

Effects of APACHE II score on mechanical ventilation ; prediction and outcome

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Abstract : *Aim :* To evaluate the influence of Acute Physiology and Chronic Health Evaluation (APACHE II) score on the choice of mechanical ventilation method and treatment outcome.

Methods : A prospective, randomized trial was carried out at the multidisciplinary Intensive Care Unit over 22 months. Research sample consisted of 129 patients who required mechanical ventilation, divided in two groups : APACHE II \leq 20 and APACHE II $>$ 20. Both groups were then randomized for either noninvasive or invasive mechanical ventilation. Comparison was made based on patient characteristics, objective parameters and influence of APACHE II score on treatment success and failure.

Results : APACHE II scoring was shown to have statistical significance on outcome assessment. Statistical significance was in favour of patients with APACHE II score \leq 20 vs $>$ 20 (ventilator associated pneumonia 0 vs. 10, tracheotomy 0 vs. 16, Intensive Care Unit mortality 0 vs 12). Furthermore, in the group with APACHE II score $>$ 20, after randomization, there was a statistical significance in favour of noninvasive mechanical ventilation in need for tracheotomy 2 (4%) vs. 14 (28%) ($p < 0.001$).

Conclusion : Using good patient selection and applying strict protocols, in the group of patients with APACHE II \leq 20 all patients had successful mechanical ventilation, while in the group of patients with APACHE II $>$ 20, noninvasive mechanical ventilation can be applied.

Key words : APACHE, respiration, mechanical ventilation, Intensive Care Unit, intubation.

INTRODUCTION

Mechanical Ventilation (MV) is one of the most important and often performed procedures in the Intensive Care Unit (ICU) (1). It often saves lives but also presents an invasive, aggressive procedure accompanied by a series of serious early and late complications. These complications are proportional to the duration of MV (2). MV is applied when maintaining appropriate oxygenation and ventilation or diminishing respiratory distress and patient dyspnoea, isn't possible using conservative methods (3).

Invasive Mechanical Ventilation (IMV) procedure includes : airway intubation, positive pressure ventilation and often application of sedatives and muscle relaxants (4). Endotracheal tube can cause damage to the trachea producing ulceration, oedema and haemorrhage (5, 6). High ratio of ventilator associated pneumonia (VAP) is the most important complication of this MV method (7).

Noninvasive Mechanical Ventilation (NIMV) includes similar techniques for alveolar ventilation improvement, but without endotracheal intubation. Avoiding complications from endotracheal intubation, improving patient comfort, maintaining airway defence mechanisms, speech and swallowing process are the definite NIMV advantages (8, 9). It is easier for patients to interact with the respirator, both in the beginning of NIMV, as well as during the weaning process. Besides these advantages, there are also side effects from using this MV method. These include damage to the nose and face skin, gastric distension with possible aspiration, sleeping disorders and conjunctivitis (10). There are also conditions that present a problem for NIMV application. These are coma, unstable respiratory centre, mental immaturity, shock and cardiorespiratory arrest (11). Both MV methods require continuous patient monitoring, secured with reliable alarm system. They also require the presence of medical staff that is well educated in the forms of MV as well as continuous adjustment of the ventilator parameters according to the patients' condition (12, 13).

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None of the many clinical trials was able to establish if and in what measure severity of illness influences the choice of MV method (14, 15). Therefore, we decided to compare these two MV methods and treatment outcome in connection to severity of illness based on Acute Physiology and Chronic Health Evaluation (APACHE) II score.

PATIENTS AND METHODS

Patients

This prospective randomized study was conducted at the medical-surgical ICU at Dr. Josip Benčević General Hospital in Slavonski Brod, Croatia, between January 2004 and October 2005, during which time, a total of 502 adult patients required MV. Of the 502 patients, 373 patients were excluded because they didn't meet the strict defined criteria. These exclusion criteria were expected MV duration shorter than 24 h, use of MV on admission to the ICU, patients being scheduled for organ donation, central nerve system disorders unrelated to hypercapnic encephalopathy or hypoxemia, cardiac arrest within 5 days. These conditions present contraindications for application of NIMV and including them in the research would influence patient randomisation.

