – overall mechanical ventilation time (days), Pinsp – peak inspiratory pressure (cm H$_2$O), PEEP – the highest level of positive end-expiratory pressure (cm H$_2$O), FiO$_2$ – the highest oxygen concentration in the ventilator circuit, TS – tracheostomy, re-MV – need for reconnection to mechanical ventilation after previous weaning, BSC – pulmonary hygiene bronchoscopy LOS-ICU – length of ICU stay, LOS-hosp – length of hospital stay

In the group of patients with pneumonia (n=520) statistically significant differences were found in all the studied parameters (*P*<0.0001), see Table 1.

In the subgroups of patients with various pneumonia types (CAP, early-onset HAP, late-onset HAP) and in the subgroup of patients without pneumonia, statistically significant differences were found in all the studied parameters (*P*<0.0001), see Table 2.

There was a significant association between the HAP type and patient age, with the mean age of 55.4 and 62.0 years in patients with early-onset and late-onset HAP, respectively (*P*=0.048). The HAP patients' mean APACHE II score was 22.241 (range, 8-41; median, 22.0). No association was found between the initial APACHE II score and pneumonia type.

At a high level of statistical significance, differences in the frequency of necessary MV-related interventions and mortality were also noted between the subgroups, as seen from Table 3.

DISCUSSION

Epidemiological data from a six-year retrospective study, which shows considerable differences in all assessed parameters, is presented. This data points to a dif-

Table 2. Parameters of mechanical ventilation depending on the pneumonia type.

	Subgroup				P
	no HAP (n=1,927)	CAP (n=131)	early-onset HAP (n=63)	late-onset HAP (n=326)	
	Median (min,max)	Median (min,max)	Median (min,max)	Median (min,max)	
PCV	3.0 (1.0-7.0)	6.0 (3.0-9.0)	6.0 (3.0-9.0)	12.0 (3.0-22.0)	<0.0001
MV	4.0 (2.0-8.0)	8.0 (3.0-11-0)	8.0 (3.0-11.0)	12.0 (3.0-24.0)	<0.0001
Pinsp	20.0 (5.0-40.0)	25.0 (18.0-30.0)	25.0 (20.0-30.0)	27.0 (18.0-34.0)	<0.0001
PEEP	5.0 (5.0-14.0)	8.0 (5.0-12.0)	8.0 (6.0-14.0)	11.0 (6.0 – 14.0)	<0.0001
FiO$_2$	45 (30-100)	70 (50-100)	70 (50-100)	80 (50-100)	<0.0001
LOS-ICU	5.0 (2.0-9.0)	9.0 (3.0-13.0)	9.0 (3.0-13.0)	12.0 (3.0-26.0)	<0.0001
LOS-hosp	8.0 (2.0-30.0)	15.0 (3.0 – 24.0)	15.0 (3.0 -24.0)	17.0 (3.0 – 25.0)	<0.0001

PCV – pressure-controlled ventilation time (days), MV – overall mechanical ventilation time (days), Pinsp – peak inspiratory pressure (cm H$_2$O), PEEP – the highest level of positive end-expiratory pressure (cm H$_2$O), FiO$_2$ – the highest oxygen concentration in the ventilator circuit, LOS-ICU – length of ICU stay, LOS-hosp – length of hospital stay

Table 3. Frequency of selected diagnostic and therapeutic interventions related to mechanical ventilation depending on the type of pneumonia.

		Subgroup				P
		no pneumonia	CAP	early-onset HAP	late-onset HAP	
		n	n	n	n	
TS	0	1,791 (92.9%)	119 (90.8%)	57 (90.5%)	205 (62.9%)	< 0.0001
	1	136 (7.1%)	12 (9.2%)	6 (9.5%)	121 (37.1%)	
Re-MV	0	1,788 (92.8%)	106 (80.9%)	51 (81.0%)	217 (66.6%)	< 0.0001
	1	139 (7.2%)	25 (19.1%)	12 (19.0%)	109 (33.4%)	
BSC	0	1,658 (86.0%)	114 (87.0%)	51 (81.0%)	214 (65.6%)	< 0.0001
	1	269 (14.0%)	17 (13.0%)	12 (19.0%)	112 (34.4%)	
Mort	0	1,586 (82.3%)	126 (96.2%)	57 (90.5%)	224 (68.7%)	< 0.0001
	1	341 (17.7%)	5 (3.8%)	6 (9.5%)	102 (31.3%)	