After using these exclusion criteria, 129 patients remained and were included in the research and they present the research sample. These patients were then divided in two groups based on the value of APACHE II score. This score includes 12 physiological variables: body temperature, mean systemic arterial blood pressure, heart rate, respiratory rate, oxygenation status, pH, blood serum sodium, potassium and creatinin, hematocrit, white cell count, neurological status expressed by the Glasgow Coma Score (GCS), age and underlying conditions. APACHE II score is important because of the possibility to predict hospital mortality which means treatment success prediction. In APACHE II score, value of 20 is set as statistically important for survival rate, because if APACHE II score is under 20 mortality rate is about 20%, and above 20 mortality rate is 40% and more (16). Based on this score we have established whether and how severity of illness influences MV method. Patients were therefore divided in two groups: group with APACHE II score ≤ 20 , and the group with APACHE II score > 20 . In both of these groups patients were than randomly assigned to either NIMV or IMV method by use of two closed, non-

transparent, identically looking envelopes, each containing information on one of the MV methods investigated. After a patient was included in the study, and placed in the specific group based on the value of APACHE II score, a third party not involved in the study was asked to choose one of the envelopes. Depending on the information in the chosen envelope, the patient was allocated to undergo either NIMV or MV method.

On admission, following patient data were collected: sex, age, co morbidities (hypertension, diabetes mellitus, and congestive heart disease) and previous use of MV. Reasons for MV were also recorded: Chronic Obstructive Pulmonary Disease (COPD), Polytrauma, Pneumonia, Pulmonary Oedema and Acute Respiratory Distress Syndrome (ARDS). Objective patient data were measured and recorded on admission to the ICU, 1 h, 4 h and 12 h after admission. After that, every 24 h of ICU stay, and if necessary more often than that. Following objective data were measured and recorded during MV procedure: respiratory frequency (RR), tidal volume (Vt), heart rate, systolic and diastolic blood pressure, arterial blood oxygen saturation (SatO₂), negative logarithm of H⁺ concentration (pH), arterial oxygen tension (PaO₂), carbon dioxide arterial tension (PaCO₂) and bicarbonate blood level, arterial oxygen tension/inspiratory oxygen fraction (PaO₂/FiO₂ ratio), RR/Vt ratio.

Methods

Following objective parameters were used as indications for MV application: worsening of clinical status, spontaneous RR $> 25 \text{ min}^{-1}$, spontaneous Vt $< 0.005 \text{ L/kg}$, heart rate $> 140 \text{ min}^{-1}$, PaO₂ $< 60 \text{ mmHg}$, PaCO₂ $> 45 \text{ mmHg}$, pH < 7.30 , systolic blood pressure > 180 or $< 80 \text{ mmHg}$, SatO₂ $< 88\%$, PaO₂/FiO₂ < 200 , RR/Vt > 100 , restless patient. Each patient had to fulfil at least eight of these objective parameters to be included in the study.

During the research, following data were also collected for each MV method: total MV duration, length of ICU stay, success of MV, need for intubation and tracheotomy, incidence of VAP and ICU mortality. Need for tracheotomy was assessed using evidence-based guidelines for weaning and discontinuing ventilatory support (17). They recommended considering a tracheotomy for patients after an initial period of stabilization on the ventilator when it becomes apparent that the patient will require prolonged ventilatory assistance. According to these guidelines, a tracheotomy should than be per-

formed for the following patients : those requiring high levels of sedation to tolerate translaryngeal tubes, those with marginal respiratory mechanics in whom a tracheotomy tube having lower resistance might reduce the risk of muscle overload, those who may develop psychological benefit from the ability to eat orally, communicate by articulated speech, and experience enhanced mobility, and those in whom enhanced mobility may assist physical therapy efforts (18). VAP was identified based on the algorithm of clinical pulmonary infection score (CPIS). This algorithm consists of 6 parameters : radiographic image showing new infiltration, body temperature $> 38.5^{\circ}\text{C}$, leukocytosis over $10000\text{ (mm}^3\text{)}^{-1}$, purulent tracheal secretion, respiratory index $\text{PaO}_2/\text{FiO}_2 < 200$ and absence of other infection source (19).

NIMV and IMV were compared based on the statistically determined difference in objective parameters and MV treatment outcome. Based on these results the advantage of one of the methods was established. During ICU stay, patients received all necessary treatment required by their condition. All laboratory and clinical parameters were evaluated and corrected if necessary. Enteral nutrition was preferred to parenteral whenever possible, applied through nasogastric tube or orally (20).

IMV protocol

Patient with respiratory insufficiency, who had IMV applied, was orotracheally intubated. During IMV patients received the lowest respiratory support level that secured $\text{SatO}_2 > 90\%$ with $\text{FiO}_2 \leq 0.6$, satisfying CO_2 elimination ($\text{PaCO}_2 \leq 45\text{ mmHg}$) and stable hemodynamic patient condition. Weaning process was conducted using pressure support ventilation (PSV) (21). Initial positive pressure support was $18\text{ cmH}_2\text{O}$. This support was then reduced by $2\text{-}4\text{ cmH}_2\text{O}$ depending on the patients' clinical status and values of the measured parameters of pulmonary mechanics, biochemistry and circulation. Patients were extubated after fulfilling general extubation criteria, where $5\text{ cmH}_2\text{O}$ of pressure support was enough for spontaneous patient breathing. After the conclusion of the weaning process, continuous patient monitoring was performed, side effects and complications as well as need for further MV were observed and evaluated. Weaning procedure was considered successful when the unassisted spontaneous breathing was sustained for 48 consecutive hours without respiratory distress, with $\text{pH} > 7.35$ and $\text{PaO}_2 > 60\text{ mmHg}$ in a patient breathing through a mask at $\text{FiO}_2 \leq 0.4$.

Patients were continuously monitored till they were either dismissed from ICU, or death occurred.

NIMV protocol

Patients head-pad was raised to 45° , necessary equipment was prepared next to patients head and the procedure that follows was explained. An appropriate facemask was chosen and connected to the respirator. Starting respirator parameters were set to : continuous positive airway pressure (CPAP) to $0\text{ cmH}_2\text{O}$, PSV $10\text{ cmH}_2\text{O}$ and FiO_2 was adjusted to reach $\text{SatO}_2 > 90\%$. The nose was protected using strapping to prevent skin damage. Patient was calmed down and the mask was gently held applied to the patients' face simultaneously trying to harmonise patients' respiration with the respirator. Next step was to secure the firm mask positioning using head stripes. Respirator was then set to : CPAP $3\text{-}5\text{ cmH}_2\text{O}$ and PSV $10\text{-}25\text{ cmH}_2\text{O}$ in order to reach $\text{Vt} > 5\text{ ml kg}^{-1}$ and $\text{RR} < 25\text{ min}^{-1}$. After that, the alarms on the respirator and respiratory support level were set. Right communication with the patient was ensured, and the patient was explained how to signalize if in need of help or in case of complications occurrence. According to patients state development, clinical status and objective parameters, respiratory support level was reduced until MV could be discontinued. NIMV was discontinued when the patient could sustain spontaneous breathing without evidence of respiratory distress, with $\text{SatO}_2 > 90\%$ at $\text{FiO}_2 \leq 0.4$, with $\text{PSV} + \text{PEEP} \leq 10\text{ cmH}_2\text{O}$. Endotracheal intubation in NIMV patients was performed in case of respiratory arrest, loss of consciousness, severe psychomotor agitation that requires sedation, hemodynamic instability (systolic blood pressure > 180 or $< 80\text{ mmHg}$ and heart rate $< 50\text{ min}^{-1}$ with loss of consciousness), failure to reach $\text{SatO}_2 > 90\%$ with $\text{FiO}_2 \leq 0.6$ and $\text{PaCO}_2 > 60\text{ mmHg}$.