TS – tracheostomy, re-MV – need for reconnection to mechanical ventilation after previous weaning, BSC – pulmonary hygiene bronchoscopy, Mort – mortality

ferent level of severity of pulmonary damage depending on the type of pneumonia. The results contribute to the identification of the risk for individual pneumonia types with respect to the incidence of MV-related diagnostic and therapeutic interventions and MV parameters. The results show that the lung damage and deterioration in pulmonary function, associated with the increased use of MV, is graduated from CAP over early-onset HAP, after late-onset HAP, which causes the most serious lung damage. Similarly differences in the frequency of assessed interventions correlated with type of pneumonia for tracheostomy, reconnection to MV after previous weaning and the frequency of pulmonary hygiene bronchoscopy. Further, the median Pinsp was lower by more than 5 cm H_2O in patients without pneumonia than in both CAP and early-onset HAP patients and the highest median Pinsp was observed in the late-onset HAP subgroup. The distribution of median PEEP values was similar, in CAP and early-onset HAP were also identical, the highest in late-onset HAP patients. The increasing severity of the clinical course of pneumonia, from CAP to early-onset HAP and to late-onset HAP, was correlated with the length of ICU stay and the length of hospital stay. The benefit of the study is that it documents the actually applied pressure parameters of MV that were selected to ensure elimination of hypoxia and hypercapnia. The MV parameters were selected in a protective manner, with respect to potential ventilator-induced lung injury (VILI). This is because ARDS was shown to be developed and/ or aggravated by VILI that accompanies inappropriate MV (ref.[18]). Yet further reductions in plateau pressures or tidal volumes below certain thresholds ($\leq$ 30 cm of water and $\leq$ 7 mL per kilogram of predicted body weight, respectively) were found to have no effect on survival[18]. It has also been shown that implementing a MV protocol in the early beginning of MV is associated with significant improvements in the delivery of lung-protective, safe MV and clinical outcome[19]. Another study hypothesised that the ventilator-related causes of lung injury may be unified in a single variable: the mechanical power. Assessed was, whether the mechanical power measured by the pressure-volume loops can be computed from its components: tidal volume, Pinsp, flow, PEEP, and respiratory rate. Computed and measured mechanical powers were similar at 5 and 15 cm H2O PEEP both in normal subjects and in ARDS patients. The mechanical power increases exponentially with volume tidal, Pinsp and flow as well as with respiratory rate and PEEP. Authors concluded that the mechanical power equation, that can be easily implemented in every ventilator's software, may help estimate the contribution of the different ventilator-related causes of lung injury[20]. The present study shows considerable differences between pneumonia types in all epidemiological parameters. To a great extent, variations in the clinical course of pneumonia are associated with its etiological agents[21-24]. While patients with early-onset HAP are more at risk from bacterial strains causing CAP, those with late-onset HAP are mainly threatened by MDR strains[21-24]. However, authors of recent studies are inconsistent as to when the risk for infection with MDR strains starts to pre-

vail. This may be after four[21,23], five[22,25] or even seven days[26] from hospital admission. According to the 2016 Infectious Diseases Society of America guidelines, the risk of HAP increases from day 5 of hospital stay (not intubation) (ref.[21]). But Nair et al. reported that the epidemiology of HAP has been changing in that the distinction between early-onset and late-onset HAP has become less apparent, that is, resistant strains are detected even in patients with early-onset HAP while susceptible strains may be observed in both early-onset and late-onset HAP (ref.[27]).