In all patients included in the research, MV was administered by use of Evita Dräger dura 2 respirators (Dräger, Lubeck, Germany), with software option for NIMV and Puritan Bennet 7200 respirators (Puritan Bennet, Carlsbad, CA, USA). Nasal and face masks were applied for NIMV (Respironics Inc, Herrsching, Germany). Parameters of pulmonary mechanics were directly measured on the respirator. For patients with spontaneous breathing, tidal volume and respiratory frequency were measured using spirometer (Ohmeda Biox, Louisville, CO, USA), and maximal inspiratory pressure using manometer (Ohmeda Biox). Pulmonary biochemistry parameters were measured

using blood gas analysis on Ciba Corning (Ciba Corning, Halsted, England). Cardio-respiratory functions including systolic and diastolic blood pressure, heart rate, and end-tidal CO₂ were continuously monitored using Datex monitors (Datex Ohmeda, Helsinki, Finland), and ventilation and oxygenation using Datex Engstrom AS3 and CS3 Compact (Datex Ohmeda, Helsinki, Finland).

Statistical analysis

Qualitative and numerical data were analyzed with descriptive statistic parameters : median, minimum value, maximum value, interquartile (IQ) range. Frequency tables were used to present qualitative data. Contingency tables with chi-square test were employed for comparison of two independent for qualitative variables. In the case of small sample size, Fishers exact test was used. Mann-Whitney test was employed for the comparison of two independent groups on numerical data. Normality of distribution was tested by the Kolmogorow-Smirnov test. $P < 0.01$ was considered statistically significant. The statistical analysis was performed using the SPSS statistical software package for Windows (Release 9.0, Standard version, SPSS Inc., Chicago, IL, USA). Based on a power analysis, the study aimed to recruit 129 patients in order to have 70% power of detecting a clinically significant difference in proportion of patients experiencing MV failure at the 5% level of significance, with the assumption that 50% of APACHE II > 20 trial group failure would fulfil the criteria for MV failure and that a reduction to 20% in the APACHE II ≤ 20 group would be clinically relevant.

The study was carried out in line with ethical principles and was approved by the Hospital Ethics Committee. An informed consent was obtained for all patients, either directly from them, or from closest relatives according to patient's condition.

No author has a conflict of interest in regard of devices discussed in this publication. Support was provided from institutional and departmental sources.

RESULTS

The results of the study are presented through one flow chart and in two tables.

Flow chart of patients through the study based on APACHE II score and treatment outcome is presented. In the group of patients with APACHE II score ≤ 20 there were 26 patients, after randomization 12 patients had NIMV and 14 had IMV

applied. In the group with APACHE II > 20 , there were 103 patients. After randomization, 53 patients had NIMV and 50 had IMV applied (Fig. 1).

Furthermore, comparison of two MV methods based on the study population characteristics is shown. Based on the study population characteristics patients were compared according to basic patient data (age, sex), co morbidities, prior MV application, APACHE II score and reason for MV, (Table 1).

Furthermore, influence of APACHE II score on MV treatment outcome is presented. Based on the parameters of MV treatment outcome, patients were compared according to age, MV duration, time spent in ICU, successful treatment, VAP, need for tracheotomy and ICU-mortality (Table 2).

DISCUSSION

The major finding of our study was that both NIMV and IMV present appropriate MV methods for treatment of acute respiratory failure (ARF).

Of the total 502 patients with ARF treated in our ICU, all patients who didn't meet the strict defined criteria were excluded from the research, and only 129 (26%) patients remained. These 129 patients present the research sample. This substantial number of excluded patients arose from the need to achieve better objectivation and research groups that are as alike as possible. Furthermore, strict rules and protocols were applied in patient selection as well as during the study.

CONFALONIERI *et al.* (22) in their research in 2005 had 1033 patients. They looked for predictive factors of MV treatment success. The advantage of their research is the high number of patients, but it also has limitations. Most important one is that the research was conducted in 13 ICU-s in 8 countries that all have a different approach to the problem of ARF, and specific ICU-s have affinities towards different MV methods.

Our research has confirmed that APACHE II score has strong influence on the success of the MV procedure. We expected such result, because of the parameters included in this scoring system. The fact alone that patients with GCS < 8 should be intubated, shows how important this parameter is. Patients with better acute physiologic state are better able to tolerate MV, and that contributes to better results in these patients. Patients' age also has similar and already confirmed influence on MV success (younger patients are easier adjustable to the MV, in most cases they respond better to MV and the

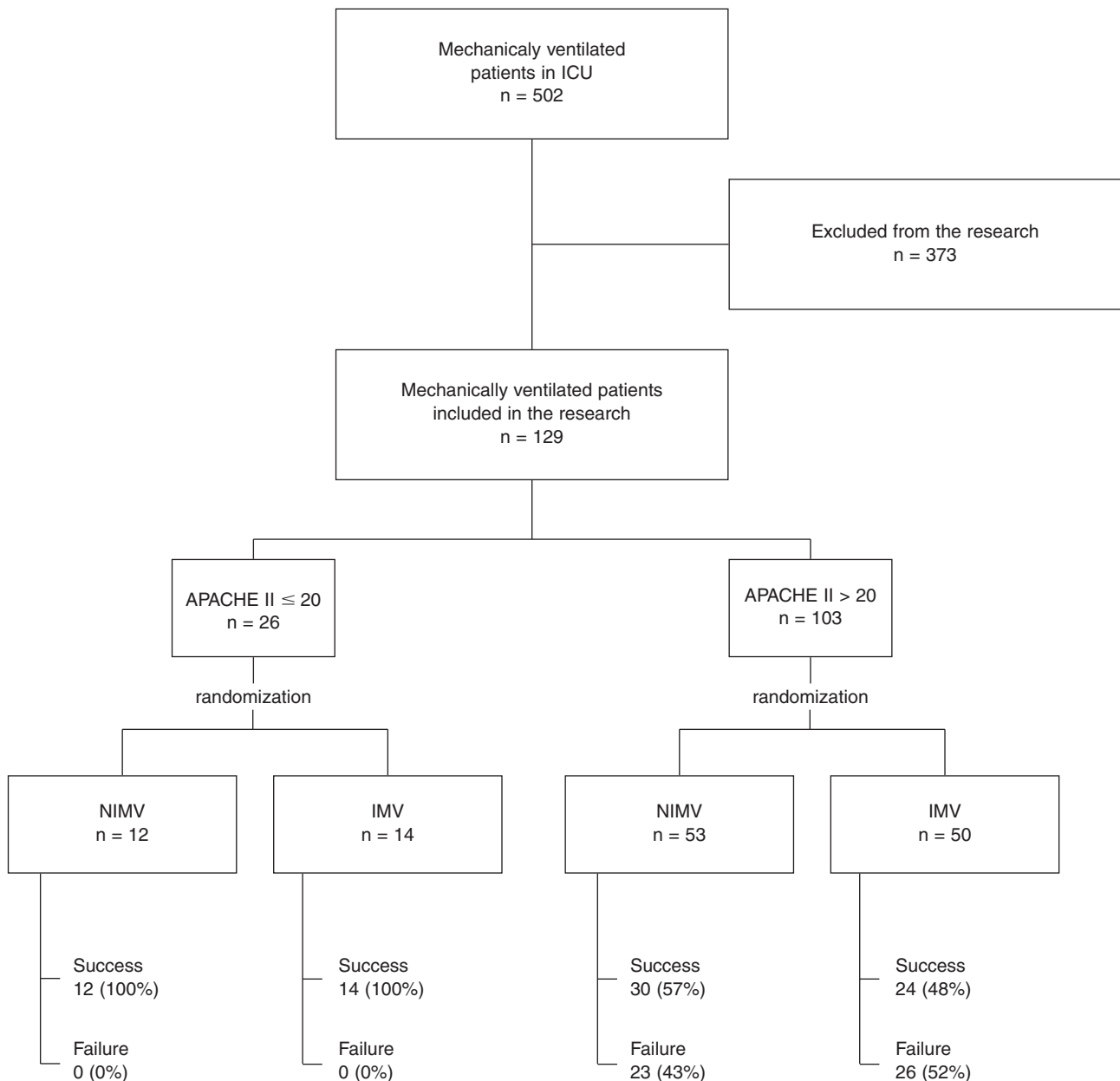


Fig. 1. — Flow of patients through the study.

Abbreviations : ICU – Intensive Care Unit, IMV – Invasive Mechanical Ventilation, NIMV – Noninvasive Mechanical Ventilation, APACHE – Acute Physiology and Chronic Health Evaluation.

changes it produces in the organism). Existence of a ongoing chronic disease also influences treatment success and MV outcome.

In the group of patients with APACHE II ≤ 20 , there was no statistically significant difference, except that all patients with IMV were intubated. Based on these results we can conclude that some patients in this group were probably unnecessary intubated and that it could have been avoided, together with all the complications that go with endotracheal intubation and were mentioned earlier.