Greatest differences between the pneumonia subgroups were noted for mortality. The lowest mortality has been expectedly demonstrated in the subgroup without pneumonia, after stratification of the cohort into pneumonia types, the highest mortality was associated with late-onset HAP. A similar epidemiological study showed that mortality of patients with acute respiratory failure (ARF) due to pneumonia is lower (37%) than in ARF caused by sepsis (54%) (ref.[28]). With respect to prolonged ICU and hospital stay and higher mortality of pneumonia patients, the present study results are consistent with those reported by Vincent et al. The authors documented longer ICU stay (6 and 4 days, respectively; $P<0.001$) and more than two-fold higher ICU mortality (34% and 16%, respectively; $P<0.001$) in patients with ARF than in those without ARF (ref.[29]). The studied MV-related epidemiological parameters are influenced by numerous variables. For example, in a large study of more than two thousand patients, early tracheostomy did not lower the incidence of VAP, MV time, LOS-ICU and mortality but reduced the time of patients' sedation[30]. According to other authors, daily weaning trials and sedation holidays had been repeatedly described and validated as strategies that limit the time of mechanical ventilation[31]. Therefore, guidelines for discontinuing mechanical ventilation claim that sedation protocols reduced LOS-ICU and transitioning to non-invasive ventilation reduced LOS-ICU and short- and long-term mortality. Similarly, protocolised rehabilitation leading to early patient mobilisation is associated with shorter ventilation time[32]. By contrast, MV may be strongly negatively affected by fluid management since volume overload was shown to be associated with increased HAP incidence[33]. Independent risk factors for the development of HAP/VAP are also both duration of mechanical ventilation[34] and established ARDS. The risk of VAP increases by 3% daily for the first 5 days of MV, then by 2% daily on days 6-10 and by 1% daily on day 11 or later[16]. The risk for HAP/VAP peaks at day 5 of MV. The median time from ICU admission to the onset of HAP/VAP is seven days[35]. A potential way of reducing the incidence of HAP/ VAP has been suggested in randomised studies conducted using patients with a variety of illnesses. The use of non-invasive positive-pressure ventilation (NPPV) has been shown to significantly lower the risk of HAP/VAP and has also demonstrated a mortality benefit[36,37]. A similar study showed a lower incidence of HAP in NPPV as compared with MV in a group of patients undergoing abdominal surgery, with continuous positive airway pressure being used for treatment of postoperative hypoxemia[38].

The main advantage of the presented study is the large

study group; in this file we collected complete data on mechanical ventilation for a long period according to the records. Further, we obtained this data without the use of other than standard practice. The limitation of the study is the absence of assessment certain imaging techniques (X-ray, computer tomography), by which the degree of lung damage could be objectively addressed. Further, the correlation between data obtained by mechanical ventilation and microbiological agents of pneumonia was not found.

CONCLUSIONS

Based on the obtained epidemiological data, parameters of MV setting may be determined in a wide cohort of ICU patients with CAP and early-/late-onset HAP as compared with controls without pneumonia. During mechanical ventilation, the late-onset HAP subgroup was shown to have the highest Pinsp, PEEP and FiO_2, the longest MV time, LOS-ICU and LOS-hosp, the highest frequency of TS, reconnection to MV and pulmonary hygiene BSC and the highest mortality when compared to the early-onset HAP and CAP subgroups. The lowest values of the parameters were noted in the subgroup of mechanically ventilated patients without pneumonia. The lung damage and deterioration in pulmonary function, directly related to MV parameters, is graduated from CAP over early-onset HAP after late-onset HAP. The results contribute to the identification of the risk for individual pneumonia types with respect to MV parameters and the incidence of MV-related diagnostic and therapeutic interventions. At the same time, they are helpful in setting as gentle MV parameters as possible and in preventing the development and/or aggravation of VILI that accompanies inappropriate MV.

ABBREVIATIONS

APACHE II, Acute Physiology and Chronic Health Evaluation II; ARDS, acute respiratory distress syndrome; ARF, acute respiratory failure; BSC, bronchoscopy; CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; ICU, intensive care unit; LOS, length of stay; MDR, multiple drug-resistant; MV, mechanical ventilation; NPPV, non-invasive positive-pressure ventilation; PCV, pressure-controlled ventilation; PEEP, positive end-expiratory pressure; Pinsp, peak inspiratory pressure; PPS, positive pressure support; TS, tracheostomy; VAP, ventilator-associated pneumonia; VCV, volume-controlled ventilation; VILI, ventilator-induced lung injury.

Author contributions: RU, TH, PJ: manuscript writing; RU, TH: study design; RU, TH, PJ, KL: analysis and interpretation of data; RU, TH, PJ: drafting the manuscript and revising it critically for important intellectual content; RU, TH: agreed to be accountable for all aspects of the work in ensuring that queries relating to the accuracy and

integrity of the work are appropriately investigated and resolved; RU, TH, PJ, KL: final approval.

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