In the group with APACHE II > 20 , statistical significance in favour of NIMV was found in MV duration, time spent in ICU and 43% of patients with NIMV were intubated. Furthermore, 4% of patients with NIMV needed tracheotomy, and in IMV group 28% of patients needed tracheotomy ($p < 0.001$).

AMBROSINO *et al.* (23) showed similar results in their research performed in 1995 on COPD patients, where patients with high APACHE II score also had high NIMV failure, accompanied with higher total MV treatment failure. The difference is

Table 1

Comparison of non-invasive and invasive mechanical ventilation based on study population characteristics

Study population characteristics		MV method		Statistical difference between groups (p)
		NIMV n = 65	IMV n = 64	
Age (years) : median ; IQ.range (min-max)		54 ; 28 (19-80)	51 ; 30 (18-73)	0.608
APACHE II score median ; IQ.range (min-max)		24 ; 7 (18-36)	26 ; 6 (17-42)	0.784
Sex	Male n (%)	37 (57)	35 (55)	0.798
	Female n (%)	28 (43)	29 (45)	
Reason for MV n (%)	COPD	17 (26)	19 (30)	0.979
	Polytrauma	27 (42)	24 (37)	
	Pneumonia	8 (12)	8 (13)	
	Pulmonary oedema	7 (11)	6 (9)	
	ARDS	6 (9)	7 (11)	
Prior MV application n (%)		15 (23)	10 (16)	0.284
Co morbidities * n (%)	Hypertension	16 (25)	17 (27)	0.800
	Diabetes Mell	12 (19)	4 (6)	0.035
	Heart disease	15 (23)	11 (17)	0.404

* Co morbidities : hypertension, diabetes mellitus, and congestive heart disease.

Abbreviations : MV – Mechanical Ventilation, NIMV – Non-invasive Mechanical Ventilation, IMV – Invasive Mechanical Ventilation, APACHE – Acute Physiology and Chronic Health Evaluation, IQ – interquartile range, COPD – Chronic Obstructive Pulmonary Disease, ARDS – Acute Respiratory Distress Syndrome.

Table 2

Influence of APACHE II score on MV treatment outcome

MV treatment outcome				APACHE II > 20		
	MV method		Difference between groups (p)	MV method		Difference between groups (p)
	NIMV n = 12	IMV n = 14		NIMV n = 53	IMV n = 50	
Age (years) Median ; IQ.range (min-max)	30 ; 31 (19-76)	23 ; 37 (18-62)	0.485	55 ; 22 (19-70)	52 ; 20 (21-73)	0.784
MV duration (hours) Median ; IQ.range (min-max)	88 ; 21 (68-122)	166 ; 128 (28-190)	0.180	103 ; 36 (68-230)	152 ; 80 (52-464)	< 0.001
Time spent in ICU (hours) Median ; IQ.range (min-max)	104 ; 24 (84-168)	204 ; 153 (66-288)	0.064	137 ; 70 (86-280)	201 ; 116 (84-576)	< 0.001
Successful treatment n (%)	12 (100)	14 (100)	1.000	30 (57)	24 (48)	0.382
VAP n (%)	0 (0)	0 (0)	1.000	3 (6)	7 (14)	0.182
Tracheotomy n (%)	0 (0)	0 (0)	1.000	2 (4)	14 (28)	< 0.001
ICU-mortality n (%)	0 (0)	0 (0)	1.000	5 (9)	7 (14)	0.470

Abbreviations : APACHE – Acute Physiology and Chronic Health Evaluation, MV – Mechanical Ventilation, NIMV – Noninvasive Mechanical Ventilation, IMV – Invasive Mechanical Ventilation, ICU – Intensive Care Unit, n – number of patients, IQ – interquartile range, p – statistical difference between groups, VAP – Ventilator Associated Pneumonia.

that we studied the influence of APACHE II score on all patients with ARF, while their research was based only on patients with COPD.

Contrary to those results, FERNANDES *et al.* (24) in their study in 1993 report that APACHE II score

has no influence on NIMV success prediction for patients with COPD.

AFESSA *et al.* (25) in their study in 1999 established that APACHE II score value correlates better with success of weaning from MV than other

weaning indexes. Patients with weaning success had significantly lower APACHE II score which correlates with our results in the group of patients with APACHE II \leq 20 were all patients were successfully treated. Those with higher values of APACHE II had lower weaning success rates.

Our study had limitations, because of the small sample size when patients were divided according to specific reasons for MV. But, the aim of the study wasn't to study the influence of APACHE II score on the choice of MV method in specific reasons for MV but in all patients with ARF.

NIMV method has been shown to be equally successful to IMV in patients with APACHE II \leq 20. Further studies should determine the difference of NIMV application in different indications for MV, which could not be done here because of our small sample size.

In conclusion, the research has shown that APACHE II score has a high positive predictive value on treatment outcome.

Using good patient selection and applying strict protocols, NIMV procedure can be applied in patients with APACHE II $>$ 20.

References

- American College of Chest Physician Consensus Conference : Mechanical ventilation, CHEST, **104**, 1833-1859, 1993.
- Carlucci A., Richard J. C., Wysocky M., Lepage E., Brochard L., *Noninvasive versus Conventional mechanical ventilation*, AM. J. RESPIR. CRIT. CARE MED., **163**, 874-880, 2001.
- Abraham E., Andrews P., Antonelli M., Brochard L., Brun-Buisson C., Dobb G., *et al.*, *Year in review in Intensive Care Med-2003*, INTENSIVE CARE MED., **30**, 1017-1031, 2004.
- Stocker R., Biro P., *Airway management and artificial ventilation in intensive care*, CURR. OPIN. ANAESTHESIOL., **18**, 35-45, 2005.
- Dupont H., Chalhoub V., Plantefere G., Vaumas C., Kermarrec N., Paugam-Burtz C., *et al.*, *Variation of infected cell count in bronchoalveolar lavage and timing of ventilator-associated pneumonia*, INTENSIVE CARE MED., **30**, 1557-1563, 2004.
- Luyt C. E., Chastre J., Fagon J. Y., *Value of the clinical pulmonary infection score for the identification and management of ventilator-associated pneumonia*, INTENSIVE CARE MED., **30**, 844-852, 2004.
- Mehta S., Hill N. S., *Non-invasive ventilation. State of the Art*, AM. J. RESPIR. CRIT. CARE MED., **163**, 540-577, 2001.
- Girou E., Schortgen F., Delclaux C., Brun-Buisson C., Blot F., Lefort Y., *et al.*, *Association of noninvasive ventilation with nosocomial infections and survival in critically ill patients*, JAMA, **284**, 2361-2367, 2000.
- Majid A., Hill N. S., *Noninvasive ventilation for acute respiratory failure*, CURR. OPIN. CRIT. CARE, **11**, 77-81, 2005.
- Brochard L., *Mechanical ventilation : invasive versus non-invasive*, EUR. RESPIR. J., **22**, Suppl. 47, 31-37, 2003.
- Girault C., Briel A., Hellot M. F., Tamion F., Woinet D., Lesoy J., *et al.*, *Noninvasive mechanical ventilation in clinical practice : A 2-year experience in a medical intensive care unit*, CRIT. CARE MED., **31** (2), 552-559, 2003.
- Antonelli M., Conti G., Moro M., *Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure : a multi-center study*, INTENSIVE CARE MED., **27**, 1718-1728, 2001.
- Baudouin S., Blumenthal S., Cooper B., *Noninvasive ventilation in acute respiratory failure. British Thoracic Society Standards of Care Committee*, THORAX, **57**, 192-211, 2002.
- Liesching T., Kwok H., Hill N., *Acute Applications of Noninvasive Positive Pressure Ventilation*, CHEST, **124** (2), 699-713, 2003.
- Conti G., Montini L., Pennisi M.A., Cavaliere F., Arcangeli A., Bocci M. G., *et al.*, *A prospective, blinded evaluation of indexes proposed to predict weaning from mechanical ventilation*, INTENSIVE CARE MED., **30**, 830-836, 2004.
- Knaus W. A., Draper E. A., Wagner D. P., Zimmerman J. E., *APACHE II : a severity of disease classification system*, CRIT. CARE MED., **13**, 818-829, 1985.
- McIntyre N. R., Cook D. J., Ely E. W., *Evidence-based guidelines for weaning and discontinuing ventilatory support : A collective task force facilitated by the American College of Chest Physicians, the American Association for Respiratory Care, and the College of Critical Care Medicine*, CHEST, **120**, 375S-395S, 2001.
- Frutos-Vivar F., Esteban A., Apezteguia C., Anzueto A., Nightingale P., Gonzales M., *et al.*, *Outcome of mechanically ventilated patients who require a tracheotomy*, CRIT. CARE MED., **33** No. 2, 290-298, 2005.
- Luna C. M., Blanzaco D., Niederman M. S., Maturucco W., *Resolution of ventilator associated pneumonia : prospective evaluation of clinical pulmonary infection score as an early predictor of outcome*, CRIT. CARE MED., **31**, 676-682, 2003.
- Dhalival R., Jurewitsch B., Harrietha D., Heyland D. K., *Combination enteral and parenteral nutrition in critically ill patients : harmful or beneficial ? A systematic review of the evidence*, INTENSIVE CARE MED., **30**, 1666-1671, 2004.
- Matic I., Majeric-Kogler V., *Comparison of Pressure Support and T-Tube Weaning from Mechanical Ventilation : Randomized Prospective Study*, CROATIAN MEDICAL JOURNAL, **45**, 162-166, 2004.
- Confalonieri M., Garuti G., Cattaruzza M. S., Osborn J. F., Antonelli M., Conti G., *et al.*, *A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation*, EUR. RESPIR. J., **25**, 348-355, 2005.
- Ambrosino N., Foglio K., Rubini F., *Noninvasive mechanical ventilation in acute respiratory failure due to chronic obstructive pulmonary disease : Correlates for success*, THORAX, **50**, 755-757, 1995.
- Fernandes R., Blanch L. I., Valles J., *Pressure support ventilation via mask in acute respiratory failure in hypercapnic COPD patients*, INTENSIVE CARE MED., **19**, 456-461, 1993.
- Afessa B., Hogans L., Murphy R., *Predicting 3-Day and 7-Day Outcomes of Weaning From Mechanical Ventilation*, CHEST, **116**, 456-461, 1999.